

Prescribing pattern of anti diabetic drugs in patients suffering from type 2 diabetes mellitus with co-existing hypertension in a tertiary care teaching hospital

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ABSTRACT

Background: Diabetes mellitus and hypertension frequently co-exist in a patient. In such patients, the risk of complications, morbidity and mortality increases. One should be careful in management and choosing drugs. Authors undertook this study to understand the prescribing pattern of the physicians in diabetic hypertensive patients.

Methods: This cross sectional, observational study was conducted in type 2 diabetic outdoor patients with co-existing hypertension, for duration of one year. We used descriptive statistics to analyze data of 615 patients to determine prescribing pattern of drugs.

Results: 93.17% of patients were more than 40 years of age. Ratio of female to male patients was 1.30. Mean duration of diabetes was 5.81 years. Multi drug anti diabetic regimes (54.47%) were common than monotherapy (43.90%). Commonly prescribed anti diabetic drug groups were biguanides (89.27%), Sulfonylureas (43.90%) and insulin (15.28%). Metformin (89.27%), glibenclamide (29.11%) and insulin (15.28%) were commonly prescribed anti diabetic drugs. Metformin was the most common monotherapy drug and biguanide + sulfonylurea was the most common two drug combination. Commonly prescribed drugs for co-morbid conditions were enalapril (83.41%), aspirin (30.41%), amlodipine (29.76%) atorvastatin (27.32%) and famotidine (26.34%). Average number of drugs prescribed in a prescription was 4.65. Prescriptions with injections were 15.93% and with brand names were 13.15%.

Conclusions: Prescribing pattern of drugs was as per current practices and recommendations of guidelines. Still, there is room for improvement in choice of drug, prescribing drug with generic name and choosing drug from essential medicine list.

Keywords: Anti diabetic drugs, Diabetes mellitus, Hypertension, Prescribing pattern

INTRODUCTION

Diabetes mellitus is an important non communicable disease worldwide. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. WHO projects that it will be the seventh leading cause of death in 2030.¹ It is an important cause of heart attacks, stroke, blindness, kidney failure and

lower limb amputation. Prevalence of diabetes has been rising more rapidly in low and middle -income countries.² In India, burden of diabetes is increasing with more than 62 million diabetic individuals with the disease.^{3,4} Type 2 diabetes mellitus and hypertension are diseases of middle or old age. Co-existence of both these diseases appears to be increasing in industrialized nations because populations are aging.⁵ Hypertension is frequently associated with

diabetes mellitus and its prevalence doubles in diabetics compared to the general population. Diabetes co-existing with hypertension causes higher arterial stiffness and there is increased risk of cardiovascular, ophthalmic and renal complications in such patients.^{6,7} Overall, co-existence of both these diseases increases morbidity and mortality. It is essential to manage such patients carefully with attention. Type 2 Diabetic patients should be managed with lifestyle modifications, exercise, diet control and drugs to have optimum glycaemic control. Now a day, many anti diabetic drugs are available, physician can choose any, depending on patient profile and need. Prescribing practices may vary from physician to physician and from patient to patient. Authors undertook this study to understand prescribing pattern of anti diabetic drugs in type 2 diabetic patients with coexisting hypertension, rational prescribing practices of drugs among such patients and to provide recommendations regarding practices.

METHODS

This cross sectional, observational, descriptive study was conducted after approval from institutional ethics committee. Our study sample included 615 patients. The duration of study was one year, from July 2015 to June 2016. Study sample included type 2 diabetic outdoor patients with co-existing hypertension, aged more than 18 years, of both sexes, who gave consent. Authors excluded those patients, who had complications like retinopathy, neuropathy, diabetic foot, stroke, myocardial infarction and who required indoor admission. The diagnosis and management were decided by the physician in charge. Once consultation by the physician was over, patients were screened for study criteria. Written informed consent was taken from those patients, who fulfilled study criteria. Authors interviewed such patients and reviewed their prescriptions. Details like age, sex, duration of illness, ongoing treatment concurrent medicines were recorded in predesigned and pretested case record forms. These data were subjected to analysis using descriptive methods. Microsoft excel was used for data entry and descriptive analysis.

