

**ANTIHYPERTENSIVE DRUG UTILIZATION PATTERN IN PRESENCE OF
DIABETES MELLITUS**

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ABSTRACT

With the rising number of patients with hypertension and diabetes mellitus, achieving a BP of < 130/80 mm Hg is challenging. This paper was aimed at evaluating the utilization pattern of antihypertensive in presence of diabetes. 156 patients (94 male and 62 female) in general medicine department of a tertiary care teaching hospital were included in the paper conducted for 6 months.

The most common age group was 61-70 years; mean duration of hypertension and diabetes mellitus was 8.798±8.98 and 9.5678±8.937 years respectively. The antihypertensive drugs amlodipine, furosemide, telmisartan were mostly used as monotherapy and maximum patients were on 2 drug combination therapy. Metformin, glimepiride and insulin were most common antidiabetic drugs, metformin and insulin the most common combination. Antihypertensive and antidiabetic combination mostly administered drugs were amlodipine with metformin. In this paper we used prospective and observational methods.

It is concluded that with an alarming increase in twin epidemic of HTN and DM, the rational use of drugs is very important to prevent and control the associated cardiovascular complication with hypertension and diabetes mellitus.

Key words: Utilization pattern, monotherapy, combination therapy.

INTRODUCTION

Definition

Hypertension can be defined as a condition where blood pressure (BP) is elevated to an extent that clinical benefit is obtained from blood pressure lowering. There is no clear cut blood pressure threshold separating normal from hypertensive individuals.

Blood pressure measurement includes systolic and diastolic components (1).

Increased BP estimated to be attributable for nearly 10 per cent of all deaths. Adult hypertension prevalence has risen dramatically over the past three decades from 5 per cent to between 20-40 per cent in urban areas and 12-17 per cent in rural areas (2-3). The number of hypertensive individuals is anticipated to nearly double from 118 million in 2000 to 213 million by 2025. It is estimated that 16 per cent of ischaemic heart disease (IHD), 21 per cent of peripheral vascular disease (PVD), 24 per cent of acute myocardial infarctions (MI) and 29 per cent of strokes are attributable to hypertension underlining the huge impact effective hypertension prevention and control can have on reducing the rising burden of cardiovascular disease (CVD) (3).

COMPLICATIONS OF HYPERTENSION:

- stroke:
- cerebral/brainstem infarction

- cerebral haemorrhage
- Lacunar syndromes
- Multi-infarct disease
- hypertensive encephalopathy/ malignant hypertension
- dissecting aortic aneurysm
- hypertensive nephrosclerosis
- peripheral vascular disease (1)

Prevalence of Hypertension and Diabetes in India:

Hypertension and Diabetes two of the major global risks for mortality are on a rapid rise in developing nations. In India, as per the 2011 estimates reported by the Indian Council of Medical Research-India Diabetes study, 62.4 and 77.2 million people have Diabetes and prediabetes respectively. It is predicted that by 2030, Indian's diabetes burden will be almost 87 million people. Additionally there is an increasing prevalence of hypertension in the Indian population, especially in the urban areas.

Diabetes and Hypertension are manageable health conditions and can be controlled by medical intervention, exercise and diet. Moreover detection of progenitor's prediabetes and prehypertension through periodic surveillance can allow for early intervention and delay disease progression (4).

NON- DRUG MANAGEMENT OF HYPERTENSION:

Table no.1: Lifestyle Modifications for Management of Hypertension in patients with Diabetes

MODIFICATION	RECOMMENDATION
Alcohol	Limit alcohol consumption to two day for Restriction men or one drink per day for women.
Diet	Implement the dietary approach to stop hypertension (DASH) diet; eat four to five serving of fruits, four or five serving of vegetable and six to eight serving whole grain each day; increase intake of calcium (1,250mg daily), magnesium (500mg daily) and potassium (4,700 mg daily); limit intake of cholesterol to 150 mg daily and saturated fat to 6% of daily calorie.
Physical activity	Engage in 30 to 45 minute of moderate- intensity activity most days of the week.
Smoking cessation	Stop smoking to improve overall cardiovascular health.
Weight loss	Lose weight, if necessary, to maintain healthy body weight (i.e. body mass index of 19 to 25 kg per m ²)

DASH: Dietary Approach to Stop Hypertension. Information from Reference (5)

PHARMACOLOGIC THERAPY

Several classes of drugs are used in the treatment of hypertension in diabetic patients.

