RESEARCH ARTICLE

Study on Drug-associated Adverse Reactions in Diabetes Mellitus Patients

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Abstract

Purpose: This study aimed to assess the knowledge, attitudes, and practices regarding diabetes management, as well as to identify adverse drug reactions (ADRs) associated with diabetic medications among patients. Insights were gained through questionnaire-based surveys and direct patient interviews for conciseness of diabetes management and medication safety.

Methods: The study emphasized using questionnaire as the primary tool for data collection and management because of ease of access, convenience for participants, and efficient data handling capabilities. The responses were automatically collected and recorded in real-time as participants submitted the google forms. Measures were taken to ensure data integrity and prevention of duplicate submissions, by limiting responses to one per participant.

Results: After a thorough study, various ADRs were reported. These included blood and lymphatic system disorders, skin and subcutaneous tissue disorders, gastrointestinal disorders, general disorders and administration site conditions. The severity levels of the ADRs recorded were manageable.

Conclusion: Strengthening pharmacovigilance initiatives is essential for monitoring and reporting adverse drug reactions associated with diabetic medications. Pharmacist-led medication review services, patient counselling on medication safety, and proactive surveillance of ADRs could contribute to improved patient outcomes and medication management.

Keywords: Pharmacovigilance, Adverse drug reaction (ADR), Medication safety, Adverse events, Severity Level.

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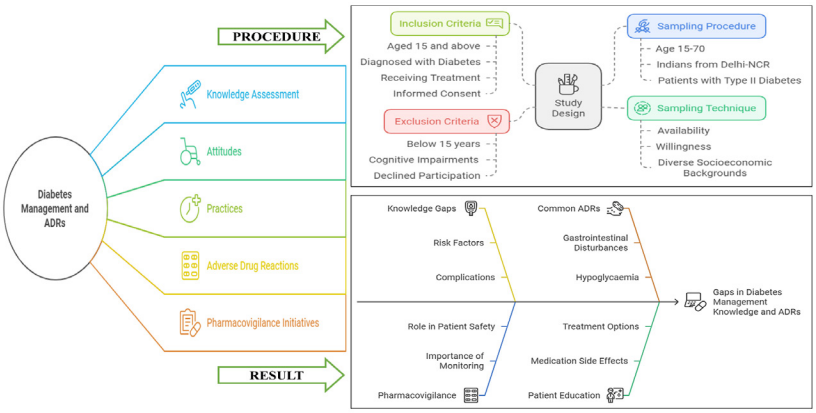

GRAPHICAL ABSTRACT

Introduction

According to the Pharmacovigilance definition given by WHO, it is "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems. Recently, its concerns have been widened to include herbals, traditional and complementary medicines, blood products, biological, medical devices and vaccines". Pharmacovigilance is defined as "the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long-term and short-term adverse effects of medicines".[1]

Integrating comprehensive diabetes education and training into the pharmacy curriculum, can provide focus on evidence-based guidelines, medication management, and patient counseling to better prepare future pharmacists for addressing diabetes-related challenges. Continued surveillance of adverse drug reactions associated with

diabetic medications is essential for identifying emerging safety concerns, optimizing treatment regimens, and enhancing patient care. Collaboration with healthcare professionals and regulatory agencies can facilitate proactive pharmacovigilance initiatives. Efforts must focus on improving patient education and empowerment regarding diabetes management and medication adherence. Pharmacists play a crucial role in providing personalized counselling, addressing patient concerns, and fostering medication safety awareness.[2,3]

Collaboration between pharmacists, physicians, nurses, and other healthcare professionals is vital for implementing holistic approaches to diabetes care. Interdisciplinary teamwork can enhance care coordination, promote evidence-based practice, and improve patient outcomes. Research endeavours should explore novel therapeutic approaches for diabetes management, including innovative drug delivery systems, pharmacogenomics-guided treatment strategies, and complementary therapies. Such advancements have the potential to revolutionize diabetes care and improve treatment efficacy and safety.[4,5]

