VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
e-ISSN 2450–8187

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Adverse Drugs Reaction and Prescribing Pattern of Antidiabetic Medications in Type 2 Diabetes Patients: An Observational Ambispective Study

ABSTRACT

Objective: Type 2 diabetes (T2D) is a global health concern and multiple medications are used for its treatment. Adverse drug reactions (ADR) pose a concern for patient health and treatment compliance. This study aimed to evaluate ADR in T2D patients receiving antidiabetic medications and to analyze the prescribing patterns.

Materials and methods: An observational ambispective study was conducted in a six-month period, enrolling 615 T2D patients. Collected data included patient demographics, comorbidities, disease duration, body mass index, prescribed medications, and ADRs. The causal relationship between ADR and drug was assessed as per WHO-Uppsala Monitoring Centre (WHO--UMC) criteria. Data was descriptively summarized using Microsoft Excel 365 software.

Results: In 615 patients, 220 experienced at least one ADR. Out of 220, percentage of ADR occurrence among female (37.6%) was higher than male (34.4%) patients. The most commonly prescribed drugs were biguanides, followed by dipeptidyl peptidase-4 inhibitors and thiazolidinediones. ADRs were higher in patients prescribed metformin followed by pioglitazone, glimepiride, sitagliptin and dapagliflozin. Thirty-two types of ADRs (424 incidents) were recorded, with gastrointestinal disturbances as most prevalent followed by weakness and tiredness. All reported ADRs were categorized as "Possible" according to WHO UMC causality categories.

Conclusions: The study emphasizes the notable occurrence of ADRs in T2D patients and highlights the need for vigilant monitoring. Although ADRs were mild to moderate in nature, optimal treatment strategies for T2D management will benefit from multicenter studies establishing a comprehensive ADR database. (Clin Diabetol 2024; 13, 3: 170–179)

Keywords: type 2 diabetes (T2D), antidiabetic medications, adverse drugs reaction, prescribing pattern

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Clinical Diabetology 2024, 13; 3: 170–179
DOI: 10.5603/cd.100105
Received: 3.04.2024 Accepted: 29.04.2024
Early publication date: 20.06.2024

Introduction

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose, progressively leading to serious damage to the heart, blood vessels, eyes, kidneys, and nerves. The most common is type 2 diabetes (T2D), usually in adults, which occurs when the production of insulin by the pancreas and/or the sensitivity of tissues to insulin is reduced (insulin resistance), leading to chronically elevated blood glucose levels [1, 2]. The countries with the largest numbers of adults with diabetes aged 20–79 years in 2021 were China, India and Pakistan. They are anticipated to remain so in 2045. India is one of the top 5 countries in the South East Asian (SEA) region with an age-standardized diabetes prevalence of 9.6% in 2021 whereas Mauritius in the SEA region had the highest prevalence rate (22.6%), followed by Bangladesh (14.2%), Sri Lanka (11.3%), and Bhutan (10.4%) [3].

The class of medications for treatment of T2D available in India are biguanides, sulfonylureas (SU), dipeptidyl peptidase-4 inhibitors (DPP4i), thiazolidinedione (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) [4]. Drugs continue to be the most common interventions used to achieve glycemic control, but drugs themselves have their adverse effect and can adversely impact mental and social health [5]. According to World Health Organization (WHO), an adverse drug reaction (ADR) is defined as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function" [6]. ADR is one of the leading causes of morbidity and mortality worldwide [7]. The consequences of ADRs burden the healthcare system with increased cost of therapy and prolongation of hospitalization. In developing countries, the cost of adverse reactions in the general population is very high and under-recognized. It is, therefore, imperative to evaluate the safety of medicines by specialized methods like Pharmacovigilance [8–11].

The detection of ADRs has become significant because of introduction of large number of drugs in the last two decades [12]. ADR may occur daily in hospitals and adversely affect patients' life, often causing considerable morbidity and mortality [13, 14]. Attention should be given to identifying the patient populations at risk, the drugs most commonly responsible and the causes of ADRs. Increased supply of drugs in the market and an upward trend in polypharmacy are contributing factors to the prevalence of ADRs worldwide [15]. ADRs may result in a loss of patient confidence, leading to negative emotions toward the treatment recommended by their physician and may result in the patient choosing self-treatment options, which may consequently precipitate additional ADRs [16, 17].

