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Research Article

Drug Utilization Pattern of Anti-Diabetic Drugs Among Diabetic Outpatients in a Tertiary Care Teaching Hospital

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Abstract: *Introduction:* Drug utilization studies provide useful insights into the current prescribing practices and also identify irrational prescribing. Diabetes mellitus is a metabolic disorder characterized by resistance to the action of insulin, inadequate insulin secretion, or both. *Material and Methods:* This is a prospective and observational study was conducted over a period of 6 months in the outpatient Departments of General Medicine and Department of Pharmacology, a tertiary care teaching hospital. Adult diabetic patients (either newly diagnosed or known cases) of either sex, who were prescribed at least one anti-diabetic medication (OHA/Insulin), were included in the study. Details about demography, medical history, diagnosis data, and duration of diabetes, family history of diabetes, co-morbid conditions, laboratory investigations, and anti- diabetic drug utilization were collected. The adverse drug reactions (ADRs) related to antidiabetic drugs were monitored and documented in suitably designed ADR monitoring forms. *Results:* In our study shows that mono and combination therapies for the treatment of type II DM. The present study revealed that most of the physicians initially prescribed mono therapy (40%) includes Metformin/Glibenclamide/Glimepiride/Gliclazide to control hyperglycaemia followed by dual therapy (35%) FDC of Metformin + Pioglitazone/Metformin + Glipizide/Metformin + Glimepiride/ Metformin + Saxagliptin/ Metformin +Voglibose and triple therapy (25%) includes Metformin + Glimepiride + Pioglitazone. *Conclusion:* In our study, males were found to be more affected by type 2 diabetes mellitus than females. In the study, the prescribing trend was found to be monotherapy followed by dual agents because of presence of higher incidences of co-morbidities. Among oral antidiabetic agents, metformin along with glimepiride was most commonly used combination.

Keywords: Drug Utilization Pattern, Anti-Diabetic Drugs, Tertiary Care Teaching Hospital.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by resistance to the action of insulin, inadequate insulin secretion, or both. The clinical appearance of diabetes mellitus is hyperglycemia i.e., increase blood glucose. The new classification system identifies four types of diabetes mellitus i.e. Type I, Type II, Gestational Diabetes and other specific types of diabetes mellitus.

Type I Diabetes Mellitus- IDDM (Insulin Dependent Diabetes Mellitus) is characterized by destruction of beta cell triggered by an autoimmune process typically leading to absolute deficiency of insulin. The DM usually begins acute, and later on over a period of a few days to few weeks.

Type II Diabetes Mellitus- NIDDM (Non-Insulin Dependent Diabetes Mellitus) is a chronic, progressive disease characterized by hyperglycemia, which rises from the progress of resistance of insulin in peripheral tissues, a failure of the pancreatic β-cells to secrete adequate insulin in response to glucose loads, and an insufficient suppression of glucagon production. In this type of diabetes mellitus is connected with a family background of diabetes, corpulence, geriatric, and deficient of exercise.

Gestational Diabetes mellitus develops diabetes mellitus during gestational period in the women. Whereas, the majority of gestational diabetes mellitus women has normal blood glucose level at the 1st half of the gestation and later on develops a relative

insulin deficiency throughout the 2nd half of the gestation, leading to hyperglycemia.

Specific types of diabetes mellitus are numerous identified etiologies. This group includes persons with genetic defects of beta-cell function or with defects of insulin action, with diseases of the exocrine pancreas such as pancreatitis, dysfunction associated with other endocrinopathies (e.g., acromegaly) and pancreatic dysfunction caused by drugs, chemicals, or infections [3].

Diabetes mellitus is a main communal health problem in the developing as well as developed countries. All over the world, one in 20 deaths due to DM; 6 deaths every minute, 8700 deaths every day, 3.2 million deaths are due to diabetes every year. At least one death in ten adults from 35 to 64 years of age because of diabetes [5].

