Review Article

A Review on Adverse Drug Reaction and Prescribing Pattern of Antidiabetic Medications in Type 2 Diabetes Patients

Sneha. P. S.*, Renisha. R. S., Soumya. R. V., Prasobh. G. R., Pavithra J., Nithin Manohar R.

Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

ABSTRACT

A number of drugs are used to treat type 2 diabetes (T2D), a global health concern. The health of patients and adherence to therapy are at risk due to adverse drug reactions (ADR). The purpose of this study was to assess ADRs in T2D patients taking anti-diabetic drugs and to examine prescribing trends. 615 T2D individuals were included in an observational ambispective study that lasted six months. Patient demographics, comorbidities, length of illness, body mass index, prescribed drugs, and ADRs were among the information gathered. The WHO-Uppsala Monitoring Centre (WHO-UMC) criteria were used to evaluate the causal link between the drug and ADR. Microsoft Excel 365 program was used to create a descriptive summary of the data. 220 out of 615 individuals had at least one ADR. Out of 220, female patients experienced a higher percentage of ADR occurrences (37.6%) than male patients (34.4%). Biguanides were the most often given medications, followed by thiazolidinediones and dipeptidyl peptidase-4 inhibitors. Patients on metformin experienced more adverse drug reactions (ADRs), followed by those on pioglitazone, glimepiride, sitagliptin, and dapagliflozin. Based on WHO UMC causation classifications, all reported ADRs were classified as "Possible". The study underlines the importance of careful monitoring and the noteworthy incidence of ADRs in T2D patients.

INTRODUCTION

Diabetes is a long-term metabolic condition marked by high blood glucose levels that gradually causes major harm to the heart, blood vessels, kidneys, nerves, and eyes. The most prevalent is type 2 diabetes (T2D), which often affects adults and is brought on by a decrease in the pancreatic synthesis of insulin and/or a decrease in tissue sensitivity to insulin (insulin resistance), which results in persistently high blood glucose levels [1]. Biguanides, sulfonylureas (SU), dipeptidyl peptidase-4 inhibitors (DPP4i), thiazolidinedione

*Corresponding Author: Sneha. P. S.

Address: Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

Email ✉: snehaps765@gmail.com

(TZD), sodium glucose co-transport 2 inhibitors (SGLT2i), alpha-glucosidase inhibitors (αGI), non-sulphonyl urea secretagogues, insulin, and glucagon-like peptide-1 receptor agonists (GLP1RA) are among the class of drugs available in India for the treatment of type 2 diabetes. Despite their adverse effects and potential to adversely affect mental and social health, medications remain the most widely used therapy for glycaemic management[2]. According to the World Health Organisation (WHO) "An adverse drug reaction (ADR) is a noxious and unintended reaction to a drug that occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function"[3].

MATERIALS AND METHODS

Study design

615 T2D patients participated in an observational ambispective study to evaluate the prescribing patterns of antidiabetic medications and ADRs.

Study population

For six months (March 2022 to May 2022 and March 2023 to May 2023), the study was carried out on outpatients at Rudraksha Hospital, Bareja and Rudraksha Institute of Medical Sciences (RIMS Healthcare), Ghodasar in Ahmedabad, Gujarat, India. With the exception of pregnant women, patients with associated malignant disorders, and patients with acute communicable diseases, the study included T2D patients of both sexes, aged 18 years or older, with or without associated conditions, and taking antidiabetic drugs.

Data collection/variables

All relevant details such as age, sex, duration of disease, and prescribed medicines were recorded. Patients were followed up and ADRs were recorded. The causal relationship between ADR and drug was assessed by the investigators as per WHO-UMC criteria.

Statistical analysis

Collected data were descriptively summarized using Microsoft Excel 365 software.

RESULTS

Demographic Distribution of Patients with T2D and ADR

Table 1: Demographic Distribution of Patients with T2D and ADR

Groups	No of patients	No of patients with ADRs	Percentage of ADRs(n=220)	Percentage of ADR occurrence
Sex distribution	266	100	45.5%	37.6%
Female	349	120	54.6%	34.4%
Male				
Age distribution(years)	9	8	3.7%	88.9%
21-30	81	28	12.7%	34.6%
31-40	163	62	28.2%	38%
41-50	235	87	39.6%	37%
51-60	116	32	14.6%	27.6%
61-70	11	3	1.4%	27.3%
Above 70				
Duration of disease distribution(years)	304	108	49.1%	35.5%
0-5	193	66	30%	34.2%
6-10	65	32	14.6%	49.2%
11-15	37	9	4.1%	24.3%
16-20	16	5	2.3%	31.3%
Above 20				