Getting more information on prescribed drugs and their side effects will be beneficial to the healthcare professional as well as to the patients [18]. Hence the present study was planned to evaluate the ADRs and prescribing patterns of the drugs.

Materials and methods

Study design

An observational ambispective study was conducted on 615 patients with T2D to assess ADR and prescribing pattern of antidiabetic drugs.

Study population/study participants

The study was conducted on out-patients of Rudraksha Institute of Medical Sciences (RIMS Healthcare), Ghodasar and Rudraksha Hospital, Bareja in Ahmedabad, Gujarat, India for a period of 6 months (March 2022 to May 2022 and March 2023 to May 2023). T2D patients with or without associated conditions, aged 18 years or above, of both sexes, taking antidiabetic medications were included in the study, except for pregnant women, patients with associated malignant condition and acute communicable diseases.

Ethical approval

Approval of Institutional Ethics Committee (IEC) "Rudraksha Hospital Ethics Committee" was obtained before initiation of the study. Patients were explained the procedure of the study and requested to provide signed Informed Consent Forms (ICFs) to Investigators before enrolment for the study.

Data collection/variables

All relevant details such as age, sex, height, weight, body mass index (BMI), duration of disease, diagnosis, comorbidities, 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. As the experiment was exploratory in nature, there were no specific hypotheses planned to be tested and no claims were made regarding treatment usage.

Results

A total of 615 T2D patients on antidiabetic medications were enrolled in the study, of which 266 (43.3%) were female, and 349 (56.8%) were male. Among 220 patients, who had ADR, 100 (45.5%) were female, and 120 (54.6%) were male. Percentage of ADR occurrence among female patients was 37.6%, and among male, it was 34.4% (Tab. 1).

The average age of the patients enrolled in the study was 52.14 years, ranging from 23 to 78 years. Out of 615 patients, 235 (38.2%) were 51–60 years old, 163 (26.5%) were 41–50, 116 (18.9%) were 61–70, 81 (13.2%) were 31–40, 9 (1.5%) were 21–30, and 11 (1.8%) were over 70 years old. In 220 patients with ADR, 87 (39.6%) were 51–60 years old, 62 (28.2%) were 41–50, 32 (14.6%) were 61–70, 28 (12.7%) were 31–40, 8 (3.6%) were 21–30 and 3 (1.4%) were over 70 years. ADR occurrence was observed as 37.0% (51–60), 38.0% (41–50), 27.6% (61–70), 34.6% (31–40), 88.9% (21–30), 27.3% (above 70 years) in patients of various age groups (Tab. 1).

The average duration of T2D was 7.31 years ranging from newly diagnosed to 33 years. Out of 615 patients, in 304 (49.4%) patients the disease duration was 0–5 years, in 193 (31.4%) patients 6–10 years, in 65 (10.6%) patients 11–15 years, in 37 (6.0%) patients 16–20 years and in 16 (2.6%) patients more than 20 years. In 220 patients with ADR, in 108 (49.1%) patients the disease duration was 0–5 years, in 66 (30.0%) patients 6–10 years, in 32 (14.6%) patients 11–15 years, in 9 (4.1%) patients 16–20 years and in 5 (2.3%) patients more than 20 years. ADR occurrence was observed as 35.5% (0–5 years), 34.2% (6–10 years), 49.2% (11–15 years), 24.3% (16–20 years) and 31.25% (above 20 years) in patients with various duration of disease for T2D (Tab. 1).