All over the world, the prevalence of DM was estimated to be 2.8% in 2000 and will reach 4.4% by 2030 in all age groups. The total number of persons all over the world with diabetes is expectable to ascend 366 million by 2030 from 171 million in 2000. In India, it is predictable that 79.4 million persons in the year 2030 cases of diabetes mellitus, while 42.3 million in the China and the United States (30.3 million) will also see significant increases of this metabolic disorder [6, 7]. As per the International Diabetes Federation (2013), roughly 50% of all people with diabetes exist in just 3 countries: India (65.1 million), the USA (24.4 million), and China (98.4 million) [9].

MATERIAL AND METHODS

This is a prospective and observational study was conducted over a period of 6 months in the outpatient Departments of General Medicine and Department of Pharmacology, a tertiary care teaching hospital. A total of 130 prescriptions of patients were screened, out of which 120 being a known case of DM under treatment of both genders and aged between 30 to 80 years were included in the study.

Adult diabetic patients (either newly diagnosed or known cases) of either sex, who were prescribed at least one anti-diabetic medication (OHA/Insulin) were included in the study. Patients with any malignancy; pregnant and lactating females were excluded. Patient data relevant to the study were obtained by patient's medical records, direct interview of the patient or his/her caregivers and the hospital information system. The data were recorded in a standard data collection form. Details about demography, medical history, diagnosis data, duration of diabetes, family history of diabetes, co-morbid conditions, laboratory investigations, and anti- diabetic drug utilization, were collected. Each prescription contained the drug, quantity, duration and date of dispensing. Each anti-diabetic medication was classified into one of the following classes: Metformin, Dipeptidyl peptidase-4 (DPP-4) Inhibitors, Glucagon-like peptide (GLP-1) receptor antagonists, Sodium-glucose co-transporter 2 (SGLT-2) inhibitors, Alpha-glucosidase inhibitors (AGIs), Thiazolidinedione (TZD), Sulfonylureas (SUs) and Insulin.

The adverse drug reactions (ADRs) related to antidiabetic drugs were monitored and documented in suitably designed ADR monitoring forms. The severity and causality of the ADR was also assessed. The severity of ADR was categorized as mild, moderate or severe as per standard definitions. The causality assessment of ADRs was done as per Naranjo scale.

STATISTICAL ANALYSIS

The data were analysed using graph SPSS version 25th. Level of significance (p value) was set at 0.05. Patient's demographic data were presented as mean± standard deviation (SD).

RESULT

Table-1: Distribution of age group.

Age Group	No. of patients	Percentage
31 - 40 years	11	9.16
41 - 50 years	19	15.8
51 - 60 years	20	16.6
61 – 70 years	33	27.5
71 – 80 years	37	30.8
Total	120	100

The table reflects that maximum number of patients belonged to age group of 71 - 80 years. The least patients were age group (31-40) years were 11 patients in table 1.

Table-2: Distribution of gender

Gender	No. of patients	Percentage
Male	71	59.1
Female	49	40.8
Total	120	100

Of the total 120 diabetic patients, distribution of Tertiary care hospital patients on the basis of gender revealed that 71 (59.1%) were male and 49 (40.8%) were female patients as shown in table 2.

Table-3: Distribution of area

Area of living	No. of patients	Percentage
Rural	51	42.5
Urban	69	57.5
Total	120	100

As shown in Table 3, study patients in health facilities were distributed on the basis of area of living into urban or rural. Of 120 subjects of Tertiary care teaching hospital, it was observed that maximum

percentage of study population was urban constituting 42.5% and 57.5% were urban.

Table-4: Comparing branded versus generic drugs

Parameters	Frequency
Total number of prescriptions	120
Total no. of drugs prescribed	386
Average drugs per prescriptions	2.41
Encounter with Branded	167
Encounter with Generic	219

In table 4 study results revealed that total 386 drugs were prescribed in 120 patients enrolled at Tertiary care teaching hospital. Average number of drugs per prescription was 2.41. The minimum and maximum number of drugs per prescription was 1 and 4 respectively used of branded and generic drugs in type II DM.