1) ACE INHIBITORS

Angiotensin-converting enzyme (ACE) inhibitors prevent or delay microvascular and macro vascular complications of diabetes and are recommended as first-line antihypertensive agents in patients with diabetes.(6-7)

Example of ACE inhibitors:

- Enalapril
- Ramipril
- Captopril

2) ANGIOTENSIN RECEPTOR BLOCKERS

Like ACE inhibitors, ARBs reduce the complications of diabetes (e.g., progression of kidney disease), and they are preferred

agents for managing hypertension in patients with diabetes(6).

ARBs are effective in delaying the onset of kidney failure

in patients with type 2 diabetes, hypertension, and macroalbuminuria. (6-7)

ARBs should be reserved for patients who cannot tolerate ACE inhibitors.

Example of ARBs:

- losarta
- telmisartan
- candesartan

3) DIURETICS

Thiazide diuretics, either as monotherapy or as part of a combination regimen, are beneficial in the treatment of hypertension in patients with diabetes (6).

In the systolic hypertention in the elderly program, chlorthalidone (thalitone) reduced cardiovascular and cerebrovascular events in patients with type 2 diabetes and isolated systolic hypertension (8) Patients treated

with chlorthalidone had a lower incidence of heart failure. Thiazide diuretics are less effective in patients with diminished renal function (9); patients with a GFR of less than 50 ml per min per 1.73 m²; may require a loop diuretic. Metabolic alterations are a potential concern with the use of thiazide diuretics. Higher dosages have been linked to elevations in cholesterol and triglyceride levels and loss of glycaemic control; however, these dosages are not routinely used in clinical practice. When used in low or moderate dosage (i.e., up to 25 mg of hydrochlorothiazide per day), the risk of clinically significant alterations in glucose metabolism is minimal.

More importantly, these drugs reduce the risk of cardiovascular events and all cause mortality.(10-11)

Example of Diuretics:

- furosemide
- hydrochlorothiazide
- spironolactone

4) BETA BLOCKERS

Beta blockers are a useful adjunct when combination therapy is needed to achieve target blood pressure in Patients with diabetes. These agents have additional antihypertensive effects when combined with ACE inhibitors in patients with a baseline pulse rate greater than 84 beats per minute.(6)

Example of BBs:

- propranolol
- atenolol

5) CALCIUM CHANNEL BLOCKERS

Dihydropyridine calcium channel blockers (CCBs) reduce cardiovascular events in patients with diabetes and hypertension; however, they may be inferior to other agents in some cardiovascular outcomes. In the systolic hypertension in Europe trial, patients treated with nitrendipine (not available in the United States) had a significant reduction in cardiovascular events and mortality compared with the control group, but many patients also received ACE inhibitors or diuretics to attain target blood pressure (12).

Example of CCBs:

- amlodipine

METHODOLOGY:

STUDY SITE

The study on Antihypertensive drug utilization pattern in presence of diabetes mellitus was carried out in the General medicine department of KIMS hospital and research Centre, Bangalore.

STUDY PERIOD

The study was conducted for a period of six months.

STUDY DESIGN

This study was a Prospective, observational study

STUDY CRITERIA

Inclusion Criteria

- i) Patients treated for hypertension and with co- morbidities like type 2 diabetes mellitus, dyslipidaemia, and other associated cardiovascular diseases.
- ii) Inpatients in the medicine department of either gender, more than 18 years of age.

Exclusion Criteria

- i) Pregnant and lactating patients.

