

Original Research Article

Prescribing pattern of antidiabetic drugs in type 2 diabetes mellitus at a tertiary care hospital in Eastern India

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ABSTRACT

Background: Chronic hyperglycemia of diabetes mellitus (DM) is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. We aimed to evaluate the prescribing pattern of antidiabetic drugs among Type 2 DM (T2DM) outpatients in Medical College, Kolkata.

Methods: A cross sectional study was conducted over a period of three months in the Department of Pharmacology and Department of Endocrinology, Medical College, Kolkata. Detailed information of the participants regarding demography, medical history, duration of diabetes, family history of diabetes, prescribed antidiabetic medicines, comorbid conditions and associated medications were evaluated.

Results: A total of 305 subjects with T2DM were included and 516 prescriptions were analyzed. 57% of the subjects were male. Majority of patients were in the age group of 51-60 (37.7%) years. Most of them had history of diabetes between 1-5 years (46.26%) and most common comorbid condition was hypertension. The average number of antidiabetic medicines per prescription was 2.90. Antidiabetic drug was prescribed as monotherapy (5.23%) as well as combination of two (32.36%), three (38.17%), four (16.47%), five (7.17%) and six (0.58%) anti-diabetic drugs combinations. Among the oral antidiabetic (OAD) agents, metformin was most commonly prescribed (92.44%) while the most commonly prescribed injectable antidiabetic medicine was lispro mix insulin (27.13%).

Conclusions: The antidiabetic medicine prescribing trend appeared to be shifting towards combination therapy. Through a thorough understanding of the existing prescribing patterns, attempts may be made to improve the quality and efficiency of drug therapy.

Keywords: Antidiabetic drug, Drug utilization, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) 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 Chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.²

Diabetes may be of several types (type 1, type 2, gestational and specific types of diabetes due to other causes) among which type 2 predominates. The prevalence of type 1 diabetes mellitus (T1DM) is about 5% to 10% and type 2 diabetes mellitus (T2DM) is about 90% to 95%.³ Type 2 DM is characterized by a variable degree of insulin resistance, impaired insulin secretion, and increased glucose production.

The World Health Organization (WHO) has projected that the global prevalence of T2DM 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 DM, from 4 to 5.4%.⁴ According to International Diabetes Federation (IDF), the number of people with diabetes in the world in 2013 was 382 million, which is going to be increased to almost 592 million by 2035. Regarding Indian scenario IDF stated that 65.1 million of adults in India suffered from diabetes in the year 2013.⁵ It was also predicted that the prevalence of diabetes in adult population in India will be 6% by the year 2025.⁶ In another study, the prevalence of diabetes is predicted to be doubled globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India.⁷

A good glycemic control is the cornerstone of the management of diabetes. Modern principles of management of diabetes focus on disease prevention, screening high risk individuals and aggressive treatment of individuals in the pre-diabetic state. The current pharmacotherapy of DM includes treatment with drugs like insulin and oral antidiabetic (OAD) agents. OAD agents are heterogeneous in their modes of action, safety profiles and tolerability. The main classes of OAD agents include agents that stimulate insulin secretion (sulfonylureas and other insulin secretagogues), reduce hepatic glucose production (biguanides), delay digestion and absorption of intestinal carbohydrate (α -glucosidase inhibitors), improve insulin action (thiazolidinediones) and incretin based therapies like dipeptidyl peptidase-4 (DPP 4) inhibitors.⁸⁻¹⁰ Besides these, there is provision for sodium glucose co-transporter inhibitor 2 (SGLT2 inhibitors).

Prescription by a clinician reflects the prescriber's attitude to disease and role of the drug in treatment. Besides, it provides insight into the nature of healthcare delivery system.

According to WHO, drug utilization is defined as the marketing, distribution, prescription and use of drugs in a society with special emphasis on the resulting medical, social and economic consequences.¹¹ The principal aim of drug utilization studies (DUS) is to facilitate the rational use of drugs in population. Drug utilization studies are important for the optimization of drug therapy. The study of drug utilization or prescribing patterns serves a component of medical audit, which seeks monitoring, evaluation and necessary modifications in the prescribing practices to achieve rational and cost effective pharmacotherapy. The consequences of irrational prescribing include non-adherence to medications, which may result in complications due to uncontrolled blood glucose levels and also escalate drug costs and health care costs.

