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Research Article

Drug utilization study on antidiabetic medications at SIMS-Shimoga a tertiary care hospital

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ABSTRACT

Background: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. DM is a leading cause of blindness, end stage renal disease, and nontraumatic lower extremity amputations. The objective of the study was to evaluate the drug utilization pattern of antidiabetic medications at a tertiary care hospital.
Methods: Demographic details of the patient were noted. Evaluation of the written prescription was carried out according to the requirements in case record form followed by computerization of data and analysis.
Results: DM was almost equal in male (51%) and females (49%), the risk of DM was high after 40 years of age. Out of all the case records and prescriptions reviewed it was found that 23% had Type 1 DM, and 77% had Type 2 DM. In 46.35% cases, there was a family history of DM while in 47.44% cases it was absent, 6% were unaware. The average number of drugs per prescription was 3.26±0.24 and antidiabetic drugs at 1.72±0.28. Insulin alone was prescribed in 25.54% cases. Single antidiabetic agents as lone drugs were seen in 39.05%; combined oral antidiabetic drugs accounted for 25.54% cases. The combination of insulin and oral antidiabetic agents were prescribed in 9.85% cases.
Conclusion: Metformin was the oral hypoglycemic agents, which was the most frequent prescribed as was insulin and its analogs. These drugs being essential in the treatment of diabetic patients should be made available to patients all the time.

Keywords: Diabetes mellitus, Drug utilization, Prescription, Analysis, Insulin, Antidiabetic

INTRODUCTION

Diabetes mellitus (DM) refers to the 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] DM is of two types Type 1 and Type 2, Type 1 diabetes is the result of complete or near total insulin deficiency other specific types of diabetes are also classified under Type 1 as per WHO guidelines:[1,2] (a) Maturity onset diabetes of young due to genetic defect of beta cell function, (b) genetic defects in insulin action, (c) diseases of exocrine pancreas, (d) endocrinopathies, (e) drug or chemical induced, (f) infections, and (g) immune mediated diabetes. Type 2 DM is characterized by a variable degree of insulin résistance, impaired insulin secretion, and increased glucose production. The third category f diabetes is gestational diabetes. The risk factors of Type 2 DM are family history of diabetes, habitual physical inactivity, race and ethnicity, history of gestational DM or delivery of baby >4 kg, hypertension (blood pressure [BP] >140/90 mm Hg), polycystic ovary syndrome, and history of vascular disease.[1,3]

The complications associated with DM are of two types acute and chronic. Acute complications of DM are diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS). Volume depletion and hyperglycemia are prominent features of both HHS and DKA.[3] The chronic complications of DM are microvascular which includes eye diseases such as retinopathy and macular edema; sensory and motor, i.e. mono and polyneuropathy, nephropathy. Macrovascular complications are coronary artery disease, peripheral arterial disease, and cerebrovascular disease. Other complications include gastrointestinal (gastroparesis, diahrea), genitourinary (uropathy or sexual dysfunction), dermatological infections, cataracts, glaucoma, and periodontal disease. The treatment goals for DM are;

control (hemoglobin A1c [HbA1c] <7), fasting blood sugar (FBS) (90-130 mg/dl), postprandial blood sugar (PPBS) (<180 mg/dl), BP<130/80 and lipids (low density lipoprotein <100 mg/dl, high density lipoprotein >40 mg/dl and triglycerides <150 mg/dl.[2,3] Diabetes is an iceberg disease, the number of estimated cases of diabetes worldwide is estimated to be around 347 million, of these more than 90% is Type 2 diabetes. In 2008, 1.2 million people died due to consequences of DM with more than 80% of deaths in low and middle income countries. There are estimated 37.7 million cases of drug in India 21.4 million in urban areas, and 16.3 million in rural areas.[4]

The different class of drugs used in treatment of DM is as follows (Table 1).[5,6]

Prescription by a clinician may be taken as a reflection of his attitude to disease and role of the drug in treatment. It also provides insight into the nature of healthcare delivery system. Drug utilization is defined as the marketing, distribution, prescription, and use of drugs in society, with emphasis on the resulting medical and social consequences.[7] Drug utilization studies create a sound socio-medical and health economic basis for health care decision-making. Drug utilization review (DUR) is the "evaluation of drug use in a given health care environment against predetermined criteria and standard to access the appropriateness of drug therapy."[7,8] Retrospective DUR involves evaluation of therapy and intervention when necessary while the patient is receiving treatment. A great extent of variability is seen in antidiabetic drug prescriptions; this is due to several factors which determine the choice of pharmacotherapy in the patient. These factors include target HbA1c levels to be achieved, presence of hypoglycemic episodes, weight of the patient, side effects due to existent antidiabetic drugs, cost of medications, presence of co-morbid conditions such as hypertension, hyperlipidemia, and adherence to polytherapy.[7]

Table 1: The various classes of drugs used in diabetes.