- i. Sulfonylureas: Tolbutamide, Glibenclamide, Glipizide, Gliclazide, Glimepiride etc.
- ii. Meglitinide analogues: Repaglinide, Nateglinide
- iii. Biguanides: Metformin
- iv. A Glucosidase inhibitors: Acarbose, Miglitol, Voglibose
- v. Thiazolidinediones: Pioglitazone

Table-5: Distribution of drug therapy

Therapy	Percentage
Monotherapy	40 %
Dual therapy	35 %
Triple therapy	25 %

In table 5, shows that mono and combination therapies for the treatment of type II DM. The present study revealed that most of the physician's initially prescribed mono therapy (40%) includes Metformin/Glibenclamide/Glimepiride/Gliclazide to control hyperglycaemia followed by dual therapy (35%) FDC of Metformin + Pioglitazone/Metformin + Glipizide/Metformin + Glimepiride/ Metformin + Saxagliptin/ Metformin +Voglibose and triple therapy (25%) includes Metformin + Glimepiride + Pioglitazone.

Table-6: Distribution of oral Antidiabetic drug therapy

Drugs	Percentage
Metformin, Glibenclamide, Glipizide, Gliclazide, Glimepiride	78%
Dapagliflozin and Tenegliptin	22%

In table 6, while at a tertiary care teaching hospital the Metformin (Biguanide) and Sulfonylureas: Glibenclamide, Glipizide, Gliclazide, Glimepiride was most commonly prescribed drug and Dapagliflozin (Sodium-glucose co-transport-2 (SGLT-2) inhibitors) and Tenegliptin (DPP-4) inhibitors was prescribed less.

Table-7: Distribution of concomitant drugs in Tertiary care teaching hospital patients

Concomitant drug	Frequency	Percentage
Ondansetron	5	4.1
Proton pump inhibitors	6	5
Pregabalin	10	8.3
Antihistamines	6	5
Antispasmodics	5	4.1
Antidiarrheal	5	4.1
Antibiotics	12	10
Calcium in combination with vitamin D3 and/or other drugs	8	6.6
Iron supplements	8	6.6
Multivitamin and Multimineral	12	10
NSAIDs	19	15.8
Vitamin D and analogues	10	8.3
Zinc supplements	8	6.6

In table 7, among the Diabetic patients enrolled at Tertiary care hospital, NSAIDs (15.8%) were the most commonly prescribed concomitant medication. Other frequently prescribed drugs were multivitamins and multimineral (10%), Pregabalin (8.3%), antihistamines (5%), antibiotics (10%).

Table-8: Descriptive statistics for price of drugs used

	Total number of drugs prescribed (N)	Minimum cost of drug	Maximum cost of drug	Mean	Std. Deviation (SD)
Tertiary care hospital	120	0.83	410	123.7	13.42

In table 8, for the management of diabetes in patients in tertiary care hospital, the minimum and maximum cost of drug was 0.83 and 410 respectively.

Table-9: Incidence of adverse drug reactions at Tertiary care teaching hospital

	Patients with ADR N (%)	Patients without ADR N (%)	Total N (%)
Tertiary care hospital	41 (34.1%)	79 (65.8%)	120 (100)

The incidence of adverse drug reaction was calculated by dividing the total number of patients who developed ADR by total number of patients recruited in the study, multiplied by 100. This gave an incidence rate of 34.1% enrolled patients at Tertiary care teaching hospital as shown in the Table 9.

Table-10: Percentage of different type of ADRs in the Health Facilities

Type of ADR	Frequency	Percentage
Type A	41	34.1%
Type B	0	0
Type C	0	0
Type D	0	0
Type E	0	0
Type F	0	0
Total	41	34.1%

The Diabetic patients that attended at hospital was observed for different types of adverse drug reactions that they suffered during the study period. In Tertiary care hospital, a total of 41 patients of various age groups, belonging to either gender suffered from the adverse drug reactions. All the reported ADRs i.e. 41 (34.1%) were of type A reactions which are predictable. None of the patients at both the health center reported to have the adverse drug reactions of type B, C, D, E and F, this is shown in Table 10.