Several DUS on antidiabetic agents are available across the world, including India.¹²⁻²³ However, there are no accepted guidelines for treating T2DM in Indian scenario, as all are formulated in western countries. More so, it is

necessary to follow a treatment protocol in common comorbidities associated with T2DM. In view of this, the present study was designed to evaluate the prescribing pattern of antidiabetic drugs among T2DM outpatients in Medical College, Kolkata.

METHODS

This cross-sectional study was conducted over a period of three months (August 2019-October 2019) in the Department of Pharmacology and Department of Endocrinology, Medical College, Kolkata. Patients were recruited from the Out Patient Department (OPD) of diabetic clinic in the hospital.

Prior to conducting the study, the study proposal, informed consent document and case record form were approved by the Medical College Ethics Committee. Participants were explained clearly about the purpose and nature of the study in the language they understood and were included in the study only after obtaining a written informed consent.

Inclusion criteria

T2DM patients of both sexes on antidiabetic medications visiting diabetic clinic, Medical College, Kolkata were included in the study.

Exclusion criteria

Patients with T1DM/gestational diabetes/diabetes due to specific causes were excluded.

The detailed information of the participants was obtained from OPD prescriptions of diabetic clinic by examination of patient's medical records, direct interview of the patient or his/her caregivers. Details about demography, medical history, duration of diabetes, family history of diabetes, prescribed antidiabetic medicines, comorbid conditions and associated medications were collected. The data were collected in a case record form (CRF). The data from the CRF were transcribed onto an excel database and analyzed using SPSS statistical software. All variables were tested for their distribution and those with normal distribution were summarized using mean and standard deviation.

RESULTS

A total of 305 subjects with T2DM were included and 516 prescriptions were analyzed. Out of these subjects 173 (57%) were male and 132 (43%) were female.

The mean age of study subjects was 51 ± 10.12 (mean \pm SD) years with a range between 21 and 75 years. Majority of the patients were in the age group of 51-60 (37.7%) years followed by age group of 41-50 (30.49%) years while patients with age group of more than 70 years (1.63%) was found to be the least (Table 1).

Table 1: Distribution of age of the study subjects.

Age (years)	Percentage (%)
≤ 30	4.26
31-40	11.8
41-50	30.49
51-60	37.7
61 -70	14.09
>70	1.63

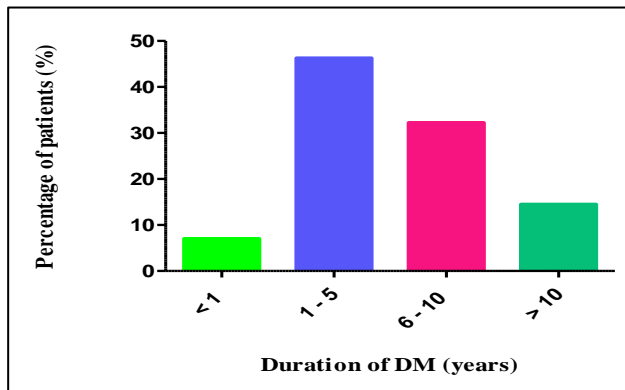


Figure 1: Distribution of patients according to duration of diabetes mellitus.

Majority of the patients had history of diabetes between 1-5 years (46.26%) followed by 6-10 year (32.24%), followed by >10 years (14.48%). 7% of the patients had history of diabetes for less than one year (Figure 1).

Most of the patients had hypertension as comorbid condition (49.18%) followed by dyslipidemia (32.78%), neuropathy (19.08%), coronary artery diseases (CAD) (8.52%) and hypothyroidism (4.91%) (Figure 2).

The average number of antidiabetic medicines per prescription was 2.90 and average number of total medicines per prescription was 4.15.

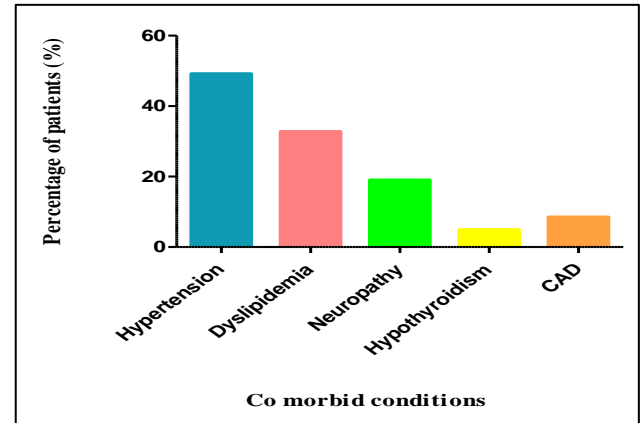


Figure 2: Comorbid conditions associated with diabetes mellitus.