Enhance insulin secretion
Sulfonylurea's (tolbutamide, glibenclamide, glipizide, glimipride)
Meglitinide analogs (repaglinide, nateglinide)
Glucagon-like peptide receptor agonist (exenatide, liraglutide)
Dipeptidyl peptidase 4 inhibitors (sitagliptin, vildagliptine)
Overcome insulin resistance
Biaguanide (metformin)
Thiazolidinediones (pioglitazone)
Miscellaneous antidiabetic
Alpha-glucosidase inhibitors (acarbose, miglitol, voglibose)
Amylin analog (pramlinitide)
Dopamine D2 receptor agonist (bromocriptine)
SGLT-2 inhibitor (dapagliflozin)
Insulin preparations
Rapid acing (lispro, actrapid, glulisine)
Short acting/regular soluble insulin
Intermediate acting NPH, isophane
Long acting (glargine, detemir)

SGLT-2: Sodium-glucose cotransport-2, NPH: Neutral protamine hagedron

METHODS

The study was conducted in patients diagnosed with diabetes and attending the medicine Out-Patient Department of a tertiary care center.

Inclusion criteria

Diabetic patients of sex between 18 and 60 years of age. The patients with confirmed DM Type 1 or 2. (Based on random blood sugar >200 mg/DL and FBS 126 mg/dl PPBS 200 mg/dl).

Exclusion criteria: The patients with gestational DM

The case records of the patients were analyzed. Demographic details included age, sex, and family, from the patient's medical records, the prescription were analyzed in detail for the; generic or brand name of the drug, dose, dosage form, frequency, and duration of therapy was noted in the case record form. Data obtained from demographic profile and disease related history of each study participant was computerized and analyzed. In addition, data related to prescription patterns and prescribed daily dose/daily defined dose (PDD/DDD) ratios were also computed to study the utilization patterns amongst the study population. The following data variables were analyzed. Age: categorized into four age groups, those <30 years of age, between 31 and 40 years, between 41 and 50 years, and those between 51 and 60 years. Sex included males and females; marital status included married, unmarried, and widow. Socioeconomic status was based on modified Kuppuswamy score which divided the patients into five categories upper (26-29), upper middle (16-25), lower middle (11-15), upper lower (5-10), and lower (<5). Literacy was based on the education status as primary, secondary, and higher secondary graduation. Disease related data of the patient included the type of diabetes, duration of disease, history of hospitalization, family history, and associated illness.

Prescription pattern data of the study participants[8]

Average number of drugs per prescription, average number of diabetic drugs per prescription, percentage prescriptions with only insulin, percentage prescription with only oral

antidiabetic agents, and percentage prescriptions with both insulin and oral antidiabetic drugs. Percentage antidiabetic drugs from hospital schedule. Percentage drugs prescribed by generic name. Percentage of incomplete prescriptions: a prescription was considered incomplete if it lacked information with regard to any of the following criteria: name of the drug, dose of the drug, dosage form of the drug, frequency of medication, duration of treatment and instructions, or nondrug therapy. Percentage distribution of the nondiabetic drugs received by the study population. Percentage distribution of diabetic drug received by the study population. Percentage distribution of the adverse effects related to antidiabetic medications reported by the study population. Ratio of PDD and DDD among the study population to study trends of drug utilization.

RESULTS

DM was almost equal in male (51%) and females (49%), the risk of DM was high after 40 years of age, which composed 75% of cases. Out of 274 cases, 244 (89%) were married, and 30 (11%) were unmarried. The education status indicated high in illiterates else was uniformly distributed among other literates. 44.16% cases were in lower class, 26.27% in upper lower; this was 28% in the middle class. This variation was because upper-class people preferred treatment in the private hospital than coming to a government hospital (Table 2).

Out of all the case records and prescriptions reviewed it was found that 23% had Type 1 DM and 77% had Type 2 DM. Majority (51.82%) prescriptions indicated diabetes of <1 year duration. In 46.35% cases, there was the family history of DM while in 47.44% cases it was absent, 6% were unaware. The average number of drugs per prescription was 3.26±0.24 and antidiabetic drugs at 1.72±0.28. Insulin alone was prescribed in 25.54% cases. Single antidiabetic agents as lone drugs were seen in 39.05%; combined oral antidiabetic drugs accounted for 25.54% cases. The combination of insulin and oral antidiabetic agents were prescribed in 9.85% cases. Percentage of drugs from hospital schedule was 76.4% (Table 3).

