



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH  
An official Publication of Human Journals

ISSN 2349-7203



Human Journals

**Review Article**

November 2023 Vol.:28, Issue:4

© All rights are reserved by Md Hasan Kashif et al.

## Managing Adverse Drug Reactions (ADRs) of Anti-Diabetic Medications: A Review on Prevalence and Clinical Pharmacist's Involvement in India



IJPPR  
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH  
An official Publication of Human Journals



ISSN 2349-7203

**Md Hasan Kashif<sup>1\*</sup>, Shakeel Ahmed<sup>2</sup>**

1) *Dr. Md Hasan Kashif, Assistant Professor, Department of Pharmacology Luqman College of Pharmacy, Kalaburagi. India.*

2) *Shakeel Ahmed, Associate Professor, Department of Pharmacology Luqman College of Pharmacy Kalaburagi. India.*

**Submitted:** 22 October 2023  
**Accepted:** 27 October 2023  
**Published:** 30 November 2023

**Keywords:** Diabetes; antidiabetic drugs; Adverse drug reactions; pharmacist; ADRs monitoring; ADRs Reporting

### ABSTRACT

The prevalence of diabetes among Indians is significantly higher and the majority of diabetic patients who are taking antidiabetic drugs to manage their condition experience ADRs which can be controlled by carefully monitoring and reporting at the proper time by health care providers. India is the second-most affected country in the world, with an estimated 77 million individuals (1 in 11 Indians) having a formal diagnosis of diabetes. The modern Indian population, which constitutes 65 % of the nation, is gradually adapting to a new lifestyle that was unknown before. They are highly susceptible to the risk of diabetes and its growing burden. As a result, it becomes necessary for a medical professional or pharmacist to monitor, report, and manage ADRs and similar issues in the hospital. Insulin and oral diabetic medications are used to treat diabetes. In addition to these medications, diabetic patients frequently receive antihypertensive medication, antiplatelet therapy, and medicines to treat dyslipidemia. Anti-diabetic therapy can cause hypersensitivity, hepatotoxicity, erythema multiforme caused by drug, photodermatitis, hypoglycemia, hypoglycemic coma, and other severe pharmacological consequences. To prevent unintended side effects from occurring during treatment, it is essential to inform the patient about their medications and any possible adverse reactions. The article's primary objective is to increase public awareness about antidiabetic drugs, their effects, and the importance of pharmacists reporting adverse drug reactions and being involved in the whole event. As experts in medicine, pharmacists in the hospital sector can be crucial in identifying, monitoring, and reporting ADRs.



[ijppr.humanjournals.com](http://ijppr.humanjournals.com)

## INTRODUCTION

Diabetes is a chronic condition that develops when the pancreas either produces insufficient amounts of insulin or when the body cannot properly utilize the insulin produced by the pancreas.

Blood sugar levels are controlled by the hormone insulin. Uncontrolled diabetes frequently results in hyperglycemia, also known as high blood glucose or raised blood sugar, which over time causes significant harm to a number of different body systems, including the nerves and blood vessels.

### Types of Diabetes

- Types 1 diabetes

Type 1 diabetes (formerly called insulin-dependent, juvenile, or childhood-onset) is characterized by inadequate insulin synthesis and requires daily insulin administration.

- Types 2 diabetes

Type 2 diabetes, also known as non-insulin-dependent or adult-onset diabetes, is turned on by the body's inefficient use of insulin. Type 2 diabetes affects more than 95% of patients with diabetes. The main causes of this progressive disease are being overweight and being physically inactive.

Although they are frequently less severe, type 2 diabetes symptoms may resemble those of type 1.

### Gestational diabetes

Gestational diabetes is defined as blood sugar levels that are higher than usual but lower than those that are indicative of diabetes. Pregnancy is when gestational diabetes develops.

Pregnancy and delivery problems are more likely to occur in women with gestational diabetes. Future type 2 diabetes risk is elevated for these mothers and potentially for their offspring as well.

Prenatal testing rather than reported symptoms is being used to identify gestational diabetes.