The study included 615 T2D patients on antidiabetic drugs, 266 (43.3%) of whom were female and 349 (56.8%) of whom were male. Out of the 220 patients with ADR, 120 (54.6%) were men and 100 (45.5%) were women. ADR incidence rates were 34.4% for male patients and 37.6% for female patients. The average age of the patients enrolled in the study was 52.14 years, ranging from 23 to 78 years. Out of 615 patients, 81 (13.2%) were 21–30, 81 (13.2%) were 31–40, 163 (26.5%) were 41–50, 235 (38.2%) were 51–60 years old, 116 (18.9%) were 61–70, 81and 11 (1.8%) were over 70 years old. In 220 patients with ADR, 8 (3.6%) were 21–30, 28 (12.7%) were 31–40, 62 (28.2%) were 41–50, ,87 (39.6%) were 51–60 years old, 32 (14.6%) were 61–70, and 3 (1.4%) were over 70 years. ADR occurrence was observed as 88.9% (21–30), 34.6% (31–40), 38.0% (41–50), 37.0% (51–60), 27.6% (61–70) and 27.3% (above 70 years) in patients of various age groups. From the time of initial diagnosis until age 33, the average duration of T2D was 7.31 years. Of the 615 patients, 304 (49.4%) had an illness duration of 0–5 years, 193 (31.4%) had a disease duration of 6–10 years, 65 (10.6%) had a disease duration of 11–15 years, 37 (6.0%) had a disease duration of 16–20 years, and 16 (2.6%) had a disease duration of more than 20 years. Of 220 patients with ADR, 108 (49.1%) had an illness duration of 0–5 years, 66 (30.0%) had a disease duration of 6–10 years, 32 (14.6%) had a disease duration of 11–15 years, 9 (4.1%) had a disease duration of 16–20 years, and 5 (2.3%) had a disease duration of more than 20 years. In patients with varying duration of disease for T2D, the incidence of ADR was found to be 35.5% (0–5 years), 34.2% (6–10 years), 49.2% (11–15 years), 24.3% (16–20 years), and 31.25% (over 20 years).

Prescribing Pattern of Antidiabetic Medications Including FDCs Formulations and Number of Patients with ADR

Table 2: Prescribing Pattern of Antidiabetic Medications Including FDCs Formulations and Number of Patients with ADR

Prescribed formulations	No of patients	No of patients with ADRs	Percentage of ADR(n=615)	Percentage of ADR(n=220)
Biguanide +SU+TZD	**336**	**118**	**19.2%**	**53.7%**
Metformin+Glimiperide+Pioglitazone	318	112	18.2%	50.9%
Metformin+Gliclazide+Pioglitazone	18	6	1.1%	2.7%
Biguanide+DPP4i	**208**	**80**	**13%**	**36.4%**
Metformin+ Sitagliptin	93	35	5.7%	15.9%
Metformin+ Vildagliptin	76	29	4.7%	13.9%
Metformin+ Teneligliptin	38	15	2.4%	6.8%
Metformin+ Linagliptin	1	1	0.2%	0.5%
Biguanide + SU	**51**	**14**	**2.3%**	**6.4%**
Metformin+ Glimepiride	35	8	1.3%	3.4%
Metformin+ Gliclazide	9	4	0.7%	1.8%
Metformin+ Glipizide	7	2	0.3%	0.9%
Biguanide + αGI	**37**	**16**	**2.6%**	**7.3%**
Metformin+ Acarbose	33	14	2.3%	6.4%
Metformin+ Voglibose	4	2	0.3%	0.9%
Biguanide	**35**	**17**	**2.8%**	**7.7%**
Metformin	35	17	2.8%	7.7%

Commonly prescribed fixed-dose combinations (FDCs) contain biguanide, SU and TZD in 336 (54.6%) patients followed by biguanide and DPP4i in 208 (33.8%), biguanide and SU in 51 (8.3%), biguanide and αGI in 37 and only biguanide in 35.

Study Limitations

The study was conducted at two hospitals which may limit the generalizability of the findings to a broader population. The study had a relatively short duration of 6 months for data collection, which might not capture long-term trends or variations in antidiabetic drug prescribing patterns and ADRs. Multicentric trials and larger sample size could provide more robust insights into the prevalence and patterns of ADRs in T2D patients. Addressing these limitations in future research can enhance the robustness and applicability of findings in similar studies.

CONCLUSIONS

The present study provided data on prescription pattern, the prevalence (35.8%) of ADRs and their distribution among different groups with respect to genders, age, duration of disease. The study indicated that percentage of ADR occurrence among female (37.6%) was higher than male patients (34.4%). Metformin (215, 35.0%) exhibited the highest ADRs, followed by pioglitazone (160, 26.0%), glimepiride (142, 23.0%), sitagliptin (108,17.6%), and dapagliflozin (107,17.4%), Voglibose (106,17.2%) and vildagliptin (46, 7.5%). FDC of biguanide, SU, and TZD (336, 54.6%) was prescribed most frequently followed by biguanide, SU and αGI (261, 42.4%). Although ADRs are not life-threatening, they can cause discomforts in many patients. Hence, healthcare providers should remain vigilant in observing and attending ADRs.

REFERENCES

1. Shi GJ, Shi GR, Zhou JY, et al. Involvement of growth factors in diabetes mellitus and its complications: A general review. Biomed Pharmacother. 2018; 101: 510–527, doi: 10.1016/j. biopha.2018.02.105, indexed in Pubmed: 29505922.

2. Hameed S, Kumar P, Kumar M, et al. Evaluation of suspected adverse drug reactions of oral anti-diabetic drugs in a tertiary care hospital of Bihar, India: An observational study. Panacea J Med Sci. 2022; 12(1): 172–176, doi: 10.18231/j.pjms.2022.032.

3. WHO. International Drug Monitoring: The Role of Hospital. Technical Report Series No. 425). Geneva, Switzerland: World Health Organization, 1969.