Completeness of prescription was seen in 65.1% of cases. In 90% of cases dosage was mentioned, in only 35% cases the duration of treatment was written. 70% of prescriptions contained instructions or nondrug therapy (Table 4). Frequency, name of drug and dosage form of drug was mentioned in almost 100% of prescriptions.

Table 2: Demographic profile of DM patients.

Demographic profile	Result (%)
Gender	
Male	140 (51)
Female	134 (49)
Age (years)	
<30	14 (5.1)
31-40	56 (20.43)
41-50	86 (31.38)
51-60	118 (43.06)
Marital status	
Married	244 (89.05)
Unmarried	30 (10.95)
Literacy	
Illiterate	73 (26.64)
Primary education	44 (16.05)
Secondary education	47 (17.15)
Higher secondary	54 (19.70)
Graduates	56 (20.43)
Socioeconomic status	
Upper (26-29)	2 (0.72)
Upper middle (16-25)	15 (5.47)
Lower middle (11-15)	64 (23.35)
Upper lower (5-10)	72 (26.27)
Lower (<5)	121 (44.16)
DM	
Type 1	63 (23)
Type 2	121 (77)
Diabetes duration	
<1 year	142 (51.82)
Between 1-5 years	72 (26.27)
Between 5-10 years	25 (9.12)
More than 10 years	35 (12.77)
Family history of DM	
Present	127 (46.35)
Absent	130 (47.44)
Unaware	17 (6.2)

DM: Diabetes mellitus

DISCUSSION

In our study, the average number of drugs per prescription was found to be 3.26±0.24. In addition, the number of diabetic drugs per prescription was 1.72±0.28. This was more than the average number antidiabetic prescribed in Adbi et al.[9] where the average number of drugs was 0.94. It was, however, <2.27 recorded in a study conducted by Sultana et al.[10] 2010. The increase in the number of drugs may be due to increased number of co-morbidities in the patient population as well as the use of combination therapy even amongst antidiabetic agents. The number of participants prescribed insulin alone was 25.54%. In a study conducted by Upadhyaya et al.,[11] the insulin usage in patients was 7.96%. The main cause was oral hypoglycemic agents (OHA) cannot suffice the depleted insulin reserves in Type 2 diabetes. There were 107 patients (39.05%) who were prescribed only OHA, these included 107 (39.05%) patients with monotherapy and 70 (25.54%) with a combination of two or more agents. This was higher compared to mono

Table 3: Prescription pattern variables.

Drug use indicators	
Average number of drugs per prescription	**Results (%)**
Average number of diabetic drugs per prescription	3.26±0.24
Percentage prescriptions with insulin alone (n=70)	1.72±0.28
Short acting insulin	25/70 (35.71)
Intermediate acting insulin	20/70 (28.57)
Long acting insulin	23/70 (32.85)
Premixed insulin	02/70 (2.8)
Percentage prescription with only antidiabetic agents alone	
Single agent	n=107 (39.05)
Metformin	63/107 (58.87)
Glibenclamide	25/107 (23.36)
Glimipride	11/107 (10.28)
Glipizide	06/107 (5.6)
Glyburide	02/107 (1.8)
More than one agent	n=70 (25.54)
Metformin+glibenclamide	22/70 (31.42)
Metformin+glimipride	32 (32.85)
Metformin+glibenclamide+ pioglitazone	25 (35.71)
Percentage prescriptions with both insulin and oral antidiabetic drugs	n=27 (9.85)
Insulin and glibenclamide	12/27 (44.45)
Insulin and metformin	15/27 (55.55)
Percentage antidiabetic drugs from the hospital drug schedule	76.4

Table 4: Prescription content analysis.

Prescription content	Result (%)
Completeness of prescription contents	178 (65.1)
Dose of drug	247 (90)
Duration of treatment	96 (35)
Instructions or non-drug therapy	192 (70)
Frequency of drug intake	274 (100)
Name of the drug	274 (100)
Dosage form of the drug	274 (100)

(33%) and lower for combination (66%) therapy in a study conducted by Rajeshwari et al.[12] Metformin was the most common prescribed in monotherapy followed by glibenclamide.