Table-11: Number and types of adverse drug reactions at Tertiary care teaching hospital

ADR	Frequency	Percentage
Hypoglycemia	11	9.1
Diarrhea	2	1.6
Abdominal pain	3	2.5
Dizziness	3	2.5
Pedal edema	4	3.3
Nausea	8	6.6
Vomiting	8	6.6
Indigestion	2	1.6
Total	41	34.1

In table 11, during the study period, 41 cases of adverse drug reactions were reported in Tertiary care teaching hospital, out of which all (100 %) were of predictable type. Hence, percentage of various kinds of ADRs for suspected drugs were calculated individually. The most commonly occurring ADR were hypoglycaemia was the most common ADR observed accountable 11 (9.1%). The percentages of other adverse drug reactions were comparatively less followed by abdominal pain, Dizziness, Pedal edema.

DISCUSSION

Although the urban population in India had right to use dependable screening methods and anti-diabetic-medications, such health compensation is not available to the rural patients. There is an unequal distribution of health remunerations between rural and urban areas, and in addition lack of money in rural areas may be multi-faceted. Food uncertainty, poor sanitation, illiterateness, and domination of transfer of diseases may all contribute, which recommends that both local governments and policy makers may be undermining and under-prioritizing the looming threat of diabetes [13].

Such inadequacies contribute to an arrangement that may outcome in poor diabetes screening and unable to do services, unbelievable to diabetic management guidelines, lack of available consultation and long-distance travel to health services. While comparing between rural and urban areas there is poor geriatric services in rural areas for management of diabetes, with these populations more likely to suffer from diabetic problems compared to their urban counterparts. More requirements to be done to report the urban-rural inequality in diabetes management [14].

Moreover, figure of Early-onset of diabetes increases accountable for longer duration of diabetic problems, whereas statistics on the incidence of diabetic problems across the whole of India is scarce.[19] A new international study stated that diabetes governor in persons seriousness with extensive period of the illness (9.9±5.5 years), by neuropathy the greatest problem (24.6 percent) followed by cardiovascular disease (23.6 percent), a nephropathy (21.1 percent), retinopathy (16.6 percent) and foot ulcers (5.5 percent) [20]. Indian diabetic population there is poor glycemic control influence are observed, which is accountable for macro- and microvascular variations existing with diabetes, and influence diabetic patients to other problems such as diabetic muscle infarction and myonecrosis [21].

The chief controlling goals in Type 2 DM are the respite of severe signs and stoppage of long lasting problems, whereas evading hypoglycemia, glycemic controls and inhibit the progress of atherosclerosis and additional complications of diabetes. The association among the degrees of glycemic control and microvascular problems in Type 2 DM is well

recognized. In addition, well control of blood glucose decreases the jeopardy of microvascular disease. Whereas, for stoppage of macrovascular disease refining glycemic control is essential but inadequate [22].

Dietetic and way of life alterations form are backbone of treatment for Type 2 DM [23]. Drug therapy is supported when target goals are not attained with way of life alterations [24]. Numerous oral anti-hyperglycemic drugs remain obtainable towards progress controlling of Type 2 DM. Established on their mechanism of action, they are split into drugs that increase insulin secretion like Meglitinides, Sulfonylureas, Glucagon-like peptide-1 (GLP-1) agonists, Dipeptidyl Peptidase-4 (DPP-4) inhibitors, decrease glucose production like Biguanides, increase insulin sensitivity like Thiazolidinediones (TZDs) and decrease carbohydrate absorption like α-Glucosidase inhibitors [25].

CONCLUSION

In our study, males were found to be more affected by type 2 diabetes mellitus than females. In the study, the prescribing trend was found to be monotherapy followed by dual agents because of presence of higher incidences of co-morbidities. Among oral antidiabetic agents, metformin along with glimepiride was most commonly used combination. Our study showed, low cost of drugs per prescription as brands with low cost has been prescribed to the patients. So, it is necessary to taken care of quality of drugs.

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