Various groups of antidiabetic medicines were prescribed. Besides oral antidiabetic drugs injectable antidiabetic drug- insulin was also prescribed (Table 2). The drugs were prescribed in different doses (Table 3).

Table 2: Different antidiabetic medicines prescribed.

Different antidiabetic medicines prescribed			
Oral		Injectable	
Group	Drug	Group	Drug
Biguanide	Metformin	Rapid acting	Lispro
Sulfonylurea	Glimepiride, Gliclazide	Short acting	Regular
PPAR gamma agonist	Pioglitazone	Long acting	Glargine
DPP4 inhibitor	Linagliptin, Vildagliptin, Teneligliptin, Sitagliptin	Combinations	Lispro/ Lispro protamine, Regular/NPH
Alpha glucosidase inhibitor	Voglibose, Acarbose		
SGLT2 inhibitor	Canagliflozine, Empagliflozine		

Out of 516 prescriptions, 15 (2.9%) contained only injectable antidiabetic medicines. 155 (30.03%) contained both oral and injectable antidiabetic medicines and 346 (67.05%) contained only oral antidiabetic medicines.

Antidiabetic drug as monotherapy were prescribed in 5.23% prescriptions. Besides monotherapy, combination of different antidiabetic drugs were prescribed as two (32.36%), three (38.17%), four (16.47%), five (7.17%) and six (0.58%) drug combinations (Figure 3).

As monotherapy most commonly prescribed oral and injectable antidiabetic drugs were metformin (37%) and lispromix (41%) respectively. Combination of metformin + glimepiride was the most commonly prescribed two antidiabetic drug combination (45.5%). Most commonly prescribed three antidiabetic drug combination was metformin + glimepiride + pioglitazone (27.92%). Most commonly prescribed four antidiabetic drug combination was metformin + glimepiride + pioglitazone + vildagliptin (25.88%). Most commonly prescribed five antidiabetic drug combination was metformin + glimepiride + pioglitazone + voglibose + vildagliptin

(67.56%) and most commonly prescribed six antidiabetic drug combination was metformin + glimepiride + pioglitazone + voglibose + vildagliptin + canagliflozine (66.67%) (Table 4).

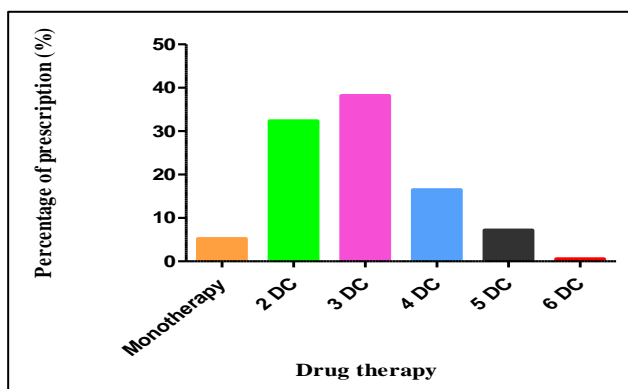


Figure 3: Distributions of prescriptions according to antidiabetic drug utilization pattern (DC: drug combination).

Among the OADs metformin was the most commonly prescribed medicine (92.44%) followed by glimepiride (57.55%) and pioglitazone (40.69%). Among the injectable antidiabetic medicines lispromix insulin was the most commonly prescribed medicine (27.13%).

Besides antidiabetic medicines, prescriptions also contained other medicines due to associated illnesses. Among those other medicines, atorvastatin was most

commonly prescribed (60.46%). This was followed by amlodipine (16.27%) and losartan (10.27%).

Table 3: Antidiabetic medicines prescribed in different doses.

Oral antidiabetic medications	
Name of drugs	Daily dose range (mg/day)
Metformin	500-2000
Linagliptin	5
Glimepiride	1-6
Pioglitazone	15-30
Vildagliptin	50-100
Teneligliptin	20
Gliclazide	60
Sitagliptin	50-100
Voglibose	0.2-0.6
Canagliflozine	100
Acarbose	25-50
Empagliflozin	10
Injectable antidiabetic medications	
Name of drugs	Daily dose range (unit/day)
Glargine	10-16
Lispro Insulin	16-80
Regular Insulin	14-34
Combination of insulin: lispro/lispro protamine (25/75)	12-70
Combination of insulin: regular/NPH (30/70)	10-70

Table 4: Most commonly prescribed antidiabetic medicines.