SOURCE OF DATA

i) Patients case notes

ii) Laboratory test data

RESULT:

The study to assess utilization pattern of antihypertensive drugs in patients with hypertension and diabetes mellitus was carried out for duration of 6 months in the general medicine department of KIMS hospital and Research Centre. The documented data was analysed and the results are shown here:

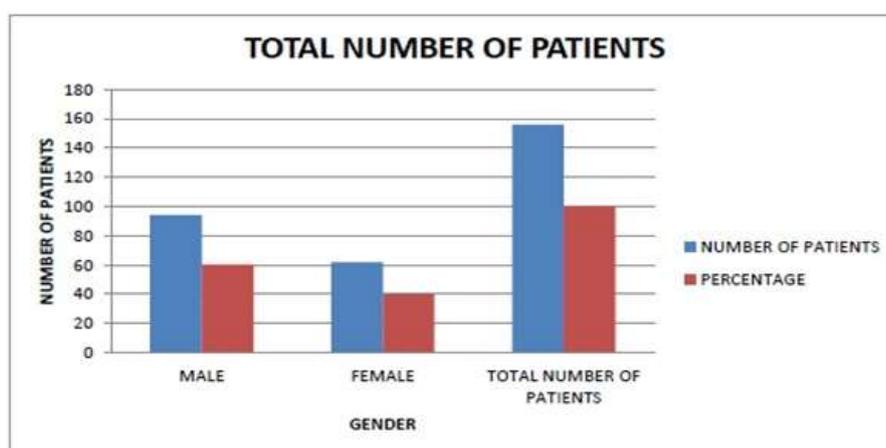


Figure1: Total Number of Patients

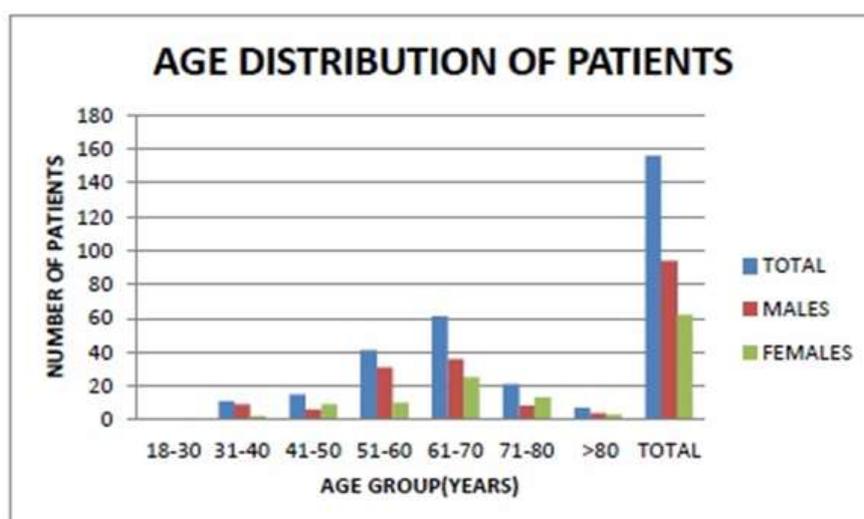


Figure 2: Age Distribution of Patients

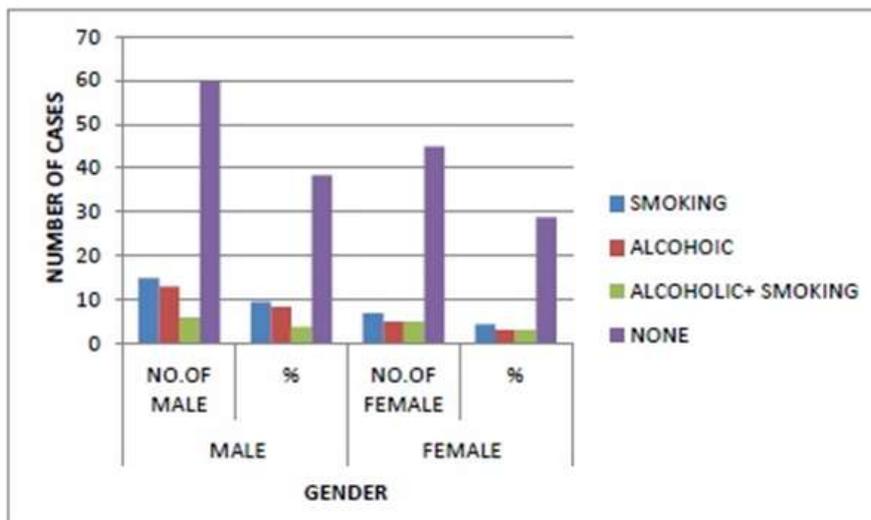


Figure 3: Social Habit

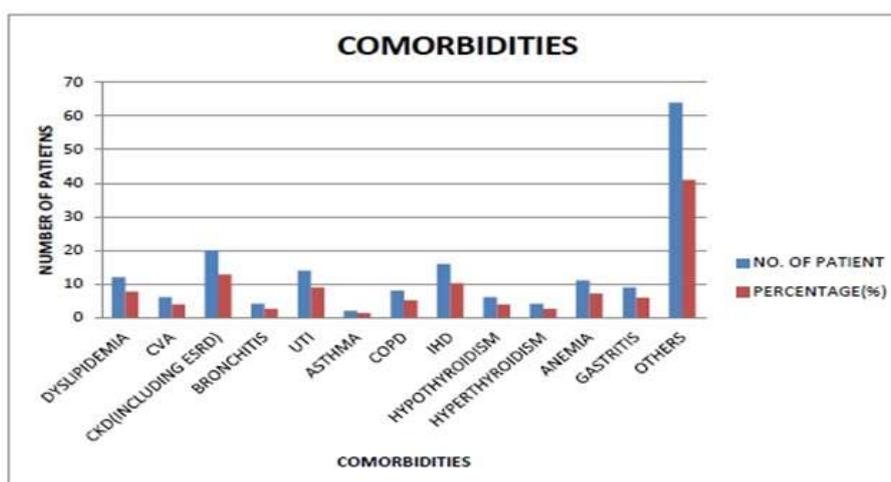


Figure 4: Comorbidities