- Pre-diabetes

Individuals have prediabetes when the blood sugar level is higher than the average. It's not high enough to be diagnosed as type 2 diabetes there yet. However, prediabetic adults and children are at a greater risk of developing type 2 diabetes without making lifestyle adjustments.<sup>1</sup>

### **Signs and symptoms**

Symptoms include frequent urination (polyuria), excessive thirst (polydipsia), persistent hunger, loss of weight, alterations in vision, and tiredness. These signs could occur unexpectedly.

### **Causes of diabetes**

Researchers believe that environmental triggers including viruses and genes play a role in the development of type 1 diabetes. When the insulin-producing beta cells of the pancreas are attacked and destroyed by the immune system, the body's defense mechanism against infection, type 1 diabetes develops. Numerous factors, including lifestyle changes and genetics, contribute to type 2 diabetes, the most prevalent type of the disease.

If you are not physically active, overweight, or obese, you are more prone to acquire type 2 diabetes. Insulin resistance can occasionally result from excess weight and is highly prevalent in type 2 diabetics.

Other factors include hormonal disorders, pancreatic damage or removal, genetic abnormalities, and certain drugs.<sup>2</sup>

### **Diabetes Issues in Elderly Patients**

Because of increased longevity and lifestyle changes, diabetes mellitus (DM) prevalence is a global issue that is getting worse. As one in two elderly people (60–65 years old) in developed and even developing nations suffer from diabetes or prediabetes, and as eight out of ten elderly people (60–65 years old) have some kind of dysglycemia, DM in this age group is becoming a serious public health concern. Older diabetics experience co-morbidities and DM problems more frequently than their younger individuals.<sup>3</sup>

## **Risk factors**

Risk factors for type 1 diabetes are not as clear as for prediabetes and type 2 diabetes. Unlike type 2 and prediabetes, type 1 diabetes has less well-defined risk factors. Family history and aging are two known risk factors.

Among the risk factors for type 2 diabetes are individuals who are prediabetic, having a weight problem, a minimum age of 45, possess a type 2 diabetic parent, sibling, or other family member.

Poor physical activity.

have given birth to a baby that weighed more than 9 pounds or had gestational diabetes (diabetes during pregnancy). Asian American peoples are also at higher risk as well.

The chance of developing type 2 diabetes may increase if you have non-alcoholic fatty liver disease.<sup>4</sup>

The only reliable method for protecting the public's health is through appropriate and efficient ADR monitoring or pharmacovigilance. In an expansive nation like India, home to nearly 1.2 billion people, has a massive illness prevalences and ethnic diversity patterns, application of several systems of prescription drugs, and individuals from various socioeconomic backgrounds, and it is it's crucial to have a reliable and standardized Drug safety surveillance and pharmacovigilance program for the country. Utilization of Antidiabetics use has grown. However, reports of major negative effects are inconsistent. Inextricably linked to the usage of these products have can into a cause for worry. Spontaneous monitoring of adverse events reporting these medications' security.<sup>5</sup>

## **Adverse drug reactions**

An adverse drug reaction (ADR) is a medication's unintended, undesirable side effect that develops during routine clinical use of prescribed medications. Adverse medication reactions nearly always happen in medical facilities and can have a negative impact on a patient's quality of life, frequently leading to significant morbidity and mortality.

### **Anti-diabetic drugs and their major adverse effects**

There are many antidiabetic drugs available, each with a different mechanism shown in Figure 1. People with diabetes frequently need to take more than one type of medication, and some even need to take multiple medications. Various antidiabetic drugs can cause side effects in some patients.

Unfortunately, several anti-diabetic drugs have significant side effects like nausea or gastrointestinal problems. Antidiabetic drugs like Metformin, only have temporary side effects. Figure. 2 displays the potential adverse effects of anti-diabetic drugs.<sup>6</sup>

### **Potential side effects of common anti-diabetic drugs**

The following class of antidiabetic drugs often causes adverse effects in long-term therapy.