RESULTS

Authors had included data of 615 patients in this analysis. 93.17% of patients were more than 40 years age and only 6.83% patients were below 40 years. The youngest patient in this study was 26 years old. Average age of patients was 54.63±10.87 years. Female patients were more compared to male in each age group. Ratio of female patients to male patients in this study was 1.30. Table 1 shows distribution of patients as per age and sex. In this study, more than half of the sample population had a diabetic history of less than 5 years. Patients suffering from type 2 diabetes mellitus for more than 10 years were only 7.32% (Figure 1). Mean duration of diabetes was 5.81±4.99 years.

Majority of patients were given either single anti diabetic drug (monotherapy) or two anti diabetic drugs

combination. Four drugs combination was prescribed to only four (0.65%) patients. 10 (1.63%) prescriptions did not have anti diabetic drug (Table 2).

Table 1: Distribution of patients as per age and sex.

Age groups	Male (n, percentage of total population)	Female (n, percentage of total population)	Total (n, percentage of total population)
20-29 years	3 (0.49%)	1 (0.16%)	4 (0.65%)
30-39 years	15 (2.44%)	23 (3.74%)	38 (6.18%)
40-49 years	58 (9.43%)	76 (12.36%)	134 (21.79%)
50-59 years	94 (15.28%)	103 (16.75%)	197 (32.03%)
60 years or more	97 (15.77%)	145 (23.58%)	242 (39.35%)
Total	267 (43.41%)	348 (56.59%)	615 (100.00%)

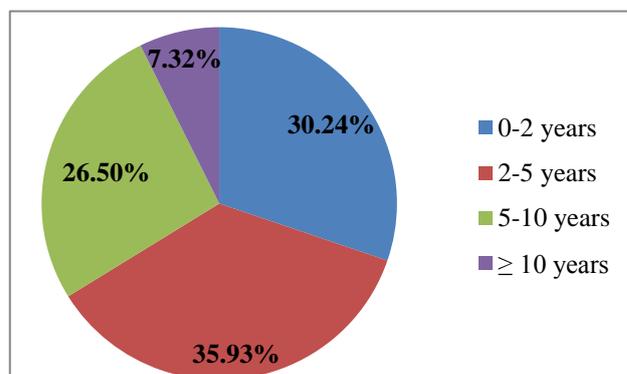


Figure 1: Distribution of patients as per duration of diabetes.

Table 2: Distribution as per number of anti diabetic drugs in a prescription.

Number of anti diabetic drug in a prescription	Number of encounters (%)
No drug	10 (1.63%)
One drug	270 (43.90%)
Two drug	311 (50.57%)
Three drug	20 (3.25%)
Four drug	4 (0.65%)

Commonly prescribed anti diabetic drug groups were biguanides (89.27% prescriptions) followed by Sulfonylureas (43.90% prescriptions) and insulin (15.28% prescriptions). Figure 2 shows prescribing pattern of anti diabetic drug groups.

The most common anti diabetic drug prescribed to the patients was metformin (89.27%) followed by glibenclamide (29.11%) and human mixtard insulin (15.28%). Glimepiride was prescribed in 8.29%

prescriptions. Repaglinide and voglibose were present in one prescription each. Glimepiride + metformin fixed dose combination (FDC) (1.46%), glimepiride + pioglitazone FDC (0.81%), gliclazide + metformin FDC (0.49%) and glimepiride + pioglitazone + metformin FDC (0.16%) were fixed dose combinations prescribed in this study. Table 3 shows prescribing pattern of anti diabetic drugs.

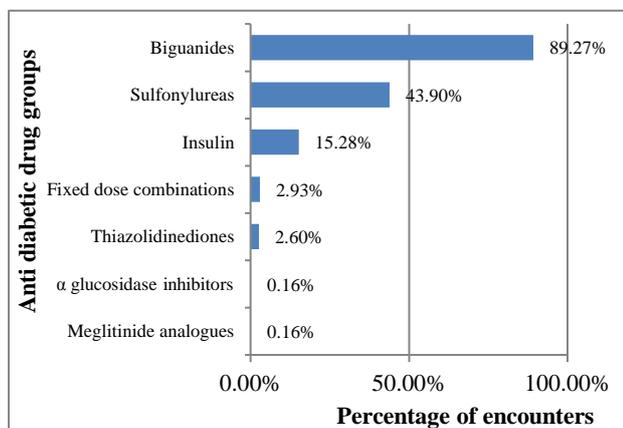


Figure 2: Prescribing pattern of anti diabetic drug groups.