The average BMI of the patients was 28.1 kg/m^2 enrolled in the study ranging from 16.6 to 54.5 kg/m^2. As per obesity classification according to WHO, out of 615

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 ADRs occurrence
Sex distribution				
Female	266	100	45.5%	37.6%
Male	349	120	54.6%	34.4%
Age distribution [years]				
51–60	235	87	39.6%	37.0%
41–50	163	62	28.2%	38.0%
61–70	116	32	14.6%	27.6%
31–40	81	28	12.7%	34.6%
21–30	9	8	3.7%	88.9%
Above 70	11	3	1.4%	27.3%
Duration of disease distribution [years]				
0–5	304	108	49.1%	35.5%
6–10	193	66	30.0%	34.2%
11–15	65	32	14.6%	49.2%
16–20	37	9	4.1%	24.3%
Above 20	16	5	2.3%	31.3%
BMI distribution (kg/m^2)				
Overweight: 25–29.9	264	99	45.0%	37.5%
Obese: > 30	181	68	30.9%	37.6%
Normal: 18.5–24.9	162	48	21.8%	29.7%
Underweight: < 18.5	8	5	2.2%	62.5%
Comorbidities distribution				
Only T2D	210	68	30.9%	32.4%
T2D + 1	214	87	39.6%	40.7%
T2D + 2	135	43	19.6%	31.9%
T2D + 3 and more	56	22	10.0%	39.3%

ADR — adverse drug reaction; BMI — body mass index; T2D — type 2 diabetes

patients, 264 (42.9%) were overweight — 25 kg/m^2 to 29.9 kg/m^2, 181 (29.4%) were obese — more than 30 kg/m^2, 162 (26.3%) had a normal body weight — 18.5 kg/m^2 to 24.9 kg/m^2 and 8 (1.3%) were underweight — less than 18.5 kg/m^2. In 220 patients with ADR, 99 (45.0%) were overweight, 68 (30.9%) were obese, 48 (21.8%) had a normal body weight and 5 (2.3%) were underweight, based on BMI categories. ADR occurrence was observed as 37.5% (overweight), 37.6% (obese), 29.6% (normal), 62.5% (underweight) in patients of various BMI range.

Out of 615 patients, no comorbidity was reported in 210 (34.2%), at least one comorbidity in 214 (34.8%), two comorbidities were reported in 135 (22.0%) and three or more comorbidities in 56 (9.1%) patients. Among 220 patients who had ADR, 68 (30.9%) patients did not have any comorbidity, 87 (39.6%) had at least one, 43 (19.6%) had two and 22 (10.0%) had three or more comorbidities. ADR occurrence was observed as 32.4% (no comorbidity), 40.7% (1 comorbidity), 31.9% (2 comorbidities) and 39.3% (3 or more comorbidities) (Tab. 1).

In 615 patients, oral antidiabetic drugs were prescribed to 527 (85.7%), oral and injectables to 86 (14.0%) and only injectables to 2 (0.3%) patients. Out of 527 patients who were on oral antidiabetic drugs, 186 (35.3%) reported ADR and out of 86 who were on oral and injectable drugs, 32 (37.2%) reported ADR. Two patients who were on only injectable drugs, both reported ADR.

Commonly prescribed fixed-dose combinations (FDCs) contain biguanide, SU and TZD in 336 (54.6%) patients followed by biguanide, αGI and SU in 261 (42.4%), biguanide and DPP4i in 208 (33.8%), biguanide, DPP4i and SGLT2i in 171 (27.8%), biguanide and SGLT2i in 95 (15.5%), biguanide and TZD in 93 (15.1%), DPP4i and SGLT2i in 75 (12.2%) and biguanide and SU in 51 (8.3%). In 220 patients, who had ADR, biguanide, SU and TZD was given to 118 (19.2%) patients followed by biguanide, αGI and SU in 100 (16.3%), biguanide and DPP4i in 80 (13.0%), biguanide, DPP4i and SGLT2i in 69 (11.2%), biguanide and SGLT2i in 28 (4.6%), biguanide and TZD in 38 (6.2%), DPP4i and SGLT2i in 22 (3.6%) and biguanide and SU in 14 (2.3%) (Tab. 2).