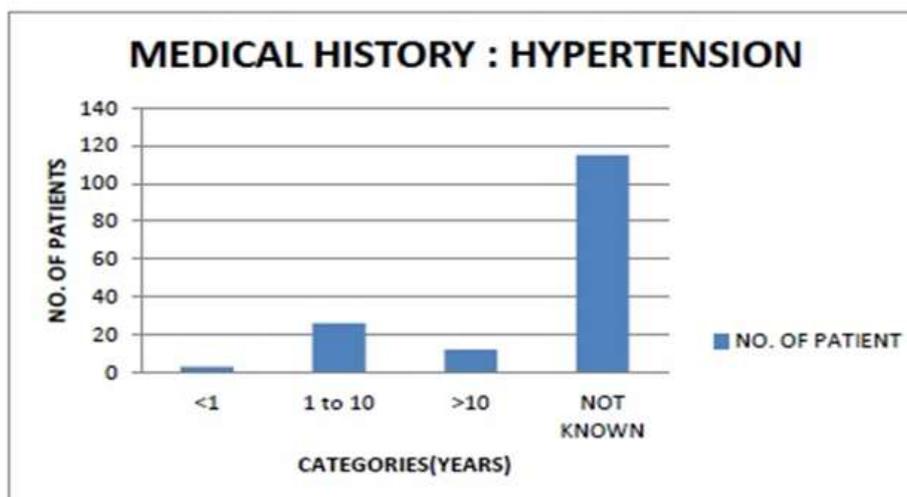


Figure 5-1: Medical History Hypertension

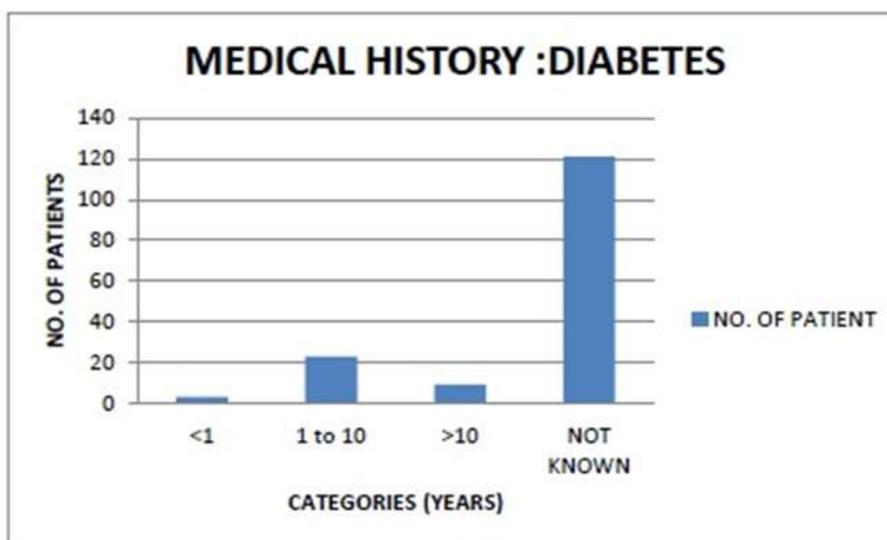


Figure 5-2: Medical History Diabetes

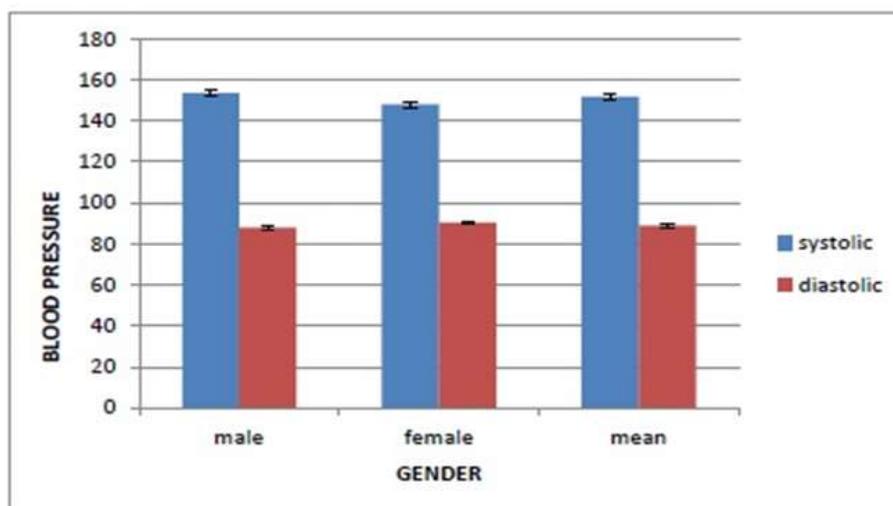


Figure 6: Clinical Parameter

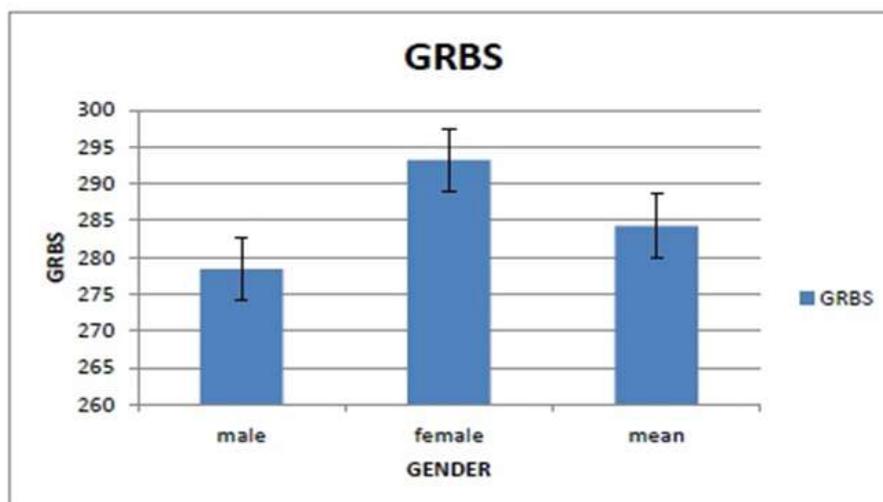


Figure 7: Clinical Parameter

Table 2: Utilization Pattern of Antihypertensives

S.NO.	CLASS OF DRUG	DRUG USED	ATC CLASSIFICATION	NO. OF PATIENTS		MALE		FEMALE	
				NO.	%	NO.	%	NO.	%
1	DIURETICS								
A	THIAZIDES	HYDROCHLORTHIAZIDE	C03AA03	18	11.53	08	44.45	10	55.56
B	LOOP DIURETICS	FUROSEMIDE	C03CA01	65	41.66	38	59.37	27	41.53
		TORSEMIDE	C03CA04	09	5.76	09	100	00	00