Table 3: Prescribing pattern of anti diabetic drugs.

Drugs	Number of encounters	Percentage of encounters
Metformin	549	89.27%
Glibenclamide	179	29.11%
Human mixtard (30:70) insulin	94	15.28%
Glimepiride	51	8.29%
Glipizide	27	4.39%
Pioglitazone	16	2.60%
Glimepiride + metformin FDC	9	1.46%
Glyburide	8	1.30%
Gliclazide	5	0.81%
Glimepiride + pioglitazone FDC	5	0.81%
Gliclazide + metformin FDC	3	0.49%
Repaglinide	1	0.16%
Voglibose	1	0.16%
Glimepiride + pioglitazone + metformin FDC	1	0.16%

Out of 270 (43.90%) prescriptions with monotherapy anti diabetic regime, majority of prescriptions contained biguanide (85.19%) followed by sulfonylurea (7.41%) and insulin (7.41%). Prescriptions with two anti diabetic drugs were 311 (50.57%). In these 311 prescriptions, biguanide + sulfonylurea (74.92%) followed by biguanides + insulin (21.54%) and biguanide + thiazolidinedione (1.93%) were commonly prescribed combinations.

Table 4: Prescribing pattern of anti diabetic monotherapy/multi drug regime.

Drug	Number of encounters	% of total encounters
Single anti diabetic drug in a prescription (n=270)		
Biguanide	230	85.19%
Sulfonylurea	20	7.41%
Insulin	20	7.41%
Total prescriptions containing single anti diabetic drug	270	100.00%
Two anti diabetic drugs in a prescription (n=311)		
Biguanide + sulfonylurea	233	74.92%
Biguanides + insulin	67	21.54%
Biguanide + thiazolidinedione	6	1.93%
Sulfonylurea + thiazolidinedione	3	0.96%
Insulin + thiazolidinedione	1	0.32%
Sulfonylurea + α glucosidase inhibitor	1	0.32%
Total prescriptions containing two anti diabetic drugs	311	100.00%
Three anti diabetic drugs in a prescription (n=20)		
Biguanide + sulfonylurea + thiazolidinedione	11	55.00%
Biguanide + sulfonylurea + sulfonylurea	6	30.00%
Biguanide + sulfonylurea + insulin	2	10.00%
Biguanide + sulfonylurea + meglitinide analogue	1	5.00%
Total prescriptions containing three anti diabetic drugs	20	100.00%
Four anti diabetic drugs in a prescription (n=4)		
Insulin + sulfonylurea + biguanide + biguanide	2	50.00%
Insulin + sulfonylurea + sulfonylurea + biguanide	1	25.00%
Insulin + sulfonylurea + biguanide + thiazolidinedione	1	25.00%
Total prescriptions containing four anti diabetic drugs	4	100.00%

Prescriptions with three anti diabetic drugs were 20 (3.25%). Biguanide + sulfonylurea + thiazolidinedione

(55.00%) followed by biguanide + sulfonylurea + sulfonylurea (30.00%) and biguanide + sulfonylurea + insulin (10.00%) were commonly prescribed combinations in such prescriptions. Four (0.65%) prescriptions contained four antihypertensive drugs. In ten (1.63%) patients, no anti diabetic drug was prescribed and they were on diet, exercise and other non pharmacological management (Table 4).

In this study, commonly prescribed drug for co morbid conditions were enalapril (83.41%) followed by aspirin (30.41%), amlodipine (29.76%) atorvastatin (27.32%) and famotidine (26.34%). Table shows prescribing patterns of drugs for co morbid conditions (Table 5).

Table 5: Prescribing pattern of drugs for co-morbid conditions.