A total of 9 classes of drugs were prescribed to 615 patients, as biguanide in 607 (98.7%), DPP4i in 494 (80.3%), TZD in 448 (72.9%), SU in 437 (71.1%),

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 + Glimepiride + Pioglitazone	318	112	18.2%	50.9%
Metformin + Gliclazide + Pioglitazone	18	6	1.0%	2.7%
Biguanide + αGI + SU	**261**	**100**	**16.3%**	**45.5%**
Metformin + Voglibose + Glimepiride	249	96	15.6%	43.6%
Metformin + Voglibose + Gliclazide	12	4	0.7%	1.8%
Biguanide + DPP4i	**208**	**80**	**13.0%**	**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 + DPP4i + SGLT2i	**171**	**69**	**11.2%**	**31.4%**
Metformin + Sitagliptin + Dapagliflozin	147	61	9.9%	27.7%
Metformin + Vildagliptin + Dapagliflozin	22	7	1.1%	3.1%
Metformin + Vildagliptin + Remogliflozin etabonate	2	1	0.2%	0.5%
Insulin	**96**	**38**	**6.2%**	**17.3%**
Insulin Glargine	54	24	3.9%	10.9%
Insulin degludec + Insulin aspart	19	5	0.8%	2.3%
Insulin degludec	8	3	0.5%	1.4%
Insulin aspart	7	3	0.5%	1.4%

Human insulin	3	1	0.2%	0.5%
Insulin isophane + Human insulin	2	1	0.2%	0.5%
Insulin glulisine	1	1	0.2%	0.5%
Insulin aspart + Insulin aspart protamine	1	0	0	0
Insulin detemir	1	0	0	0
Biguanide + SGLT2i	**95**	**28**	**4.6%**	**12.7%**
Metformin + Dapagliflozin	72	20	3.3%	9.1%
Metformin + Empagliflozin	23	8	1.3%	3.6%
Biguanide + TZD	**93**	**38**	**6.2%**	**17.3%**
Metformin + Pioglitazone	93	38	6.2%	17.3%
DPP4i + SGLT2i	**75**	**22**	**3.6%**	**10.0%**
Sitagliptin + Dapagliflozin	31	9	1.5%	4.1%
Linagliptin + Empagliflozin	19	8	1.3%	3.6%
Vildagliptin + Dapagliflozin	17	5	0.8%	2.3%
Vildagliptin + Remogliflozin Etabonate	8	0	0	0
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%
DPP4i	**21**	**7**	**1.1%**	**3.2%**
Vildagliptin	14	4	0.7%	1.8%
Teneligliptin	6	2	0.3%	0.9%
Linagliptin	1	1	0.2%	0.5%
GLP1RA	**20**	**6**	**1.0%**	**2.7%**
Semaglutide	18	6	1.0%	2.7%
Liraglutide	2	0	0	0
Biguanide + DPP4i + TZD	**19**	**3**	**0.5%**	**1.4%**
Metformin + Sitagliptin + Pioglitazone	19	3	0.5%	1.4%
SGLT2i	**16**	**11**	**1.8%**	**5.0%**
Dapagliflozin	8	5	0.8%	2.3%
Empagliflozin	7	5	0.8%	2.3%
Canagliflozin	1	1	0.2%	0.5%
Meglitinides + αGI	**6**	**5**	**0.8%**	**2.3%**
Repaglinide + Voglibose	6	5	0.8%	2.3%
αGI	**6**	**0**	**0**	**0**
Acarbose	5	0	0	0
Voglibose	1	0	0	0
SU	**3**	**3**	**0.5%**	**1.4%**
Glimepiride	3	3	0.5%	1.4%
TZD	**1**	**1**	**0.2%**	**0.5%**
Pioglitazone	1	1	0.2%	0.5%

αGI — alpha-glucosidase inhibitors; ADR — adverse drug reaction; DPP4i — dipeptidyl peptidase-4 inhibitors; FDC — fixed-dose combination; GLP1RA — glucagon-like peptide-1 receptor agonists; SGLT2i — sodium glucose co-transport 2 inhibitors; SU — sulfonylureas; TZD — thiazolidinedione