C	POTASSIUM SPARING DIURETICS	SPIRONOLACTONE	C03DA01	13	8.33	13	100	00	00
3	α -BLOCKERS	PRazosin	C02CA01	25	16.02	12	48	13	52
4	β -BLOCKERS	METOPROLOL	C07AB02	03	1.92	03	100	00	00
5	ACEI	RAMIPRIL	C09AA05	02	1.28	00	00	02	100
		ENALPRIL	C09AA02	02	1.28	02	100	00	00
6	CCBs	AMLODIPINE	C08CA01	89	57.05	54	60.67	35	39.32
7	ARBs	TELMISARTAN	C09CA07	27	17.30	15	55.56	12	44.45
		LOSARTAN	C09CA01	17	10.89	13	76.47	23.52	23.52
8	CASs	CLONIDINE	C02AC01	18	11.53	11	61.12	07	38.89

Table 3: Therapy Pattern With Antihypertensives Drugs

S.NO	TYPE OF THERAPY	NO. OF DRUGS	DRUG NAME	NO. OF PATIENT	%
	MONOTHERAPY		LOSARTAN	2	7.14
			TELMISARTAN	1	3.57
			AMLODIPINE	22	78.57
			FUROSEMIDE	1	3.57
			PRazosin	1	3.57
			ENALPRIL	1	3.57
			TOTAL	28	100
	COMBINATION THERAPY	2 DRUGS	PRAzosin+AMLODIPINE	1	1.63
			PRAzosin+LOSARTAN	6	9.83
			FUROSEMIDE+TELMISARTAN	4	6.55
			FUROSEMIDE+AMLODIPINE	30	49.18
			HYDROCHLORTHIAZIDE+LOSARTAN	2	3.27
			HYDROCHLORTHIAZIDE+FUROSEMIDE	3	4.91
			AMLODIPINE+LOSARTAN	9	14.75
			FUROSEMIDE+CLONIDINE	6	9.83
			TOTAL	61	100
		3 DRUGS	FUROSEMIDE+AMLODIPINE+CLONIDINE	4	
			TORSEMIDE+AMLODIPINE+LOSARTAN	1	
			HYDROCHLORTHIAZIDE+FUROSEMIDE+TELMISARTAN	3	
			HYDROCHLORTHIAZIDE+TORSEMIDE+CLONIDINE		
			FUROSEMIDE+METOPROLOL+AMLODIPINE	1	
				3	
			TOTAL	12	100
4	OTHER COMBINATION			52	

NOTE: OUT OF 156 PATIENTS 3 PATIENTS WERE NOT RECEIVING ANY ANTIHYPERTENSIVE DRUGS.

