

A Prospective Study of Utilization Pattern of Antihyperglycemic Agents, Cost Analysis and Adherence to Current Standard Treatment Guidelines in a Tertiary Care Hospital in North East India

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Abstract:

Introduction: Diabetes has emerged as one of the fastest growing global health emergencies of the 21st century. The real burden of diabetes is due to its micro and macrovascular complication which lead to increased morbidity and mortality. Judicious use of antidiabetic drugs by adhering to guidelines will decrease the complication and cost of drug therapy.

Aims and Objectives: The objective of this study was to evaluate drug utilization pattern of antihyperglycemic agents in Type 2 diabetes mellitus (T2DM).

Materials and Method: A single centric cross sectional prospective observational study was conducted over a period of 6 months (May 2017 to October 2017) in the diabetic clinic of Assam Medical College and Hospital (AMCH), Dibrugarh, Assam. The data were analyzed using descriptive statistics. Continuous data were expressed as mean percentage and nominal data were expressed as frequency and percentages.

Results: In this study a total of 207 prescriptions were analyzed and was observed that Metformin was the most common drug prescribed both as monotherapy (53.7%) and in combination with Gliclazide (50%). Amlodipine (16.9%) was the most common non-diabetic drug prescribed in our patients. Average number of drugs per prescription was 4.06, while average number of antihyperglycemic agents per prescription was 1.92. Average cost of antihyperglycemic agents per prescription was under Rs 100/month (55.5 %) with 42.45 % of drugs prescribed as generic drugs.

Conclusion: Metformin being the most commonly prescribed antihyperglycemic drug in T2DM should be available in sufficient quantities in health care system. Polytherapy is given adequately for the various macro and microvascular complications due to long standing diabetes mellitus. Generic drugs should be used to reduce the cost of treatment.

Keywords: Type 2 diabetes mellitus, Drug utilization studies, Antihyperglycemic agents, Metformin, World Health Organization.

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Introduction

Diabetes has emerged as one of the major public health challenges worldwide. According to WHO "Diabetes is defined as a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in the insulin secretion, insulin action or both." [1] The causes of Type 2 diabetes mellitus are not completely understood but there is a strong link with overweight and obesity, increasing age, ethnicity and family history. It is one of the fastest growing global health emergencies of the 21st century.

The International Diabetes Federation (IDF) have estimated 537 million individuals with diabetes

worldwide in 2021 and this number is set to increase to 643 million by 2030 and 783 million by 2045. It accounts for 6.7 million deaths in 2021.[2] India has also witnessed a rapidly exploding epidemic of diabetes and has the second largest number of people with diabetes in the world. The IDF estimates that there are 72.9 million people with diabetes in India in 2017, which is projected to rise to 134.3 million by the year 2045.[3] The projected increase in diabetes prevalence to is a consequence of ongoing largescale urbanization and increasing life expectancy. The real burden of diabetes is due to its micro and macrovascular complication which lead to increased morbidity and mortality. Complication due to hyperglycemia in

diabetes can be prevented by rational use of oral antidiabetic agents (OADs) or insulin. Diabetes imposes a substantial economic burden on countries health system. The increase in global health expenditure due to diabetes has been considerable, growing from USD 232 billion in 2007 to USD 966 billion in 2021 for adults aged 20 – 79 years. This represents a 316 % increase over 15 years.[3] Rational use of drug in population can be effectively studied with drug utilization review. The World Health Organization (WHO) defines “drug utilization as the marketing, distribution, prescription and use of the drug in a society considering its consequences, either medical, social or economic”.[4] It helps to identify the adherence to standard treatment guidelines and to evaluate the rational drug usage. There are various guidelines for the management of Diabetes mellitus. The American Association of Clinical Endocrinologists/ American College of Endocrinology (AAACE/ACE), American Diabetes Association (ADA), National Institute for Health Care Excellence (NICE), Indian Council of Medical Research (ICMR). In 2018, Indian Council of Medical Research (ICMR) has given guidelines for treatment of diabetes in which the selection of drugs is mainly based on Body mass index.[3]

The ADA/EASD consensus report “Management of Hyperglycemia in Type 2 Diabetes, 2022” recommends a holistic, multifaceted, person-centered approach accounting for the complexity of managing type 2 diabetes and its complications across the life span.[5] In adults with type 2 diabetes without cardiovascular and/or kidney disease, pharmacologic agents should address both the individualized glycemic and weight goals. In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, heart failure and/or chronic kidney disease, the treatment plan should include agents that reduce cardiovascular and kidney disease risk (eg. Sodium- glucose cotransporter 2 (SGLT-2) inhibitor and/or Glucagon-like peptide 1 receptor agonist (GLP-1 RA) [5] The current pharmacotherapy of DM includes Insulin and Oral hypoglycemic agents like Sulfonylureas, Biguanides, α -glucosidase inhibitors, Thiazolidinediones, Dipeptidyl peptidases-4 (DPP-4) inhibitors, Sodium-glucose linked co-transporter 2 (SGLT-2) inhibitors, Glucagon-like peptide (GLP-1) receptor agonists.[6]