Drug	Number of encounters	% of total encounters
Enalapril	513	83.41%
Aspirin	187	30.41%
Amlodipine	183	29.76%
Atorvastatin	168	27.32%
Famotidine	162	26.34%
Atenolol	129	20.98%
Vitamin B complex	81	13.17%
Furosemide	77	12.52%
Metoprolol	72	11.71%
Amitryptilline	66	10.73%
Folic acid	40	6.50%
Clopidogrel	33	5.37%
Alprazolam	16	2.60%
Calcium	8	1.30%
Telmisartan	8	1.30%
Iron	7	1.14%
Paracetamol	7	1.14%
Cetirizine	6	0.98%
Losartan	5	0.81%
Chlorthalidone	5	0.81%
Hydrochlorothiazide	4	0.65%
Diclofenac	4	0.65%
Azithromycin	3	0.49%
Rosuvastatin	2	0.33%
Carvedilol	2	0.33%
Propranolol	1	0.16%
Ciprofloxacin	1	0.16%
Amoxicillin with clavulanic acid	1	0.16%

Average number of drugs prescribed in a prescription was 4.65 ± 1.83 . Average number of anti diabetic drugs in a prescription was 1.74 ± 0.61 . Percentage of prescriptions with injections was 4.69%. Out of total 42 drugs prescribed, 27 (64.29%) drugs were prescribed from national list of essential medicines 2015.⁸ Drugs prescribed by brand names were 13.15%.

DISCUSSION

Diabetes, being a chronic disease, often requires long term treatment. Co-existence of hypertension increases risk of diabetes related complications. Lifestyle modifications, diet and exercise play an important role in management. However, pharmacotherapy becomes unavoidable in these patients. The attitude of clinician to the disease and in treatment is reflected in drugs prescribed by him. Study of prescribing pattern is an important tool to understand utilization of drugs. Type 2 diabetes mellitus occurs mainly in middle or older age group. In this study, 93.17% of patients were more than 40 years of age and only 6.83% patients were below 40 years. Patients more than 50 years of age were 71.38%. The study finding is in consonance with other similar studies.^{9,10} Diabetes in advancing age increases risk of atherosclerotic changes, stroke and myocardial infarction.¹¹ Such patients should be carefully managed with non pharmacological and pharmacological measures. Elderly patients with diabetes may require more than one drug for management. In this study, female patients were more compared to male in each age group. The finding is in consonance with other study.¹⁰ The duration of diabetes plays an important role in diabetes management. In present study, more than half of the patients had a diabetic history of less than 5 years. Mean duration of diabetes was 5.81 ± 4.99 years. In patients with longer duration of diabetes, chances of complications are high. The risk of cardiovascular complications, ocular complications, neuropathy and nephropathy increase with longer duration of diabetes.¹¹ Poor glycaemic control worsen the risk of complications. Therefore as soon as diabetes is detected, prompt management must be started to achieve glycaemic control.

Among anti diabetic drug groups, biguanides (89.27%) were commonly prescribed drugs followed by sulfonylureas (43.90%) and insulin (15.28%). The study findings are in consonance with similar studies.^{9,10,12} The most common drug prescribed to the patients was metformin (89.27%) followed by glibenclamide (29.11%) and human mixtard insulin (15.28%). Glimepiride was prescribed in 8.29% prescriptions. According to UKPDS study, ADA and consensus guidelines, metformin should be the first line foundation therapy in addition to lifestyle modifications in type 2 diabetes.^{13,14} As in other study, glibenclamide was the most common sulfonylurea prescribed in this study.¹² However, glimepiride was the most common sulfonylurea prescribed in other similar studies.^{9,10} Insulin was prescribed to 15.28% patients compared to 25% patients in study conducted by Rekha MB et al.¹² These variations can be due to choice of physician in relation to type of patients, their concurrent illness as well as availability of medicines.

Poly therapy (54.47%) was common than monotherapy (43.90%) in this study. 1.63% patients were managed with lifestyle modification, diet and exercise and they were not prescribed anti diabetic drug. In this study, 33.82% patients were suffering from diabetes for more than 5 years. Duration of diabetes was more than two years in

69.75% patients and more than half of the patients were above 50 years of age. Also, patients were suffering from co-existing hypertension. This might be the reason for two or more anti diabetic drugs in more than half of prescriptions. In other similar study also, multidrug anti diabetic regimes were prescribed in majority of patients.¹⁰

Metformin was the most common drug prescribed as monotherapy. 85.19% of single anti diabetic drug (monotherapy) containing prescriptions had metformin. The finding is in consonance with similar studies.^{9,10} This pattern of utilization is as per the recommendations of guidelines for diabetes management.^{13,14}