SGLT2i in 357 (58.1%), αGI in 309 (50.2%), insulin in 110 (17.9%), GLP1RA in 20 (3.3%) and meglitinides in 6 (1.0%). In 220 patients with ADR, biguanide was prescribed to 215 (35.0%), DPP4i to 181(29.5%), TZD to 160 (26.0%), SU to 155 (25.2%), SGLT2i to 130 (21.1%), αGI to 121 (19.7%), insulin to 42 (6.8%), GLP1RA to 6 (1.0%) and meglitinides to 5 (0.8%). ADR occurrence was observed as 35.4% (biguanide), 36.6% (DPP4i), 35.7% (TZD), 35.5% (SU), 36.4% (SGLT2i), 39.2% (αGI), 38.2% (insulin), 30.0% (GLP1RA) and 83.3% (meglitinides).

A total of 32 types of ADRs (424 incidents) were reported in 220 out of total 615 enrolled patients. Most commonly ADR reported were GI disturbances (80), followed by weakness (66), tiredness (38), hypoglycemic events (29), headache (28), sleep disturbance (24), burning and painful urination (20), restlessness and uneasiness (16), decreased appetite (15), body ache (14), pedal edema (9), etc. A total 23 antidiabetic medications from 9 classes of drugs were given to patients. Biguanide had the highest number of ADR events (414) followed by DPP4i (351), SU (306), TZD (299), αGI (244), SGLT2i (235), insulin (88), GLP1RA (12) and meglitinides (6) (Tab. 3).

None of the ADR was fatal or required hospitalization. No ADR was categorized as "Certain" or "Probable" as all the patients were on more than one drugs. Hence, all the reported ADRs were categorized as "Possible" as per WHO UMC causality categories. Reported ADRs were mild (78.77%) to moderate (21.23%) in nature. No severe ADR was reported in the study.

Discussion

The study indicates that the percentage (35.8%) of ADRs is substantial and emphasizes the importance of monitoring ADRs in T2D patients. It also highlights the need for healthcare providers to be cautious about potential adverse effects.

Although ADRs were reported in both male and female patients, it has been observed that ADR occurrence was slightly higher in female patients (37.6%) compared to male patients (34.4%). In a study conducted in Korea, antidiabetic agent-associated AEs were more frequently reported by women than men [19]. In studies conducted in Bhopal, Kerala and Odisha in India, predominance of adverse effects in female patients with diabetes was reported [20–22]. Further studies and research may be required to examine the causes behind these gender differences.

The majority of T2D patients were from age group 51–60 years, followed by 41–50. Most ADRs occurred among patients 51–60 years (39.6%), 41–50 years (28.2%), and 61–70 years old (14.6%). In a study conducted in Karnataka (India), it was found that the majority of the ADRs occurred in the age group of 40–80 years of patients on antidiabetic medications [23]. The limited number of patients (1.5%) in the 21–30 age group highlights the need for further studies focusing on this demographic.

Most patients (49.4%) have been diagnosed with T2D within the past 5 years. This group has the highest number of patients with ADRs. Percentage of ADR occurrence for disease duration group of 11–15 years is the highest (49.2%). Further research and a more comprehensive study may be required to identify specific factors contributing to ADRs in different disease duration groups.

The majority of patients fall into the overweight category followed by obese. Patients classified as overweight reported the highest proportion of ADRs (45.0%), followed by patients with obesity (30.9%), with normal weight (21.8%), and underweight (2.3%). A meta-analysis of observational studies indicated that obesity is moderately associated with T2D [24].

In patients with T2D, comorbidities are common [25, 26];. 65.9% patients had at least one or more comorbidities. The data indicates that patients with comorbidities had a higher incidence of ADRs.

Mostly oral antidiabetic drugs were prescribed to the patients (85.7%). ADRs are higher in this patient group since this patient group had highest number of patients and oral antidiabetic drugs are known to have various ADRs.

Prescribing FDCs are most common for T2D patients [27, 28]. The most frequently prescribed FDC includes biguanide, SU, and TZD, with 54.6% of patients followed by biguanide, αGI and SU (42.4%). The highest ADRs (19.2%) in FDC of biguanide, SU, and TZD may be due to the combined effect of individual drugs.