This study aims to enhance pharmacovigilance practices in diabetes management by investigating the occurrence and characteristics of adverse drug reactions associated with anti-diabetic medications among patients undergoing treatment for type II diabetes mellitus. The objectives of this study encompass a comprehensive investigation into pharmacovigilance practices in diabetes management. This includes assessing the prevalence, nature, and severity of adverse drug reactions (ADRs) linked with antidiabetic medications among patients diagnosed with diabetes mellitus. Additionally, the study seeks to identify commonly implicated antidiabetic drugs, analyze temporal patterns of ADRs in relation to medication use, and explore potential risk factors associated with their development. Furthermore, the research aims to evaluate healthcare providers' awareness, reporting practices, and management strategies concerning ADRs in diabetes pharmacotherapy.

Methods

Study design

An observational cross-sectional study was conducted from April to May 2024 for a period of one month to delve into various pharmacovigilance protocols and procedure required as per project. Questionnaire-based approach was chosen for this study shown in Fig. 1. It has advantages such as cost-effectiveness, feasibility for large-scale data collection, and ability to gather standardized responses across participants. Responses were stored securely in google Sheets, allowing for easy organization and analysis of data. The study site was MMG District Hospital, Ghaziabad.

Sampling procedure

Study population inclusive of both males and females were Indians from Delhi-NCR region, within the age group of

STUDY QUESTIONNAIRE

Personal Information:

1. Full Name: _____
2. Age: _____
3. Gender: [ ] Male [ ] Female [ ] Other

Medical History:

4. How long have you been diagnosed with Diabetes_____ years/months
5. What type of Diabetes do you experience?
   [ ] Type 1 Diabetes [ ] Prediabetes [ ] Type 2 Diabetes [ ] Gestational Diabetes
6. Are you currently on any Diabetes Therapy? [ ] Yes [ ] No
7. If yes, please specify: [ ] Allopathy [ ] Ayurveda [ ] Homeopathy

Medication Details:

8. Name of the medication you are currently taking for Diabetes: _____
9. Dosage: _____
10. Frequency of use: [ ] Daily [ ] Weekly [ ] As needed
11. How long have you been taking this medication _____ months/years ?

Symptom Monitoring:

12. Since starting the medication, have you noticed any improvement in your Diabetes.
    [ ] Significant improvement [ ] Moderate improvement [ ] No change [ ] Worse
13. Have you experienced any side effects since starting the medication? [] Yes [] No
14. If yes, please specify the Severity:
    [ ] Mild [ ] Moderate [ ] Severe [ ] Life Threatening

ADRs of Drugs taken by patients:

15. [ ] ***Metformin:*** [ ] Drug ineffective [ ] Diarrhoea [ ] Abdominal Pain [ ] Lactic Acidosis [ ] Decreased appetite [ ] Dehydration [ ] Pruritus [ ] Dyspnoea [ ] Insomnia [ ] Loss of Consciousness [ ] Headache [ ] Fatigue

16. ***[ ] Linagliptin:*** [ ] Drug ineffective [ ] Pain [ ] Fatigue [ ] Rash [ ] Pruritus [ ] Nausea /Vomiting [ ] Diarrhoea [ ] Dizziness/ Headache [ ] Back Pain

17. ***[ ] Glimepiride:*** [ ] Decreased Appetite [ ] Dizziness [ ] Rash [ ] Dry Skin [ ] Tachycardia [ ] Eye pain [ ] Chest Pain [ ] Swelling Face [ ] Obesity [ ] Abdominal pain

18. ***[ ] Insulin injection:*** [ ] Myocardial Infarction [ ] Tachycardia [ ] Fatigue [ ] Eye Pain [ ] Injection Site Pain/ rash [ ] Loss of Consciousness [ ] Burning Sensation [ ] Dehydration [ ] Pain / Chest Pain [ ] Pyrexia

19. **Additional Comments:** Please provide any other comments or observations regarding your Diabetes medication: _____

20. Consent: I consent to the use of this information for pharmacovigilance purposes and understand that my personal information will remain confidential.