Sulfonylurea and insulin were other anti diabetic drugs prescribed as monotherapy. In 7.41% of single anti diabetic drug containing prescriptions, sulfonylurea drug was prescribed. Monotherapy with sulfonylureas carries no additional benefits than metformin. Sulfonylureas may lead to progressive deterioration in glycaemic control over time and do not have protective effects against atherosclerotic complications. After initial haemoglobin A1C decline, improvement in haemoglobin A1C level may not be maintained for long period by sulfonylurea alone. There were reports of failure of sulfonylurea monotherapy in number of patients.¹⁵ Insulin was prescribed as monotherapy in 7.41% of single anti diabetic drug containing prescriptions. Selection of insulin allows a clinician to focus on either fasting or postprandial hypoglycaemia, or both, depending on a specific patient's therapeutic needs.

Two anti diabetic drugs containing prescriptions were 311 (50.57%). Among these prescriptions, biguanide + sulfonylurea (74.92%) followed by biguanides + insulin (21.54%) and biguanide + thiazolidinedione (1.93%) drug combinations were commonly prescribed combinations. The American diabetes association recommends use of these combinations as second line management for type 2 diabetes if glycaemic control is not achieved with monotherapy. The choice depends on patient specific and disease specific factors.¹⁴ The risk associated with sulfonylurea like weight gain and obesity can be balanced by adding metformin in combination. Considering cost of GLP-1 receptor agonist, side effects of thiazolidinedione and cost and injectable formulation of insulin, sulfonylurea remains preferred choice to be combined with metformin. The finding is in consonance with other studies.^{9,10}

There were three anti diabetic drugs containing prescriptions were 20 (3.25%). Biguanide + sulfonylurea drugs were present in all three drugs containing prescriptions. Third drug may be thiazolidinedione, insulin, other sulfonylurea or meglitinide analogue. As in other study, Biguanide with sulfonylurea and thiazolidinedione was the most common combination (55.00%) among these prescriptions.¹⁰ Pioglitazone may reduce the risk of cardiovascular events including stroke in patients with type 2 diabetes. Pioglitazone is associated with bladder cancer, however no direct causal relation has

been proved yet.¹⁶ Only four prescriptions included four anti diabetic drugs. Poly therapy, as in this study, is particularly useful in patients, in whom there is persistent hyperglycaemia despite of adequate lifestyle modifications and pharmacological measures.

First five commonly prescribed drugs for concomitant conditions in this study were enalapril (83.41% of total prescriptions), aspirin (30.41% of total prescriptions), amlodipine (29.76% of total prescriptions), atorvastatin (27.32% of total prescriptions) and famotidine (26.34%). Our study population had co existing hypertension. In such population, enalapril or amlodipine are preferred antihypertensive agents.¹⁷ Atherosclerotic changes and cardiovascular complications occur in diabetes, the risk increases due to co-existence of hypertension, long history and advancing age.¹¹ In this study, aspirin and atorvastatin is among first five commonly prescribed concomitant drugs. The finding is in consonance with other studies.^{9,12}

Average number of drugs prescribed in a prescription was 4.65 ± 1.83 . Average number of anti diabetic drugs in a prescription was 1.74 ± 0.61 . As diabetes and hypertension, both co morbidities were present in the patients, polypharmacy was unavoidable. The finding is in consonance with other studies.^{9,12} Percentage of prescriptions with injections was 4.69%. Injectable insulin accounted for majority of injectable formulations. Antibiotics were prescribed in 0.81% prescriptions. Out of total 42 drugs prescribed, 27 (64.29%) drugs were prescribed from national list of essential medicines 2015.⁸ Also 13.15% of drugs were prescribed by brand names. So, there is room for improvement in drug prescribing practice.

Our study concluded that mostly, prescribing pattern of drugs was as per current practices and recommendations of guidelines. The pattern of drug use was to achieve better glycaemic control. Our study was single centre study, in government setup. Also authors had not included indoor patients. Authors had not done prescription follow up. To justify sulfonylurea as monotherapy, Authors have not explored indications in detail. Further large scale and more detailed study, which includes sample from government setup and private clinics, is recommended to confirm our findings.

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