Drug therapy (mono or combination)	Name of the drugs	Frequency (%)
Monotherapy: oral	Metformin	37
Monotherapy: injectable	Lispromix	41
Two drug combination	Metformin + Glimepiride	45.5
Three drug combination	Metformin + Glimepiride + Pioglitazone	27.92%
Four drug combination	Metformin + Glimepiride + Pioglitazone + Vildagliptin	25.88%
Five drug combination	Metformin + Glimepiride + Pioglitazone + Voglibose + Vildagliptin	67.56%
Six drug combination	Metformin + Glimepiride + Pioglitazone + Voglibose + Vildagliptin + Canagliflozine	66.67%

DISCUSSION

In the present study, a total of 305 diabetic patients were evaluated and it was observed that male had preponderance in the prevalence of diabetes (males 57%; females 43%). Similar study conducted by Vengurlekar et al, Boccuzzi et al, Johnson et al, Yurgin et al and Sudha et al also showed that male had preponderance in the prevalence of diabetes.^{16,24-27} In our study DM was found to be most prevalent (37.7%) in the age group of 51-60 years which is in concordance with the earlier published literature.^{12,16,17,20} This may be due to the fact that aging

causes increase prevalence of diabetes and carbohydrate intolerance in the elderly due to associated decrease in insulin secretion in response to glucose load as well as increased insulin resistance in peripheral tissues.²⁸ Moreover insulin sensitivity also decreases with progression of age and obesity.²⁹

In our study, we found that the average number of antidiabetic medicines per prescription was 2.90. Average number of drugs prescribed in our study is less as compared to result of Upadhyay et al, (3.76 per prescription) and Karthikeyan et al, (4.83 per

prescription).^{12,30} However, the average number of drug prescribed in our study is more compared to that reported by Kannan et al, (1.4 per prescription).¹⁷

In the present study, antidiabetic drug as monotherapy were prescribed in 5.23% prescriptions. Besides monotherapy, combination of different antidiabetic drugs were prescribed as two (32.36%), three (38.17%), four (16.47%), five (7.17%) and six (0.58%) drug combinations. Present study was contradictory from a study conducted in Tamil Nadu by Sivasankari et al, who reported monotherapy and two drug combination therapies were prescribed in 21.7% and 78.3% patients, respectively.²²

Among the oral antidiabetic medicines metformin was the most commonly prescribed medicine (92.44%) followed by glimepiride (57.55%) and pioglitazone (40.69%). Among the injectable antidiabetic medicines lispro mix insulin was the most commonly prescribed medicine (92.44%). Similar result regarding biguanides and sulfonylureas had been documented in study conducted by Alex et al.³¹

Studies conducted by Boccuzzi et al and Truter et al during the late 1990s had reported sulfonylureas as the most frequently prescribed antidiabetic agent which is contradictory from the present study.^{24,32}

In this study, among the sulfonylureas, glimepiride was most commonly prescribed in combination with metformin. Similar results are found in study conducted by Sudha et al, where the most commonly prescribed sulfonylurea was also glimepiride.²⁷

Comorbidity has been shown to intensify health care utilization and to increase medical care costs for patients with diabetes. In our study most of the patients had hypertension as comorbid condition (49.18%) followed by dyslipidemia (32.78%), neuropathy (19.08%), CAD (8.52%) and hypothyroidism (4.91%). Different studies from India and other countries have reported a similar observation with regard to the comorbidity in patients with diabetes. However, the prevalence of hypertension has ranged from 31 to 70% in a study conducted by Patel et al, Alam et al, Sudha et al, and Jenny L et al.^{21,23,27,33} The combination of hypertension and diabetes is clinically important because it magnifies the risk of diabetic complications.

Cost of prescription is very important in chronic disease like diabetes as it may be a major cause for non-adherence to treatment. However, as our study was performed in a Government set up, all the antidiabetic medicines were provided free of cost by the Government.

CONCLUSION

Diabetes should be managed properly to enhance the quality of life of the patients. In our study metformin was

found to be the most commonly used drug. The prescribing trend also appears to be shifting towards combination therapy. Our study contributes to the growing body of literature on drug utilization research. It is very important that efforts from both patients and the physician should be improved to meet glycemic goal to have a better and healthy life. Therefore, through a thorough understanding of the existing prescribing patterns, attempts may be made to improve the quality and efficiency of drug therapy. Besides, setting standards and assessment of the quality of care through performance review may be taken as a part of everyday clinical practice.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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