21. **Signature:** _____ **Date:** _____

Figure 1: Study questionnaire

15-70 years which encompasses adolescence, young adults, middle-aged adults, and older adults. The study population consists of patients diagnosed with type II diabetes mellitus who are receiving treatment at MMG District Hospital Ghaziabad.

Sampling technique

Patients were approached based on their availability and willingness to participate in the survey. Inclusion of both genders is required to ensure the representation of diverse perspectives and experiences related to diabetes management. Individuals from various socioeconomic backgrounds, including different income levels, education levels, and occupations, are included in the study.

Inclusion criteria

- Patients aged 15 years and above.
- Patients diagnosed with Diabetes.
- Patients receiving treatment for diabetes at MMG District Hospital Ghaziabad
- Patients willing to participate in the survey and provide informed consent.

Exclusion criteria

- Patients below the age of 15 years.
- Patients with cognitive impairments or communication barriers that prevent meaningful participation in the survey.
- Patients who decline to participate in the survey.

Procedure

Each researcher identified eligible patients based on their presence in out-patient departments, in-patient wards, pharmacy department or other relevant areas of the hospital. Patients are approached individually, and the purpose and nature of the survey are explained to them. Informed consent is obtained from patients who agree to participate in the survey. The questionnaire on diabetes management was provided to patients and were asked about any adverse effects or reactions they may have experienced from their diabetic medications. Following this, the documentation of any ADRs, including the type of reaction, severity, and medication(s) implicated were also noted. The data collection period extends over a period of 1 month, during which the researchers were actively engaged with patients.

Result And Discussion

The study was conducted with 150 participants from the MMG District Hospital Ghaziabad, as well as family and friends from the local Delhi-NCR area, covering an age range of 15-70 years, both male and female.

Distribution of diabetes types

The analysis of diabetes types within the study population reveals a predominance of Type II diabetes, accounting for 76.5% of cases. Type I diabetes is also represented, comprising 18%, while prediabetic conditions are observed in 5%. Gestational diabetes, although less common, is identified in 0.5% of the study cohort as shown in Fig. 2.

Gender distribution

The study sample comprised 150 participants, with gender distribution showing 42% female and 58% male representation. The gender distribution reflects a balanced representation within the study population, allowing for diverse perspectives and experiences to be captured in the analysis as shown in Fig. 2.

Type of therapy utilized by patients

Allopathic therapy was utilized by 136 participants. This therapy included conventional medical treatments such as Metformin, Glimepiride, Linagliptin, and Insulin Injection. Ayurvedic therapy was utilized by 10 participants as shown in Fig. 2. This traditional system employed herbal medicines and dietary modifications to manage diabetes. Also, Homeopathic therapy was taken by 4 participants, which involved the use of highly diluted substances with the aim of triggering the body's natural healing processes.

Current therapy utilization:

When asked if they were currently on any diabetes therapy, 96% of participants (146 out of 150) responded affirmatively, indicating a high engagement with diabetes management practices. Conversely, 4% of participants (4 out of 150) reported not being on any therapy as shown in Fig. 2.

Frequency of diabetes therapy use

The analysis of therapy frequency revealed that the overwhelming majority of participants, comprising 97.9%, reported using their diabetes therapy on a daily basis. In contrast, no participants reported using therapy on a weekly basis. A small proportion of participants, representing 2.1%,