In the earlier studies,[13,14] metformin followed by sulfonylurea were the most common used OHA as mono or combined therapy, in the present study also metformin 58.87% and sulfonylurea such as glibenclamide 23.36% and glimipride 10.28 were the most frequent used agents. When PPD/DDD ratios for metformin, glibenclamide, glimipride, and glipizide prescribed in monotherapy were further determined, optimal utilization of these drugs was seen for metformin glimipride and glibenclamide. Among the combination therapy metformin + glibenclamide was (32.42%), metformin + glimipride (32.85%) and last was metformin + glibenclamide + pioglitazone (35.71%). The rationale for the use of combination of biaguanide and sulfonylurea is the different site of action, additive and potentiating effects and reduced side effects.[13] The combination of metformin + glibenclamide + pioglitazone in earlier studies has shown to bring about improvement in HbA1c levels, FBS, and PPBS levels and also known to delay the requirement of insulin in Type 2 DM. During the study, it was found that out of drugs prescribed 76% were by generic name the practice of prescribing drugs by their generic name will help curtail expenditure and minimize the influences of medical practice. Prescriptions were also analyzed to the level of adherence to legal and procedural requirements of prescription writing.[7] Prescribing errors caused by poor handwriting, failure to communicate clearly and by the use of inappropriate abbreviations can lead to serious adverse effects particularly in conditions like diabetes. To overcome this problem relating to prescription incompleteness, it is essential to ensure education and training of physicians.

The number of drugs prescribed to patients for indications other than diabetes was noted and analyzed. It was seen that. 36.56% patients received statins, 32% received anti-hypertensive, 6% were prescribed calcium and vitamin supplements, aspirin was prescribed in 31.5%, folic acid in 5.6%, and hematinics in 5.6%. Hypertension is the common co-morbid condition in diabetes, substantially increasing the risk of both microvascular and macrovascular complications.[15] Calcium channel blockers were frequently prescribed followed by angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and finally beta blockers. Guidelines suggest that statin therapy be added to lifestyle therapy regardless of baseline lipid levels,[16] for diabetic patients. Substantial evidence states that low dose of aspirin therapy should be used as a primary prevention strategy in men and women with diabetes who are at risk for cardiovascular events.[17] Despite its proven efficacy aspirin is underutilized in patients with diabetes. A large number of study participants were dependable, and it is required that health policy makers see that essential drugs are available to patients either free of cost or at subsidized rates. It was also seen in the study that proportion of the drugs were not available in the hospital drug schedule and had to be purchased from the local pharmacies. Care should be taken to prescribe the drugs by their generic names.

Apart from the daily management nutritional recommendations are also very essential in DM. The caloric requirement should be derived from fat (20-35%),

Table 5: DDD/PDD calculation for antidiabetic agents.

Drug	DDD	PDD	DDD/PDD
Metformin	2000	2000	1
Glibenclamide	7	7	1
Glimipride	2	1	0.5
Glipizide	10	10	1
Pioglitazone	30	20	0.66
Repaglinide	4	3	0.75
Insulin lispro	40 U	30	1
Insulin detemir	40 U	30	0.75
Insulin glargine	40 U	18	0.45
Insulin aspart	40 U	40	1

PDD: Prescribed daily dose, DDD: Daily defined dose

carbohydrates (45-65%), and proteins (10-35%). Dietary cholesterol should be <200 mg/dl should contain fish or provide omega 3 polyunsaturated fatty acids. Low carbohydrate and high protein diets are not recommended, sucrose-containing foods may be taken by adjustment of insulin dosage. Fiber rich diet is essential to reduce PPBS3.[15] Type 1 DM be treated with insulin and Type 2 DM is a progressive disease and requires therapy intensification with time. The multiple daily dose of insulin providing basal, prandial, and supplemental insulin is a mainstay of insulin treatment. Early detection of microvascular and neuropathic complications and implementation of appropriate strategies, such as laser therapy (retinopathy), use of ARB (nephropathy), and proper foot care (neuropathy) will reduce the adverse outcomes. The rates of microvascular complications are similar in Type 1 and 2 DM. Once developed retinopathy; nephropathy and neuropathy are for the most part irreversible.[18]

CONCLUSION

DM is a leading cause of blindness, end stage renal disease, and nontraumatic lower extremity amputations. It increases the risk of coronary heart disease by two to five folds. Glycemic control is associated with reduced risk of microvascular and nephropathy complications of DM, insulin sensitizers and incretin-based drugs used early in the course of the disease. Lifestyle interventions for preventing Type 2 DM in high risk has reduced the incidence of DM by 35-58%, glycemic control in people with HbA1c >9 has reduced 30% incidence in macrovascular disease. Annual eye examination has reduced 60-70% serious vision loss. Use of metformin a biaguanide an OHA has reduced 25-31% incidence, while ACE inhibitors have a reduction of 42% in nephropathy and 22% drop in cardiovascular cases. Foot care in people with high risk of ulcers has reduced 50-60% of serious foot disease. Thus, we find that preventive measures have a more important role in reducing diabetic complications.

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