Diabetes mellitus (DM) is a chronic metabolic disease which requires lifelong treatment. So, cost of antidiabetic agent is a major deciding factor of patients’ compliance.

Judicious use of antidiabetic drugs by adhering to these guidelines will decrease the complication and cost of drug therapy. The objective of this study was to evaluate drug utilization pattern of

antihyperglycemic agents in a tertiary care hospital in North East India with focus on cost analysis and adherence to standard treatment guidelines.

Materials and Method

This single centric cross sectional prospective observational study was conducted over a period of 6 months (May to October 2017) in the diabetic clinic of Assam Medical College and Hospital (AMCH), Dibrugarh, Assam. All the participants included in the study were well explained about the purpose of the study in the language they understood and were included in the study only after obtaining a written Informed Consent (ICF).

Source of Data: The source of data was primary in nature and was obtained through a predesigned Structured Case Record Form (CRF) with detailed sociodemographic information, relevant medical history, and pattern of prescription of drugs, adverse drug reaction which were questioned directly to patients and also recorded from prescription and then recorded in the CRF.

Study Population: The study was carried out among the diabetic patients attending the diabetic clinic of Assam Medical College and Hospital (AMCH), Dibrugarh, Assam, India

Inclusion Criteria:

1. All type 2 diabetic patient attending diabetic clinic of AMCH
2. Patients of either sex and age more than 18 years

Exclusion Criteria:

1. Gestational diabetes patients
2. Patients on corticosteroid and estrogen therapy or diabetes due to other secondary causes.
3. Diabetes in- patients admitted in the hospital.

Ethical Clearance: The ethical clearance was obtained from the Institutional Ethics Committee (H) of Assam Medical College & Hospital, Dibrugarh, Assam bearing No. AMC/EC/1304 dated 17/05/2017.

Sample Size: A total of 207 patients who were known case of DM under treatment of both gender aged above 18 years visiting the medical outpatient department during the 6 months of study period were included in the study.

Body mass index (BMI) was calculated as:

$BMI = \text{weight in kg} / \text{height in sq.m}$

Anatomical therapeutic classification (ATC) was used to designate each drug prescribed. [7] Generic name and price of the drugs were obtained from CIMS (current index of medical speciality) and Indian drug review (IDR).

For calculation of adherence to standard diabetes guidelines, we followed the ICMR Guidelines 2018. The ADR related to antidiabetic drugs was monitored and documented in suitably designed ADR documentation form.

Statistical Analysis: Results obtained were recorded on Microsoft excel sheet and analysis was done using Statistical Package for the Social Sciences software program version 24.0. The data were analyzed using descriptive statistics. Continuous data were expressed as mean percentage and nominal data were expressed as frequency and percentages.

Results

Demographic Details: Results shows that 58.93% patients were males and 41.06% patients were females.

Distribution of patients based on the age group and gender shows that 3.27% males and 4.70% females was in the age group o 18 to 30 years, 18.03% males and 20% females was in the age group 31-40 years, 27.86% males and 29.4% females was in the age group 41-50 years, 27.04% males and 23.52% females was in the age group 51-60 years and 23.77% males and 22.35% females was in the age group >60 years. (Table 1)

Table 1: Demographic details

	No of patients (n=207)	Percentage
Gender		
Male	123	58.93
Female	84	41.06
Age-wise distribution (years)	Male (%)	Female (%)
18-30	3.27	4.70
31-40	18.03	20
41-50	27.86	29.40
51-60	27.04	23.52
>60	23.77	22.35
Co-morbidities	Male (%)	Female (%)
Hypertension	64 (52.45)	43 (50.58)
Neuropathy	24 (19.67)	18 (21.17)
Nephropathy	19 (15.57)	18 (21.17)
ASD/CAD	17 (13.93)	6 (7.05)
CVA	4 (4)	2 (2.35)
Diabetic foot	6 (4.91)	0 (0)
Retinopathy	3 (2.45)	3 (3.52)
Pancreatitis	4 (4)	0 (0)
Dyslipidemia & fatty liver	8 (6.55)	5 (5.88)
Hypothyroidism	8 (6.55)	9 (10.58)
Fungal infection & other infection	9 (7.37)	13 (15.29)

Based on the type of diabetes it was seen that all the patients were of Type 2 DM out of which 82.6% were known cases of Type 2 DM and 17.39% were newly diagnosed cases.

