Rathore et al. Scr Med. 2026 Mar-Apr;57(2):295-301. DOI:10.5937/scriptamed57-60113

ORIGINAL ARTICLE

Pharmacovigilance and Adverse Drug Reactions in Type 2 Diabetes Mellitus: Insights From a Tertiary Care Hospital in Central India

Rajveer Singh Rathore,[1] Akash Vishwe,[1] Susheel Kumar,[2] Lokendra Sharma,[2] Alka Bansal,[2] Punam Jakhar[2]

Abstract

Background/Aim: Type 2 diabetes mellitus (T2DM) is a chronic condition that frequently necessitates prolonged pharmacological treatment and is frequently complicated by polypharmacy and comorbid conditions. These components elevate the likelihood of adverse drug reactions (ADRs) that demand active pharmacovigilance to enhance drug safety and patient adherence. This study aimed to generate actionable insights to improve prescribing practices, strengthen pharmacovigilance infrastructure and enhance patient safety in chronic disease management by systematically evaluating the incidence, severity, causality and preventability of ADRs in T2DM patients attending a tertiary care hospital in Central India.

Methods: A prospective observational study was carried out over duration of 12 months at a tertiary care teaching hospital located in Central India. A total of 964 adults diagnosed with type 2 diabetic patients were enrolled. Data on demographics, comorbidities and drug prescriptions were recorded. Adverse events were identified through clinical evaluation and assessed for causality, severity and preventability. Chi-square tests and logistic regression were utilised for statistical evaluation. Binary logistic regression determined independent predictors of adverse events, with findings presented as adjusted odds ratios (OR) and 95 % confidence intervals (CI).

Results: Among 964 patients (mean age 46.9 ± 12.4 years), the highest prevalence was observed in the 41–50 age group (32.6 %). Adverse events were reported in 231 patients (23.96 %). Hypoglycaemia (notably with sulfonylureas, $p < 0.01$) and gastrointestinal disturbances (mainly with metformin) were the most common adverse event. The Naranjo assessment categorised 62.3 % of adverse events as probable, with 89.1 % classified as mild-to-moderate in severity. According to Schumock and Thornton criteria, 54.5 % of adverse events were preventable. Logistic regression revealed polypharmacy (OR = 2.73, $p < 0.01$) and kidney dysfunction (OR = 2.21, $p < 0.01$) as significant predictors of adverse events.

Conclusion: This research underscores a significant prevalence of adverse events in patients with T2DM, with many being preventable. Sulfonylureas and metformin were frequently implicated. Strengthening pharmacovigilance practices and promoting rational drug use are necessary for improving patient safety and therapeutic results in diabetes management.

Key words: Diabetes mellitus, type 2; Pharmacovigilance; Drug-related side effects and adverse reactions; Naranjo scale; Drug safety; Polypharmacy.

1. Department of Pharmacology, Index Medical College Hospital and Research Centre, Indore, Madhya Pradesh, India.
2. Department of Pharmacology, RUHS College of Medical Sciences, Jaipur, Rajasthan, India.

Citation:
Rathore RS, Vishwe A, Kumar S, Sharma L, Bansal A, Jakhar P. Pharmacovigilance and adverse drug reactions in type 2 diabetes mellitus: insights from a tertiary care hospital in Central India. Scr Med. 2026 Mar-Apr;57(2):295-301.

Corresponding author:
RAJVEER SINGH RATHORE
E: rsr3579@gmail.com
T: 9782711134

Received: 12 July 2025
Revision received: 6 October 2025
Accepted: 6 October 2025

Introduction

Type 2 diabetes mellitus (T2DM) is a persistent and progressively worsening metabolic disorder that is becoming increasingly prevalent across the globe. In 2021, it impacted around 537 million adults, a figure anticipated to rise to 783 million through 2045, with the most significant growth forecast in developing nations, including India.[1] The complexity of managing T2DM, often compounded by comorbid conditions like hypertension, dyslipidaemia and cardiovascular disease, necessitates long-term polypharmacy significantly elevating the risk of adverse drug reactions (ADRs).[2]