- **Sulfonylureas:** low blood sugar, upset stomach, skin rash or itching, weight gain
- **Biguanides/Metformin:** sickness with alcohol, kidney complications, upset stomach, tiredness or dizziness, metal taste
- **Alpha-glucosidase inhibitors:** gas, bloating and diarrhea
- **Thiazolidinediones:** weight gain, risk of liver disease, anaemia risk, swelling of legs or ankles,
- **Meglitinides:** weight gain, low blood sugar.<sup>7</sup>

### **Identification of adverse drug reactions**

The earliest sign of an ADR may be a patient's new or worsening symptom, for both the inpatient and outpatient domain. Patients frequently ask the pharmacist for help in a local clinic about how to treat various illnesses at present. The pharmacist may take advantage of this to ask the patient about their symptoms in order to ascertain whether an ADR may have affected to them.

For example, if a patient asks the pharmacist for a recommendation to treat gastritis, the pharmacist could inquire about other medications the patient is taking to determine whether gastritis is a known ADR associated with the anti-diabetic drug therapy.

When a patient develops a new symptom while being treated in an inpatient setting, their nurse or doctor might approach the pharmacist. Instead of making a treatment recommendation right away, ask the patient a lot of questions about their symptoms to help identify any ADRs and stop any further ADR symptoms or unnecessary drug therapy.

An ADR can also be identified with the help of common laboratory testing. It may be a sign that an ADR has occurred if you notice that an unusual laboratory test or diagnostic procedure has been ordered.

Some less obvious methods are screening of prescribed medications in both inpatient and outpatient, a sudden, unexpected withdrawal of a medication or a significant dosage increase or decrease are frequent signs of an ADR. Orders for new medications may occasionally alert the pharmacist that an ADR has occurred.

ADRs can also be identified by reviewing the daily multidisciplinary notes in a patient's chart clinical notes. Some electronic medical record systems can produce reports for changes in vital signs that satisfy certain measures.<sup>8</sup>

### **Reporting of adverse drug reactions (ADRs)**

In order to ensure drug safety, pharmacists play a crucial role in identifying and reporting adverse drug reactions (ADRs). The concept of an ADR (Adverse Drug Reaction) monitoring and reporting system has been out for a long time and is currently slowly but steadily receiving the focus it needs in terms of drug safety measures.

The lack of accurate ADR reporting and monitoring in the Indian population for medication safety continues to be a major problem for medical professionals. Therefore, it's vital to improve healthcare providers' understanding, perspective, and practice about ADR in order to increase the reporting rate.

Investigating adverse drug reactions, a major cause of illness and death is a key function of pharmacovigilance. ADRs are currently ranked as the fourth to sixth leading cause of death, according to epidemiological studies. The national health budget is significantly impacted by 4-5 ADRs. It leads to increasing the expense of patient care and it may resemble disease, causing unnecessary tests and a delay in treatment. Therefore, there is a need to take ADRs

seriously, to raise patient awareness of ADRs, and to encourage healthcare professionals to report ADRs to lower the risk.<sup>9</sup>

Patients with incur the risk of adverse drug effects must be protected, according to the pharmacist and prescriber. The pharmacist is a crucial link between the patient and the healthcare provider this is proven throughout the whole medication administration process.

The most often used techniques include prompted spontaneous reporting by physicians and pharmacists, thorough collection by qualified specialists, and, more recently, computer-assisted techniques employing normal data from hospital information systems. ADR frequencies and types vary depending on the various ADR detection techniques that are employed, and as a result, different medication classes are ultimately accountable for these ADRs.<sup>10</sup>

Another factor that influences descriptive analysis is how the term "adverse drug reactions" (ADR) is interpreted. While some authors use the World Health Organization's strict definition, many others include intentional and unintentional poisoning as well as errors in the prescription and dispensing of drugs when referring to ADRs. Depending on the approach employed for patient screening, a large number of potential ADRs and only a small number of confirmed ADRs are detected, or the risk is higher.<sup>11</sup>

When comparing the outcomes of additional analyses conducted using these data, these variations must be taken into consideration. Only a few surveys and projects have assessed ADR rates and incidences in proportion to the number of medications administered or patients exposed, and this unique pharmacoepidemiological approach demands more research. Additionally, using various methods, the pharmaco-economic impact of ADRs that either cause hospitalization or lengthen hospital stays has been calculated. There is still not a recognized standard operating procedure for these calculations.<sup>12</sup>

Although the possibility to detect severe ADRs of recently approved medications is provided by hospital ADR detection, these ADRs are still found through spontaneous reporting methods. The capabilities and importance of ADR detection in hospitals are increased by the use of pharmacoepidemiological techniques and the prospects provided by electronic hospital information systems.<sup>13</sup>