The BMI calculated for males was 22.37% and 22.1% for females. Common co- morbidities were hypertension (52.45% in males and 50.58% in females), neuropathy (19.67% in males and 21.17% in females), nephropathy (15.57% in males and 5.8% in females), ACS/CAD (13.93% in males and 7.05% in females). Other co-morbidities that were

seen were retinopathy, pancreatitis, dyslipidemia and fatty liver, hypothyroidism, fungal infection and diabetic foot. (Table 1)

Utilization Pattern of Antihyperglycemic agents:

The overall utilization pattern of antihyperglycemic agents shows that Metformin (83.57%) was the most commonly utilized antihyperglycemic drug with a mean utilization of 83.60% in males and 84.52% in females and Glipizide (1.63%) was the least utilized drug with a mean utilization of 1.63% in males. (Table 2)

Table 2: Utilization pattern of antihyperglycemic agents

Antihyperglycemic agents	ATC code	No. of diabetic patients (n %)	DDD	DDD/1000/day
Metformin	A10BA02	173 (83.57)	2 g	2.32
Gliclazide	A10BB09	68 (32.85)	60 mg	1.82
Glimepiride	A10BB12	60 (28.98)	2 mg	1.34
Teneligliptin	A10BH04	41 (19.80)	20 mg	1.10
Insulin Human mixtard	A10AE30	18 (8.70)	40U	0.48

Insulin Human actrapid	A10AB01	25 (12.07)	40 U	0.67
Insulin Glargine	A10AE04	7 (3.38)	40 U	0.18
Pioglitazone	A10BG03	5 (2.41)	30 mg	0.13
Voglibose	A10BF03	4 (1.93)	0.6 mg	0.05
Vildagliptin	A10BH02	3 (1.44)	0.1 g	0.05
Glipizide	A10BB07	2 (1.63)	10 mg	0.04

Distribution of diabetic patients based on number of antihyperglycemic agents prescribed shows that 26.08% of the study population was on monotherapy with Metformin as the most commonly prescribed drug (53.7%) followed by Insulin (37.03%) and Tenelegliptin (7.40%). Distribution of diabetic patients based on fixed drug combination (FDC) of antihyperglycemic agents revealed that 54.10% of the study population was on dual therapy, 18.84% was on triple drug

therapy and 0.96% was on 4-drug therapy. Metformin + Gliclazide (50%) was the most commonly prescribed combination followed by Metformin + Glimepiride (34.82%) and Glimepiride + Metformin + Tenelegliptin (46.15 %) whereas Vildagliptin + Metformin + Voglibose (0.48%) and Gliclazide + Tenelegliptin + Pioglitazone (0.48%) were the least prescribed combinations. (Table 3)

Table 3: Prescription pattern based on number of antihyperglycemic drugs used

Antihyperglycemic therapy	Male (n)	Female (n)	Total (%)
Monotherapy	27	27	54 (26.08)
Dual therapy	66	46	112 (54.10)
Triple therapy	28	11	39 (18.84)
4-drug therapy	1	1	2 (0.96)

Other Drugs: Utilization pattern of other drugs shows that Amlodipine (16.9 %) was the most utilized drug followed by Telmisartan (14.01%) and Hydrochlorothiazide (3.84) as the least prescribed among all prescribed antihypertensive agents. Utilization pattern of cardiovascular drugs shows Atorvastatin (12.07%) as the most utilized

drug and Fenofibrate (0.96 %) as the least utilized drug. Utilization pattern of gastrointestinal tract drug therapy shows Rabeprazole (9.66%) was the highest utilized drug whereas Ranitidine (1.93%) was the least utilized drug. (Table 4) Besides results shows use of various multivitamin supplements and oral iron preparations.