The data shows that wide range of antidiabetic drugs were prescribed to T2D patients, with the most commonly biguanide (98.7%) followed by DPP4i (80.3%), TZD (72.9%), SU (71.1%), SGLT2i (58.1%), αGI (50.2%), insulin (17.9%). Other classes, including GLP1RA and meglitinides, have a lower prescription rate.

The systematic review of various publications suggests that FDCs of various oral hypoglycemic agents (OHAs) are beneficial to T2D patients to achieve their target glycemic levels by effectively controlling hyperglycemia. Most widely used component of FDCs is metformin with other OHAs such as glimepiride, pioglitazone, rosiglitazone, acarbose, and sitagliptin [29].

The study reveals that 32 types of ADRs were recorded, with a cumulative total of 424 incidents.

Table 3. Class and Name of the Drugs vs. ADR Events

Class and name of the drugs	No. of ADR events
Biguanide	414
Metformin: GI disturbances (76), Weakness (65), Tiredness (38), Hypoglycemic events (28), Headache (28), Sleep disturbance (23), Burning and painful urination (20), Restlessness and uneasiness (16), Decreased appetite (14), Body ache (14), Pedal edema (8), Weight gain (8), Increased appetite (8), Dizziness (7), Blurred vision (7), Back pain (7), Joint pain (6), Itching (6), Chest pain (5), Throat pain (4), Itching and redness over penile foreskin (3), Urinary incontinence (3), Eructation (3), Itching at vaginal region (3), Chills (3), Cough (2), Breathlessness (2), Swelling on face (2), Excess thirst (2), Vulvar rashes (1), Rash (1), Muscle pain (1)	414
Dipeptidyl peptidase-4 inhibitors	351
Sitagliptin: GI disturbances (36), Weakness (35), Tiredness (21), Hypoglycemic events (20), Headache (14), Sleep disturbance (12), Restlessness and uneasiness (11), Burning and painful urination (7), Decreased appetite (7), Body ache (5), Pedal edema (5), Weight gain (4), Increased appetite (4), Joint pain (4), Itching (4), Dizziness (3), Blurred vision (3), Throat pain (3), Back pain (2), Chest pain (2), Cough (2), Eructation (2), Chills (2), Breathlessness (2),Swelling on face (2), Urinary incontinence (1),Excess thirst (1), Vulvar rashes (1)	215
Vildagliptin: GI disturbances (16), Weakness (15), Tiredness (7), Sleep disturbance (5), Headache (4), Weight gain (4), Restlessness and uneasiness (3), Body ache (3), Hypoglycemic events (2), Burning and painful urination (2), Decreased appetite (2), Pedal edema (2), Increased appetite (2), Blurred vision (2), Chest pain (2), Itching and redness over penile foreskin (2), Itching at vaginal region (2), Joint pain (1), Itching (1), Throat pain (1), Urinary incontinence (1), Eructation (1), Excess thirst (1)	81
Teneligliptin: GI disturbances (7), Weakness (5), Headache (5), Burning and painful urination (4), Body ache (4), Decreased appetite (3), Back pain (3), Tiredness (2), Sleep disturbance (2), Hypoglycemic events (1), Restlessness and uneasiness (1), Increased appetite (1), Dizziness (1), Chest pain (1), Itching and redness over penile foreskin (1), Urinary incontinence (1)	42
Linagliptin: Hypoglycemic events (4), GI disturbances (3), Burning and painful urination (3), Weakness (2), Sleep disturbance (1)	13
Sulfonylureas	306
Glimepiride: GI disturbances (52), Weakness (45), Tiredness (22), Headache (19), Hypoglycemic events (18), Sleep disturbance (18), Burning and painful urination (13), Restlessness and uneasiness (10), Decreased appetite (10), Body ache (9), Increased appetite (6), Dizziness (5), Back pain (5), Itching (5), Weight gain (4), Blurred vision (4), Pedal edema (3), Joint pain (3), Chest pain (3), Throat pain (3), Itching and redness over penile foreskin (3), Urinary incontinence (3), Itching at vaginal region (3),Chills (3), Cough (2), Eructation (2), Swelling on face (2), Excess thirst (2), Breathlessness (1), Muscle pain (1)	279
Gliclazide: Weakness (3), Hypoglycemic events (3), GI disturbances (2), Tiredness (2), Burning and painful urination (2), Pedal edema (2), Headache (1), Sleep disturbance (1), Restlessness and uneasiness (1), Weight gain (1), Increased appetite (1), Dizziness (1), Vulvar rashes (1)	21
Glipizide: Burning and painful urination (2), Tiredness (1), Hypoglycemic events (1), Restlessness and uneasiness (1), Itching (1)	6
Thiazolidinedione	299
Pioglitazone: GI disturbances (50), Weakness (50), Tiredness (30), Hypoglycemic events (20), Sleep disturbance (20), Headache (19), Burning and painful urination (15), Body ache (11), Restlessness and uneasiness (9), Decreased appetite (7), Weight gain (6), Dizziness (6), Back pain (6), Pedal edema (5), Itching (5), Increased appetite (4), Blurred vision (4), Joint pain (4), Chest pain (3), Throat pain (3), Urinary incontinence (3), Eructation (3), Chills (3), Itching and redness over penile foreskin (2), Itching at vaginal region (2),Swelling on face (2), Excess thirst (2), Cough (1), Breathlessness (1), Vulvar rashes (1), Rash (1), Muscle pain (1)	299
Alpha-glucosidase inhibitors	244
Voglibose: GI disturbances (46), Weakness (32), Hypoglycemic events (17), Headache (16), Tiredness (12), Sleep disturbance (11), Burning and painful urination (10), Decreased appetite (9), Restlessness and uneasiness (6), Body ache (6), Increased appetite (5), Weight gain (4), Dizziness (4), Blurred vision (4), Back pain (4), Itching (4), Pedal edema (3), Joint pain (3), Itching and redness over penile foreskin (3), Itching at vaginal region (3), Chest pain (2), Throat pain (2),Cough (2), Urinary incontinence (2), Eructation (2), Swelling on face (2), Chills (1), Breathlessness (1)	216