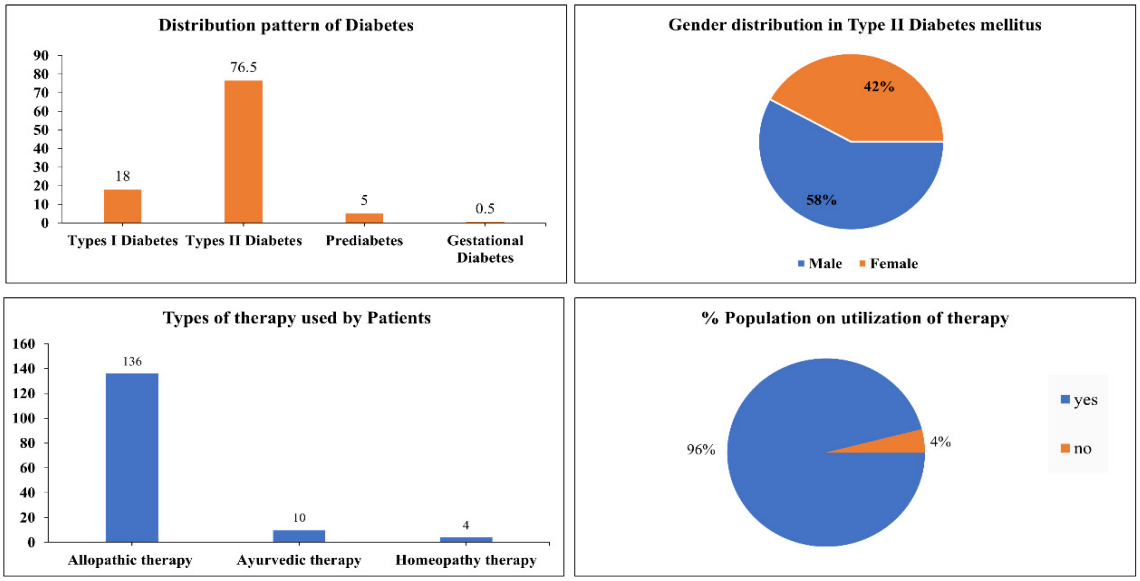

Figure 2: Distribution pattern of diabetes, gender distribution, types of therapy and %population on therapy utilization

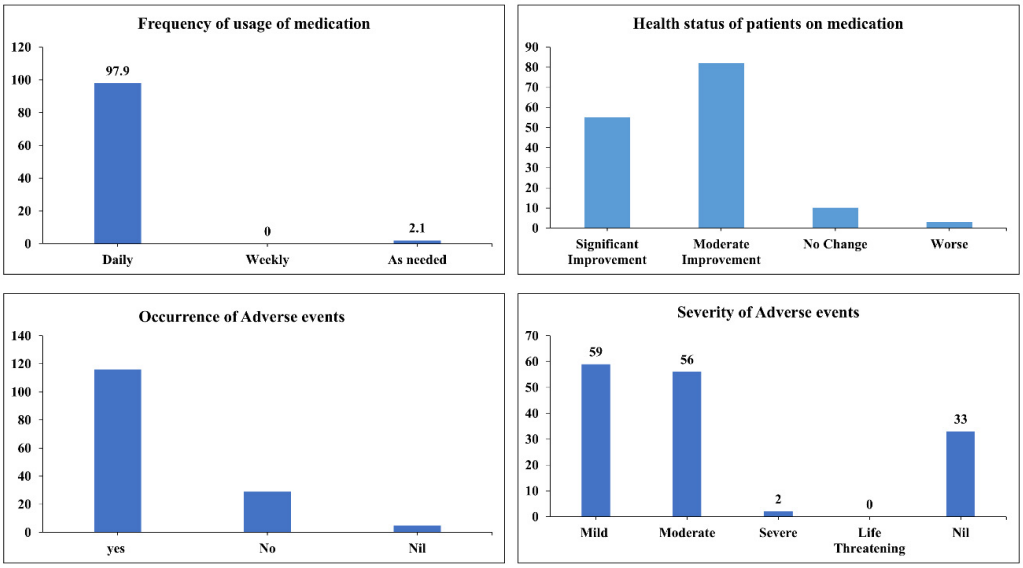

Figure 3: Frequency of medication usage, health status of patients, adverse event occurrence & its severity

reported using therapy on an as-needed basis as shown in Fig. 3.