ADRs in T2DM patients can lead to poor adherence, diminished quality of life and increased healthcare burden. Hypoglycaemia, gastrointestinal (GI) disturbances, weight gain and oedema are some of the most frequently encountered ADRs, particularly with sulfonylureas, biguanides and insulin. Despite established guidelines, inappropriate prescribing and lack of individualised drug pharmacovigilance is essential for the post-marketing surveillance of drugs by detecting, assessing and preventing ADRs. Although clinical trials yield safety data, they frequently lack the generalisability necessary for clinical practice owing to restricted sample size, short duration and stringent inclusion criteria. In contrast; pharmacovigilance systems capture data on broader populations, enabling early signal detection and ongoing safety evaluation.[3, 4]

Standardised tools such as the Naranjo ADR Probability Scale and the Hartwig and Siegel Severity Scale offer validated methods for classifying ADRs by causality and severity, respectively.[5, 6] Nonetheless, the incorporation of these techniques into standard clinical monitoring remains inconsistent, especially within Indian healthcare environment. Moreover, few region-specific studies from Central India have evaluated the prevalence, characteristics and preventability of ADRs in T2DM patients using structured pharmacovigilance methodologies.[7]

This study addresses these gaps by systematically evaluating the incidence, severity, causality and preventability of ADRs in T2DM patients attending a tertiary care hospital in Central India. By applying validated scales and statistical analysis, the study aimed to generate actionable insights to improve prescribing practices, strengthen pharmacovigilance infrastructure and enhance patient safety in chronic disease management.

Methods

A prospective, single-centre observational pharmacovigilance cohort study was conducted from 1 January to 31 December 2023, in the outpatient departments of Pharmacology and Medicine at Index Medical College Hospital and Research Centre (IMCHRC), Indore. IMCHRC is a tertiary-care teaching hospital that serves both urban and rural communities of Central India. Methodological reporting followed the STROBE recommendations for observational studies.

Based on an anticipated ADR incidence of 22 % in treated Indian T2DM populations, with k (N of predictors) = 12 and events per variables = 15, the minimum required sample was calculated to be 818. To allow for potential attrition, the recruitment target was set at ≥ 941 participants.[8]

Participants and recruitment

Consecutive adults (≥ 20 years) diagnosed with T2DM who had received at least one antidiabetic medication for ≥ 3 months were screened during routine clinic visits.

Inclusion criteria were: Age ≥ 20 years; Diagnosis of T2DM; On pharmacological therapy for ≥ 3 months; Written informed consent.

Exclusion criteria were: Type 1 or gestational diabetes; Terminal illness or critical clinical condition; Cognitive impairment precluding consent; Refusal to participate.

Data sources and collection procedures

Data were collected utilising a structured case report form (CRF) encompassing demographic details (age, sex, address), clinical characteristics (diabetes duration, comorbidities, body mass index - BMI), a detailed medication history (generic name, formulation, strength, route, daily dose and duration) and baseline laboratory parameters (fasting plasma glucose, HbA_1c, serum creatinine, estimated glomerular filtration rate

and lipid profile). Polypharmacy was predefined as the concurrent use of five or more prescription medications, regardless of therapeutic class.

ADR surveillance and classification

Adverse events were actively monitored through a triad of methods: structured patient interviews conducted at baseline and every 4-6 weeks using a bilingual symptom checklist (Hindi/English), targeted clinical examinations by the study physician and systematic review of laboratory parameters to detect biochemical indicators of ADRs, such as abrupt ALT elevations or signs of lactic acidosis.

Every suspected adverse event was independently assessed by Causality Assessment Committee; disagreements were resolved by consensus. The reported adverse events were systematically evaluated for causality using the Naranjo ADR Probability Scale,[9] for severity using the Modified Hartwig and Siegel Scale[10] and for preventability using the Schumock and Thornton criteria.[11]

Primary outcome was occurrence of ≥1 ADR during the 12-month follow-up. While the secondary outcomes included ADR causality category, severity grade, preventability status. Predictor variables included demographic and clinical factors such as age, sex, BMI and duration of diabetes, polypharmacy (yes/no), renal impairment (estimated glomerular filtration rate (eGFR) < 60), hypertension, dyslipidaemia, cardiovascular disease.