Table 4: Utilisation Pattern of Antidiabetic Drugs

S.NO	CLASS OF DRUG	DRUG USED	ATC CLASSIFICATION	TOTAL		MALE		FEMALE	
				NO.	%	NO.	%	NO.	%
1	BIGUANIDES	METFORMIN	A10BA02	55	35.25	30	54.54	25	45.45
2	INSULIN	INSULIN	A10AD01	79	50.64	50	63.29	29	36.70
3	SULFONYL UREAS	GLIMEPRIDE	A10BB12	47	30.12	28	59.57	19	40.42

Table 5: Therapy Pattern Of Antidiabetic Drugs

S.NO.	TYPE OF THERAPY	DRUG NAME	NO. OF PATINET	PERCENTAGE
1	MONOTHERAPY	METFORMIN	19	12.17
		INSULIN	03	1.92
		GLIMEPRIDE	02	1.28
TOTAL			24	15.37
2	COMBINATION THERAPY			
A	ORAL+ORAL(2 DRUG)	METFORMIN+GLIMEPRIDE	13	8.33
B	ORAL+INSULIN	METFORMIN+INSULIN	16	12.77
		METFORMIN+INSULIN +GLIMEPRIDE	03	
TOTAL			32	20.5
C	OTHER COMBINATION		73	46.79

NOTE: IN THIS STUDY IT WAS FOUND THAT AMONG 156 PATIENTS 129 WAS FOUND TO BE RECEIVING ANTIDIABETIC DRUGS.

Table 6: Therapy Pattern Of Antihypertensive And Antidiabetic Drugs

S.NO.	TYPE OF DRUG COMBINATION	NO. OF PATIENTS
1	BIGUANIDES+CCB	14
2	BIGUANIDES+INSULIN+DIURETIC+CCB	10
3	INSULIN+DIURETIC+CCB	09
4	DIURETICS+CCB	11
5	INSULIN+DIURETICS+CAS	05
6	BIGUANIDES+INSULIN+ α -BLOCKERS+ARBs	03
7	OTHERS	104

DISCUSSION:

The study on **Antihypertensive Drug Utilization Pattern In Presence Of Diabetes Mellitus** included 156 patients figure No1 and 2, depict distribution of study patients indicating 94(60.25%) were male and 62(39.74%) were female patients. Maximum number of patients 61(39.1%) suffering from hypertension and diabetes were found between the age of 61-70 years with 36(23.07%) being males and 25(16.02%) females. In the range of 51-60 years there were 41(26.28%) patients, 31(19.87%) were males and 10(6.41%) were females. Patients with the age of greater than 80 years were least with 07(4.48%) patients, out of which 04(2.56%) were males and 03(1.92%) were females. No patients were found between 18-30 years of age group, this distribution shows that the higher age group of patients are more common to be hypertensive and diabetic in nature. Figure no 3, depicts Out of 156 patients, we found that 22(14.17%) patients were smokers alone in which 15(9.61%) and 7(4.4%) was males and females respectively. It is also shown that, out of the whole study population (n=156), 18(11.53) patients were alcoholic in which

13(8.33%) were males and 5(3.20%) were in female category. Patients having habit of both alcoholic and smoking were found to be 11(7.5%) and in that 6(3.84%) were males and 5(3.2%) were females. We also found that 105(67.30%) patients have not had any habits mentioned Figure No 4, shows 20 (12.8%) patients had CKD as the comorbidity in this study. In a study done by Dutta and Udupa it was found that among 198 hypertensive diabetes 14.8% of patients had nephropathy 17. 16(10.25%) patients were diagnosed with IHD as a comorbid condition with hypertension and diabetes. 65(41.0%) were diagnosed with other comorbid conditions. Figure No 5-1, depicts In the medical history of the population under study 41 patients were showing past medical history of hypertension was 10 years with the mean and standard deviation of 8.798 ± 8.98 years, and in 115 patients the history was not known regarding the same. In a study conducted by Waleed M. and others the median duration of history of hypertension was five years while that for DM was ten years 18. figure No 5-2, shows with respect to medical history of diabetes 35 patients were showing past medical history with the