Table 4: Drug utilization of other drugs prescribed

Drugs prescribed	No. of prescriptions (n %)
Amlodipine	35 (16.9)
Metoprolol	24(11.59)
Atenolol	13 (6.28)
Aspirin	25 (12.07)
Hydrochlorothiazide	8 (3.84)
Atorvastatin	25 (12.07)
Telmisartan	29 (14.01)
Ramipril / Enalapril	12 (5.79)
Carvedilol	10 (4.83)
Pantoprazole / Rabeprazole	20 (9.66)
Ranitidine	4 (1.93)
Fenofibrate	2 (0.96)

Index of Adherence: Regarding adherence to standard treatment guidelines it was observed that antihyperglycemic agents prescribed in this hospital were in compliance with ADA guidelines with Metformin (83.57%) being the first line of treatment followed by Gliclazide (32.85%), Glimepiride (28.98%), Tenelegliptin (19.80%), Insulin (19.32%), Pioglitazone (2.4%), Voglibose (1.93%) and the least prescribed drug was Vildagliptin (1.44%) which were used as second

line therapy in addition to Metformin according to patient requirement, tolerability and cost.

Cost of Antihyperglycemic agents: Cost of antihyperglycemic agents in the prescription shows that cost of most of the agents was under Rs 100/month (55.5%) and least percentage of prescriptions were in the cost range of Rs 251- Rs 300 (1%).

Key Prescribing indicators: Average number of drugs per prescription was 4.06, whereas average

number of antihyperglycemic agents per prescription was 1.92. 42.45% drugs prescribed were generic drugs.

Most common adverse drug reaction documented was hypoglycemia (9.6%) followed by nausea and gastrointestinal upset.

Discussion

In the present study, simple random sampling was used to recruit diabetic patients visiting diabetic clinic of Assam Medical College and Hospital (AMCH), Dibrugarh, Assam during the study period of 6 months and were assessed for studying the utilization pattern of antihyperglycemic agents. Data was collected from a total of 207 patients through a predesigned Structured Case Record Form (CRF) and analysis of the prescriptions showed that T2DM was more prevalent in males (53.93%) than females (41.06%). Similar study was conducted by Chaudhary K. Pankaj et al.[8] Ravi Kumar P et al.[9], Mahamad Daud Ali et al. [10] Kayamkani Abdulla Khan [11] showed high prevalence of T2DM in males than females. Highest percentage of diabetic patients in the study were in the age group of 41 – 50 years (57.26%) showing highest prevalence of T2DM in middle age group which was also observed with the studies conducted by Mandal et al.[12], John et al.[13], Das et al.[14] Results also suggest that diabetes starts early in Indian population.

In the present study, Metformin (83.57%) was the most commonly utilized antihyperglycemic agent both as monotherapy and in combination with other AHA followed by Sulfonylurea drugs Gliclazide (32.85%) and Glimipiride (28.98%), which is in consistent to the recent treatment guidelines of T2DM from ADA/EASD (2022) and ICMR (2018). Sayed Aliul Hasan Abdi et al [15] revealed in their study that Metformin in combination with Sulfonylurea commonly Glimipiride was highly prescribed oral antidiabetic combination. Similar studies conducted by Soumya Mary Alex et al.[16], Vengulekar S et al.[17], Jambu Jain et al.[18], Khushali G et al.[19] revealed Metformin as the most frequently prescribed drug in a diabetic patient.

In our study, analysis was also done to show the utilization pattern of other drugs other than antihyperglycemic agents in T2DM and was observed that highest utilization was of antihypertensives (46.85 %) followed by cardiovascular drugs (41.54%) followed by gastrointestinal drugs (11.59%). The reason of prescribing other drugs in T2DM is the high incidence of long-term complication associated with diabetes. Similar studies conducted by Ravi Kumar P et al.[9] also similar pattern of use of antihypertensives and other cardiovascular and related drugs in T2DM.

In our present study, average number of drugs per prescription was 4.06, which is more compared to the studies done by Pankaj CK et al (1.94)[8], Ravi Kumar P et al (3.12)[9], whereas average number of antihyperglycemic agents per prescription was 1.92 which is comparable to the study conducted by Ravi P et al (1.81)[9]

Cost of drug therapy is a cause of non-adherence in chronic disease like diabetes. A huge variation in the cost of antidiabetic medications have been observed all over the world. So rational and cost-effective prescribing keeping in mind the quality of the drug is of utmost importance.

In our study, it was observed that 42.45 % of the drugs were prescribed by generic name and most of the patients who were prescribed antihyperglycemic drugs fell in the cost of less than Rs100 /month (55.5 %) which is more than that showed in the study by Kumar PR et al.[9]

Conclusion

Diabetes is a chronic disease with varied complication if left untreated or irrationally treated that may hamper the quality of life of the patient in the long run. In the present study, Metformin was the most commonly prescribed drug both as monotherapy and in combination therapy and Metformin + Gliclazide was the most common combination to be prescribed. There is still scope for improving adherence to antidiabetic drugs by prescribing more of the generic drugs which are cheaper than the brand drugs keeping in mind of not compromising the quality of the drug.

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