Statistical analysis

Data were input into Microsoft Excel and analysed using IBM SPSS version 30.0. Continuous variables were expressed as mean ± SD. Categorical variables were characterised by frequency and percentage. Comparisons between groups employed t-tests or ANOVA for continuous data and χ^2 or Fisher's exact test for categorical variables. Binary logistic regression determined independent predictors of adverse events, with findings presented as adjusted odds ratios (OR) and 95 % confidence intervals (CI). The model's fit was evaluated using the Hosmer–Lemeshow test and Nagelkerke R^2. The threshold for statistical significance was established at $p < 0.05$. No interim analyses were performed.

Results

The cohort comprised 964 patients (mean ± SD age 46.9 ± 12.4 years, 56.3 % men). The 41–50-age group represented the single largest age stratum (32.6 %). Mean duration of diagnosed diabetes was 7.8 ± 5.9 years; 68.4 % of patients had ≥ 1 macro- or micro-vascular comorbidity, most frequently hypertension (58.7 %) and dyslipidaemia (44.1 %). Polypharmacy (≥ 5 concurrent medicines) was present in 42.8 % of patients. Middle-age predominated. The 41–50-year group accounted for one-third of patients. The male-to-female ratio was 1.3:1 (Table 1).

Table 1: Demographic characteristics of patients

Variable	n (%)
Age (years) (mean SD)	46.9 ± 12.4
20–30 years	97 (10.1)
31–40 years	179 (18.6)
41–50 years	314 (32.6)
51–60 years	213 (22.1)
61–70 years	161 (16.7)
Sex	
Male	549 (56.3)
Female	415 (43.7)

Incidence and spectrum of adverse events

Overall, 231 patients (23.96 %) experienced at least one adverse drug reaction (ADR) during the 12-month observation period. GI events (39.0 %) and hypoglycaemia (32.5 %) predominated.

Metformin accounted for the greatest absolute number of adverse events (n = 75), almost exclusively dyspepsia and diarrhoea. Sulfonylureas (glimepiride) produced the highest proportion of clinically significant hypoglycaemia (88.5 % of 61 events; $\chi^2 = 17.4$, $p < 0.01$ versus other classes). Sodium-glucose cotransporter 2 (SGLT-2) and dipeptidyl peptidase 4 (DPP-4) inhibitors generated fewer events overall but showed the expected organ-specific profiles (urogenital infections and peripheral oedema, respectively) (Table 2). Frequency of adverse events by antidiabetic drug class is presented in Figure 1.

Table 2: Adverse events by antidiabetic drug class

Drug class (index agent)	**Adverse events** (n)	**Leading clinical event(s)**
Biguanide (metformin)	75	Dyspepsia, diarrhoea, nausea
Sulfonylurea (glimepiride)	61	Hypoglycaemia
DPP-4 inhibitor (vildagliptin)	21	Peripheral oedema
DPP-4 inhibitor (sitagliptin)	15	Hypoglycaemia, weight gain
SGLT-2 inhibitor (dapagliflozin)	13	Constipation
α-Glucosidase inhibitor (voglibose)	18	Dyspepsia, diarrhoea
TZD (pioglitazone)	9	Pedal oedema
Human insulin	19	Hypoglycaemia, local allergy

DPP-4: dipeptidyl peptidase 4; TZD: thiazolidinedione; SGLT-2: sodium-glucose cotransporter 2;