## **Optimization of drug therapy**

Diabetes therapy optimization is a challenging therapeutic task that requires significant patient education and motivation. The objective is to increase glycemic control while minimizing unfavourable weight gain or hypoglycemia and with minimal or no impact on blood pressure or cholesterol levels. Choosing the right medication requires figuring out which one is most likely to increase control and which is least likely to have interactions, negative side effects, or adherence issues. As a result, it may alter patient outcomes and the financial burden on healthcare systems.<sup>14</sup>

In the current healthcare system, after doctors and nurses, pharmacists comprise up the third largest health profession. A limited proportion of pharmacists work in hospital pharmacies, academia, industry, and research, whereas the majority of them are employed in the community.

Community pharmacies offer a variety of services (including dietary supplements, blood glucose meters, test strips, and needles) as well as services for people with diabetes (such as medication review, vaccination, unit dose dispensing, needle exchange, point of care testing, disposal of unwanted medicines, etc). Since appointments are not necessary to see a community pharmacist, they are regarded as the healthcare providers with the highest amount of patient contact and who are also the most easily accessible. As a result, they are in a good position to contribute greatly to the treatment of diabetic patients.<sup>15</sup>

## **METHODS**

The above study, that used the data bases, comprised a thorough textual assessment of the roles and significance of pharmacists in the identification and reporting of adverse drug reactions related to anti-diabetic drugs and in improving the quality of life of diabetic patients. A large amount of relevant reviews and research articles were discovered using search engines like Google, Google Scholar, MEDLINE, Wiley Library, MEDSPACE, and others. We utilized terms like adverse drug reactions, pharmacist, quality of life, and diabetes in our search. Only articles that addressed pharmacist interventions in improving clinical outcomes and monitoring ADRs were selected.



## RESULTS

There were 60 articles of which appeared related to the subject of interest. 10 were removed after a thorough review because they did not meet the inclusion criteria, remaining 20 had been thoroughly examined. To optimize drug therapy and produce better clinical outcomes, safety, effectiveness, and economy, a variety of pharmacist interventions were shown in literature reviews.

| S/N | Drug class                   | Example of drugs | Adverse effects   |
|-----|------------------------------|------------------|---|
| 1   | Insulin and analogues        | Regular Insulin  | Low blood glucose level, Increased Body Weight, allergy to Insulin, Lipodystrophy at injection locations.                             |
| 2   | Sulphonylureas               | Glibenclamide    | Low blood glucose level, Increased Body Weight, Cardiovascular risk, rash, Cholestatic jaundice, Bone marrow damage, Photosensitivity |
| 3   | Meglitinides                 | Repaglinide      | Low blood glucose level, Sensitivity  |
| 4   | Biguanides                   | Metformin        | Gastrointestinal effects, Lactic acidosis   |
| 5   | GLP-1 agonists               | Exenatide        | Gastrointestinal effects, Pancreatitis, risks for cancer and cardiovascular events  |
| 6   | DPP-4 inhibitors             | Saxagliptin      | Pancreatitis, cancer risk, acute hepatitis and kidney impairment  |
| 7   | Thiazolidinedions            | Pioglitazone     | Hepatitis, Cardiovascular risk, Bladder cancer, Water retention and Increased Body Weight   |
| 8   | Dual PPAR agonists           | Saroglitazar     | Gastritis, asthenia and pyrexia   |
| 9   | Alpha-glucosidase inhibitors | Acarbose         | Gastrointestinal effects, Hepatitis,  |
| 10  | Amylin analogues             | Pramlintide      | Low blood glucose level, Allergy  |
| 11  | SGLT 2 inhibitors            | Canagliflozin    | Glycosuria, Cardiovascular concern  |

### Conventional antidiabetic drugs and their major adverse effects

## CONCLUSION

The article focuses on the importance of pharmacists in improving patient outcomes in diabetic patients by monitoring and analyzing adverse drug reactions related to anti-diabetic medications and obtaining high therapeutic levels of drug therapy. Our research found that a pharmacist's participation in the healthcare team is encouraged by the essential services they provide in hospital settings. These kinds of studies will be carried out in the future for the benefit of patients who are at risk of ADRs related to antidiabetic drugs in order to strengthen relationships amongst healthcare professionals, which will ultimately improve patient care.