Perceived improvement in diabetes management

Participants were asked to report any perceived changes in their diabetes management. The majority of respondents, comprising 55 patients, reported experiencing a significant improvement in the health status with diabetes management. Additionally, a substantial proportion of participants i.e. 82, reported a moderate improvement in their condition. Only a minority of participants, accounting for 10, reported no change in their diabetes condition. A small percentage of respondents, constituting 3, reported a worsening of their diabetes as shown in Fig. 3.

Occurrence of adverse events from diabetes therapy

Out of the total 150 participants, 116 individuals reported experiencing side effects from their diabetes therapy. In contrast, 29 participants reported no side effects, while 5 participants indicated that they had not experienced any side effects, resulting in a total of 34 participant who did not report side effects as shown in Fig. 3.

Severity of adverse events from diabetes therapy

Among participants who reported experiencing side effects from their diabetes therapy, the severity varied. The majority of individuals, comprising 59 participants, reported experiencing mild side effects. Additionally, 56 participants reported moderate side effects, while only 2 participants reported severe side effects. Notably, no participants reported experiencing life-threatening side effects. Furthermore, 33 participants indicated that they had not experienced any side effects from their diabetes therapy, shown in Fig. 3.

Severity assessment of ADRs

The severity of adverse drug reactions (ADRs) was assessed among participants who reported experiencing side effects from their diabetes therapy. Severity Level Assessment of ADRs is depicted in Table 1.

Table 1: Severity Level Assessment of ADRs

Severity	*Levels*	*Numbers of cases*	*% Patients*
Mild	Level 1	47	31.33
	Level 2	12	8
	Level 3	23	15.33
Moderate	Level 4a	20	13.34
	Level 4b	13	8.67
	Level 5	2	1.33
Severe	Level 6	0	00
	Level 7	0	00
None	-	33	22
Total	-	150	100

Table 2: Causality Assessment Using WHO-UMC Scale

Types of causality	*Numbers of adrs*	*Percentage*
Certain	12	10.26
Probable	37	31.62
Possible	58	49.57
Unlikely	6	5.13
Conditional	3	2.56
Unassessable	1	0.86
Total	117	100

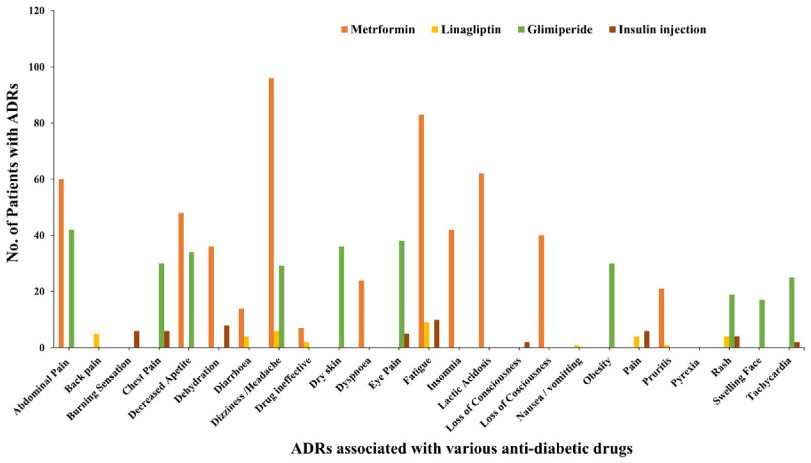

Figure 4: ADRs Associated with Drugs

Table 3: Management of adverse drug reactions

Management of adverse drug reactions	*No. of patients*
Modification Of Dosage	17
Discontinuation of Medication if Necessary	24
Switching to a different Medication	9
Home Remedy	67
None	33