Acarbose: GI disturbances (5), Weakness (4), Tiredness (3), Sleep disturbance (3), Hypoglycemic events (2), Headache (1), Burning and painful urination (1), Restlessness and uneasiness (1), Decreased appetite (1), Weight gain (1), Increased appetite (1), Dizziness (1), Blurred vision (1), Throat pain (1), Chills (1), Excess thirst (1)	28
Sodium glucose co-transport 2 inhibitors	235
Dapagliflozin: GI disturbances (39), Weakness (33), Tiredness (19), Hypoglycemic events (13), Headache (13), Restlessness and uneasiness (10), Sleep disturbance (9), Decreased appetite (6), Body ache (5), Increased appetite (5), Pedal edema (4), Dizziness (4), Itching (4), Burning and painful urination (3), Weight gain (3), Blurred vision (3), Joint pain (3), Chest pain (3), Throat pain (3), Chills (3),Eructation (2), Breathlessness (2), Excess thirst (2), Back pain (1), Cough (1), Urinary incontinence (1), Itching at vaginal region (1), Swelling on face (1), Vulvar rashes (1), Muscle pain (1)	198
Empagliflozin: Sleep disturbance (6), Burning and painful urination (6), GI disturbances (5), Weakness (5), Hypoglycemic events (3), Headache (2), Blurred vision (2), Decreased appetite (1), Pedal edema (1), Increased appetite (1), Dizziness (1), Joint pain (1), Rash (1)	35
Remogliflozin etabonate: GI disturbances (1)	1
Canagliflozin: Chills (1)	1
Insulin	88
Insulin glargine: GI disturbances (8), Weakness (8), Burning and painful urination (5), Hypoglycemic events (3), Sleep disturbance (3), Tiredness (2), Decreased appetite (2), Body ache (2), Pedal edema (2), Weight gain (2), Increased appetite (2), Throat pain (2), Cough (2), Urinary incontinence (2), Headache (1), Restlessness and uneasiness (1), Back pain (1), Itching (1), Itching at vaginal region (1), Breathlessness (1)	51
Insulin aspart: Weakness (3), Increased appetite (3), GI disturbances (2), Tiredness (2), Weight gain (2), Blurred vision (2), Hypoglycemic events (1), Sleep disturbance (1), Pedal edema (1), Itching at vaginal region (1)	18
Insulin degludec: GI disturbances (3), Weakness (3), Tiredness (2), Sleep disturbance (2), Blurred vision (2), Weight gain (1), Increased appetite (1), Itching at vaginal region (1)	15
Insulin isophane + Human insulin: Weakness (1), Tiredness (1), Muscle pain (1)	3
Insulin glulisine: Hypoglycemic events (1)	1
GLP1RA	12
Semaglutide: GI disturbances(8), Tiredness(1), Headache(1), Decreased appetite(1), Joint pain(1)	12
Liraglutide	0
Meglitinides	6
Repaglinide: GI disturbances(3), Hypoglycemic events(2), Weakness(1)	6