## ACKNOWLEDGEMENT

We are grateful to Associate Professor SS Biradar, Department of Pharmacy Practice HKE's MTRIPS for valuable help with the manuscript.

## CONFLICT OF INTEREST

No potential conflicts were reported regarding the manuscript.

## ABBREVIATIONS

ADR(s): Adverse Drug Reaction(s); WHO: World Health Organization; HRQOL: Health-Related Quality of Life; ADEs: Adverse Drug Events; QOL: Quality of Life.

## REFERENCES

1. American diabetes association. Standards of medical care in diabetes—2009. *Diabetes Care*. 2009 Jan;32 Suppl 1:S13-61.
2. Mohan H, Damjanov I. Textbook of pathology. New Delhi: Jaypee Brothers Medical Publishers; 2019.
3. Kalra S, Sharma SK. Diabetes in the Elderly. *Diabetes Ther*. 2018 Apr;9(2):493-500. doi: 10.1007/s13300-018-0380-x. Epub 2018 Feb 19. PMID: 29460258; PMCID: PMC6104259.
4. Magnus Kaijser, Anna-Karin Edstedt Bonamy, Olof Akre, Sven Cnattingius, Fredrik Granath, Mikael Norman, Anders Ekblom; Perinatal Risk Factors for Diabetes in Later Life. *Diabetes* 1 March 2009; 58 (3): 523–526.
5. Sharma Hemant, Singh G.N., Adverse events associated with antidiabetics: An analysis of Vigiflow data, *Innovations in Pharmaceuticals and Pharmacotherapy* 1(2), 2013, 91-94.
6. Patton K, Borshoff DC. Adverse drug reactions. *Anesthesia*. 2018 Jan;73 Suppl 1:76-84.
7. Tripathi KD. Essentials of Medical Pharmacology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers; 2019.
8. Warrer P, Jensen PB, Aagaard L, Jensen LJ, Brunak S, Krag MH et al. Identification of possible adverse drug reactions in clinical notes: The case of glucose-lowering medicines. *J Res Pharm Pract*. 2015 Apr-Jun;4(2):64-72.
9. Pathak AK, Kumar M, Dokania S, Mohan L, Dikshit H. A Retrospective Analysis of Reporting of Adverse Drug Reactions in a Tertiary Care Teaching Hospital: One Year Survey. *J Clin Diagn Res*. 2016 Aug;10(8):FC01-4.
10. Srisuriyachanchai W, Cox AR, Kampichit S, Jarernsiripornkul N. Severity and Management of Adverse Drug Reactions Reported by Patients and Healthcare Professionals: A Cross-Sectional Survey. *Int J Environ Res Public Health*. 2023 Feb 20;20(4):3725.
11. Mekonnen AB, Alhawassi TM, McLachlan AJ, Brien JE. Adverse Drug Events and Medication Errors in African Hospitals: A Systematic Review. *Drugs Real World Outcomes*. 2018 Mar;5(1):1-24.
12. Mukherjee S, Sharmasarkar B, Das KK, Bhattacharyya A, Deb A. Compliance to anti-diabetic drugs: observations from the diabetic clinic of a medical college in Kolkata, India. *J Clin Diagn Res*. 2013 Apr;7(4):661-5.
13. Singh A, Dwivedi S. Study of adverse drug reactions in patients with diabetes attending a tertiary care hospital in New Delhi, India. *Indian J Med Res*. 2017 Feb;145(2):247-249.
14. Lopes A, Roque F, Morgado S, Dinis C, Herdeiro MT, Morgado M. Behavioral Sciences in the Optimization of Pharmacological and Non-Pharmacological Therapy for Type 2 Diabetes. *Behav Sci (Basel)*. 2021 Nov 3;11(11):153.

15. Hughes JD, Wibowo Y, Sunderland B, Hoti K. The role of the pharmacist in the management of type 2 diabetes: current insights and future directions. *Integr Pharm Res Pract.* 2017 Jan 16; 6:15-27.