Table 4: Number of ADRs reported globally

Continents	*No. of patients*				*Total*
	Metformin	*Glimepiride*	*Linagliptin*	*Insulin*	
Africa	2241	675	30	252	3198
America	51917	3208	5204	9847	70176
Asia	39558	8416	3752	3849	55575
Europe	29757	3462	1856	1812	36887
Oceania	1425	92	120	235	1872

Causality assessment using WHO-UMC scale

The causality assessment of adverse drug reactions (ADRs) was conducted using the WHO-UMC (World Health Organization-Uppsala Monitoring Centre) scale. This scale allows for the systematic evaluation of the likelihood that a reported adverse event is related to the administration of a particular medication shown in Table 2.

Adverse drug reactions (ADRs) associated with drugs

The analysis of adverse drug reactions (ADRs) associated with Metformin, Linagliptin, Glimepiride and Insulin injection revealed several reported adverse effects among the study participants as shown in Fig. 4. These adverse effects underscore the necessity for meticulous monitoring and personalized treatment strategies for patients using these medications to manage diabetes. The complexity of diabetes management is compounded by the potential for serious side effects, making it critical to tailor treatment to each patient's unique needs and circumstances.[6,7] Key considerations include: Regular Monitoring; Patient Education; Dose Adjustments; Lifestyle Modifications; Multidisciplinary approaches; Alternative Therapies etc. By integrating these strategies, healthcare providers can optimize diabetes management, enhance patient outcomes, and minimize the risks associated with these essential medications. This approach ensures that each patient receives comprehensive, personalized care that addresses their unique needs and circumstances.[8-10]

Management of adverse drug reactions (ADRs)

The analysis of management strategies for adverse drug reactions (ADRs) revealed several approaches employed by healthcare providers and are included in Table 3.

Number of ADRs reported globally

This summary provides an overview of the reported adverse drug reactions (ADRs) associated with Metformin, Glimepiride, Linagliptin, and Insulin Injection globally, highlighting the distribution of reported ADRs across different continents as shown in Table 4.

Conclusion

The findings revealed a moderate level of knowledge among patients regarding diabetes, with notable gaps in understanding certain aspects such as risk factors, complications, and treatment options. Moreover, the identification of adverse drug reactions associated with diabetic medications highlighted the importance of pharmacovigilance in ensuring patient safety and optimizing therapeutic outcomes. Commonly reported ADRs included gastrointestinal disturbances, hypoglycaemia, and allergic reactions, underscoring the need for vigilant monitoring

and patient education regarding medication side effects. Furthermore, our study identified several adverse drug reactions (ADRs) reported by patients receiving treatment for diabetes, highlighting the importance of pharmacovigilance in ensuring medication safety and optimizing patient care.

In conclusion, this study contributes valuable insights into diabetes management knowledge, attitudes, and practices among pharmacy students, while also shedding light on the importance of pharmacovigilance in identifying and mitigating adverse drug reactions associated with diabetic medications. By addressing the identified gaps and embracing future prospects, one can work towards optimizing diabetes care, enhancing medication safety, and ultimately improving the quality of life for individuals living with diabetes.

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Approval and Consent to Participate

Physically verbal interaction with the patients willing to participate in the survey were provided with the study questionnaire online and their consent was taken as approved by the ethical committee, ITS-CDSR, Ghaziabad, India (ECR/697/Inst/UP/2014/RR-21). This research was conducted on humans by the Helsinki Declaration of 1975, as revised in 2013.

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Competing Interests Statement

The authors declare no conflict of interests.

Author contribution

Study conception and design: SM. Sagarika Majhi; *Data collection:* HS. Himanshu Singh, DS. Dheeraj Sahu, MT. Medha Tyagi; *Analysis and interpretation of results:* SM. Sagarika Majhi, HS. Himanshu Singh, DS. Dheeraj Sahu; *Draft manuscript:* MT. Medha Tyagi, HK. Harshit Kumar, ES. Ena Singh.

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