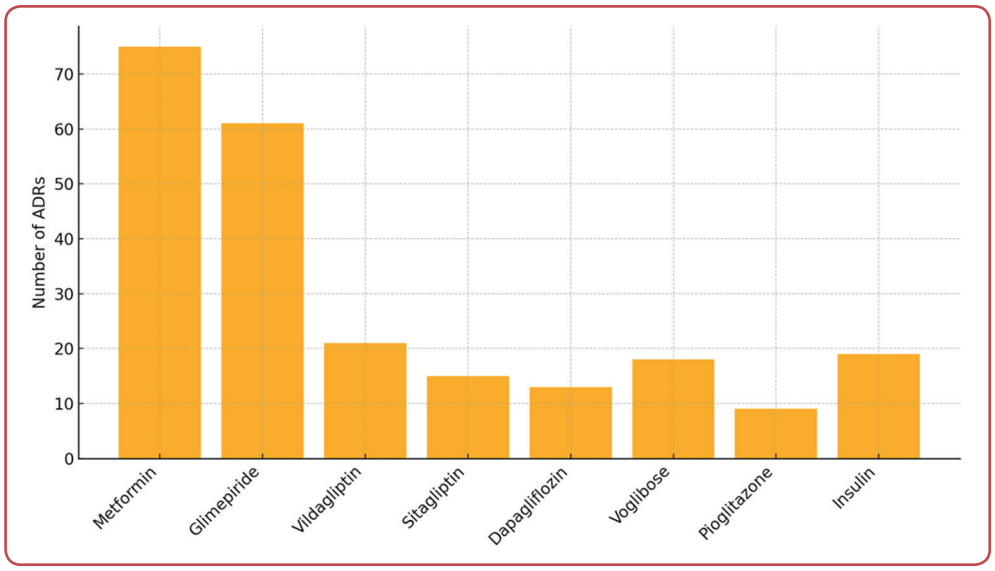

Figure 1: Frequency of adverse events by antidiabetic drugs

Causality, severity and preventability

Using the Naranjo algorithm, 62.3 % of adverse events were classified probable, 29.0 % possible and 8.7 % doubtful (Table 3). Severity grading by the Modified Hartwig–Siegel scale indicated that 89.1 % were mild to moderate (Levels 1-4); only two severe reactions (0.9 %, both insulin-related hypoglycaemic seizures) required hospital admission

On the Schumock-Thornton criteria, 54.5 % were definitely or probably preventable, largely attributable to avoidable drug–drug interactions or lack of dose adjustment in renal impairment. Most reactions were possible (83.6 %); 7.4 % were probable; none were definite as per Causality assessment scale. The severity of adverse events was assessed as 88.7 % were mild, 10.4 % moderate and < 1 % severe. The preventability (Schumock-Thornton) of adverse events showed 54.5 % were considered preventable (Table 3).

Table 3: Causality, severity and preventability profiles of observed adverse events

Domain	**Category**	**n (%)**
Causality	Possible	193 (83.6)
	Probable	17 (7.4)
	Doubtful	21 (9.1)
Severity	Mild	207 (88.7)
	Moderate	24 (10.4)
	Severe	2 (0.9)
Preventability	Definitely / probably preventable	126 (54.5)
	Not preventable	105 (45.5)

Determinants of adverse event risk

Univariable analyses showed higher adverse event rates in participants with polypharmacy (31.5 % vs 17.2 %, $\chi^2 = 28.6$, $p < 0.001$) and in those with eGFR < 60 mL min^{-1} 1.73 m^{-2} (30.9 % vs 21.0 %, $\chi^2 = 8.9$, $p = 0.003$). No statistically significant changes were observed based on sex (25.0 %

men vs 22.4 % women, $\chi^2 = 1.2$, p = 0.27) or by age group (< 60 vs ≥ 60 years, $\chi^2 = 2.7$, p = 0.10).

In the multivariable logistic model (Table 4), polypharmacy remained the strongest independent predictor of adverse events (adjusted OR 2.73, 95 % CI 1.85–4.01; p < 0.01), followed by renal impairment (OR 2.21, 95 % CI 1.41–3.47; p < 0.01). The model exhibited satisfactory calibration (Hosmer–Lemeshow, p = 0.58) and accounted for 22 % of the variance in outcomes (Nagelkerke R^2). Binary logistic regression identified two independent risk factors: polypharmacy and renal impairment.