mean and standard deviation of 9.568 ± 8.937 years and 121 cases were not known regarding the same Figure No 6, shows During the study the BP values (systolic and diastolic of the patients were documented). The mean systolic value was 151.89 ± 24.21 mmHg and diastolic value was 88.85 ± 13.82 . male systolic BP has a mean and standard deviation of 153.709 ± 21.620 , male diastolic BP has a mean and standard deviation of 87.840 ± 13.319 . In females the systolic BP has a mean and standard deviation of 148.064 ± 26.061 and diastolic BP has a mean and standard deviation of 90.40 ± 14.422 , Figure No 7, shows The glucometer random blood sugar value of the study patients was documented. The overall GRBS value was found to be 284.28 ± 133.01 mg/dl. In case of males was 278.414 ± 132.0307 and female 293.177 ± 133.971 . There GRBS values are indicative of uncontrolled diabetes in the study population. There mean values of elevated systolic BP and GRB values indicate that the patients need to be monitored more closely and adhere to physicians advice to prevent complications that can arise out of uncontrolled HTN and DM. The study shows that the second highest prescribed drug is furosemide in 65(41.66%) of patients, out of which

38(59.37%) were males and 27(41.53%) were females.

The third highest prescribed drug was telmisartan administered to 27(17.30%) patients among which 15(55.56%) were males and 12(44.45%) were females.

The least prescribed drug was found to be ramipril, administered to 2(1.28%) female patients. And enalapril prescribed to 2 male patients (Table No 2).

In this study it was observed that amlodipine was the most prescribed drug in monotherapy given to 22(78.57%) patients out of a total of 28 patients who were prescribed with monotherapy. The patients on monotherapy were mostly receiving ACEI/ARBs. The majority of (70.7%) treated patients were on multidrug regimens 18.

61 patients were prescribed with 2 drug combination therapy and it was observed that furosemide+amlodipine combination was the highest given to 30(49.18%) patients, followed by amlodipine+losartan combination prescribed for 7(14.75%) patients.

12 patients were found to be taking the 3 drug combination therapy, and furosemide + amlodipine + clonidine combination was prescribed to 4(33.33%) patients (Table No 3). The utilization pattern of antidiabetic drugs was also analyzed. It was noticed that 79(50.64%) patients were prescribed with

Insulin, out of which 50(63.29%) were males and 29(36.70%) were females. Metformin, a biguanide derivative was given to 55(35.255) patients, in which 30(54.54%) were males and 25(45.45%) were females.

Glimepride which is a sulfonyl urea, was recommended to 47(30.12%) patients, in which 28(59.57%) were males and 19(40.42%) were females (table No 4).

After analysing the therapy pattern of antidiabetic drugs, it was observed that in combination of oral therapy metformin with glimepride was prescribed to 13(8.33%) patients where as in case of oral with injectable drugs, metformin with insulin were administered to 16(12.17%) patients. It was also seen that the combination of metformin with insulin and glimepride was found to be prescribed in only 3(1.92%) patients (table No 5). While analysing the therapy pattern of both antihypertensive and antidiabetic class of drugs we found that the most commonly prescribed drug combination were Biquanides with CCB, prescribed to 14 patients sequenced by Diuretics with CCB, given to 11 patients. The least prescribed drug combination Biguanides, insulin with α – blocker and ARBs which was found to be given only in 3 patients, out of whole study population insulin with diuretics and CAS were also seen under the least

prescribed combination, given to only 5 patients.

As per the guidelines thiazides, β – blockers, ACEIs, CCBs, ARBs antihypertensive and antidiabetic drug combination most commonly preferred is However in our research it was found the combination to be diuretics and CCBs.

CONCLUSION

Treatment and control of hypertension in the presence of diabetes mellitus is usually difficult. The variation in blood pressure values in diabetic patients is very large and this necessitates constant monitoring of the patients BP to treat hypertension.

Achievement of the target BP goal with a regimen that reduces burdensome side effects and is at a reasonable cost to the patient is probably more important than the specific drug strategy.

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