ADR — adverse drug reaction; GI disturbances — gastrointestinal disturbances; GLP-1 — glucagon-like peptide-1 receptor agonists

Gastrointestinal disturbance (GI), weakness and tiredness were common ADRs across various drug classes, followed by hypoglycemic events, headache, sleep disturbances, burning and painful urination, restlessness and uneasiness, Decreased appetite, body ache and pedal edema. GI disturbances is the most commonly reported ADR followed by weakness and tiredness across various classes of antidiabetic drugs. Hypoglycemic events are frequent with several classes of drugs, including SU, DPP4i, SGLT2i and biguanides, αGIs and TZD when used in combination with one or more drugs. Managing blood glucose levels is the primary goal of T2D management, but severe hypoglycemia can be dangerous, so close monitoring is necessary. Sleep disturbances, headache, weight gain, pedal edema, burning and painful urination are reported with multiple drug classes, such as biguanides, TZD, SU, DPP4i, and SGLT2i, αGI when used in combination with one or more drugs. No pancreatic related ADR was reported in this study. Treatment adherence and daily life can be affected by these ADRs. Few drugs have limited ADR data, as they were less commonly prescribed. For example, meglitinides and GLP1RA have relatively fewer ADR reports. In a study conducted in 220 T2D patients in New Delhi, it was found that most commonly observed ADRs were related to endocrine and gastrointestinal system [30].

The assessment to categorize all ADRs as "Possible" because of the complexity of managing T2D. Patients

in the study were on multiple antidiabetic drugs, which can make it difficult to conclusively attribute specific ADR to a single drug. The "Possible" classification indicates that while there may be a reasonable link between the ADRs and the drugs, causality cannot be established with certainty. The study results indicate that patients generally experience mild to moderate ADRs from antidiabetic medications.

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, BMI, duration of disease, comorbidities and prescribed FDCs. 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%). Gastrointestinal disturbances (80, 36.4%) emerged as the most prevalent ADR trailed by weakness (66, 30.0%) and tiredness (38, 17.3%). 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.

Article information

Ethics statement

Approval of Institutional Ethics Committee (IEC) "Rudraksha Hospital Ethics Committee" was obtained before initiation of the study.

Authors contribution

Conception and design of study: Dr Jalpa Suthar, Sani Prajapati, Acquisition of data: Sani Prajapati, Dr. Dhruvi Hasnani, Dr. Vipul Chavda, Analysis, or interpretation of data: Sani Prajapati, Dr Jalpa Suthar, Dr. Dhruvi Hasnani, Dr. Vipul Chavda, Drafting the work and revising it critically for important intellectual content and Final approval of the version to be published: Sani Prajapati, Dr Jalpa Suthar, Dr. Dhruvi Hasnani, Dr. Vipul Chavda.

Funding

This publication was prepared without any external source of funding.

Conflict of interest

The authors declare no conflict of interest.

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