Table 4: Multivariable logistic regression identifying independent predictors of adverse events

Predictor	Adjusted OR (95 % CI)	p-value
Polypharmacy (≥ 5 drugs)	2.73 (1.85-4.01)	< 0.01
Renal impairment (eGFR < 60 mL min^{-1} 1.73 m^{-2})	2.21 (1.41-3.47)	< 0.01

eGFR: estimated glomerular filtration rate; OR: odds ratio; CI: confidence interval;

These data demonstrate that nearly one in four treated patients experienced an adverse event, most often mild GI symptoms with metformin or hypoglycaemia with sulfonylureas/insulin. More than half the events were preventable, underscoring the need for stringent pharmacovigilance and rational prescribing in polypharmacy and renal impaired subgroups.

All assumptions for binary logistic regression were tested and met. There was no multicollinearity among predictors (VIF < 2.5), continuous variables showed linearity with the logit (Box-Tidwell p > 0.05) and no influential outliers were detected (Cook's D < 1). The Hosmer-Lemeshow test (p = 0.58) confirmed good model fit, validating the suitability of the regression model.

Discussion

The present pharmacovigilance cohort demonstrates that almost one in four ambulatory adults with T2DM experienced at least one adverse event within 12 months, with hypoglycaemia and metformin-related GI intolerance predominating. These findings confirm the high burden of drug-related morbidity in diabetes care and address the data gap highlighted in earlier, smaller Indian studies that reported adverse event incidences of 13-26 % but lacked power to explore independent predictors.[12]

Sulfonylureas and human insulin together accounted for > 60 % of clinically important events. This aligns with multicentre data showing a two- to three-fold higher risk of symptomatic hypoglycaemia with sulfonylureas compared with DPP-4 inhibitors.[13] Modern, low-dose sulfonylureas may mitigate but do not abolish this risk.[7]

The 32 % share of adverse events attributable to metformin mirrors pooled estimates (25-30 %) from Indian and global cohorts. GI symptoms, although rarely severe, frequently impair adherence and can precipitate therapeutic inertia.

A genital or urinary infection rate of 13-17 % with dapagliflozin in presented cohort concurs with recent Indian series reporting 16-17 % genital mycoses and 3-5 % urinary tract infections.[14] While typically mild, these events reinforce the need for patient counselling on hygiene and early symptom recognition, especially in women and the elderly.

Multivariable analysis revealed a near-threefold rise in adverse event odds with five or more drugs and a twofold rise with eGFR < 60 mL min^{-1} 1.73 m^{-2}. Similar effect sizes have been reported[7] and others, underscoring the pharmacokinetic pharmacodynamics vulnerability conferred by drug burden and impaired clearance.[15]

Presented overall adverse event incidence (23.9 %) sits between the 20 % reported in a South-Indian tertiary centre cohort (n = 200) and the 28 % pooled prevalence from a recent meta-analysis of Asian studies.[16] Differences likely reflect heterogeneity in surveillance intensity, drug mix and patient comorbidity. The pattern of events is nevertheless consistent: sulfonylurea/insulin-related hypoglycaemia, metformin GI intolerance and SGLT-2 inhibitor GU infections form the "classic triad" of adverse events in modern glucose-lowering therapy.[17]

Structured medication review, particularly in patients with polypharmacy or renal impairment, could have preventable adverse events, as 54.5 % of events in this cohort were classified definitely/probably preventable. Preferential use of low-hy-

poglycaemia agents (eg DPP-4 or GLP-1 receptor agonists) for high-risk patients may reduce emergency visits and hospitalisations linked to sulfonylurea/insulin hypoglycaemia.

Targeted counselling on SGLT-2 inhibitor hygiene and early UT/GU infection management should accompany prescriptions, balancing these manageable risks against proven cardiovascular and renal benefits.[14] Integration of smartphone apps, automated electronic medical-record prompts and continuing medical-education workshops could increase spontaneous ADR reports and help PvPI refine safety signals sooner.[17]

Strengths and limitation of the study

Strengths include prospective design, robust sample size exceeding a priori power, use of validated causality/severity/preventability tools and adjustment for major confounders. Limitations encompass single-centre scope, potential under-detection of subclinical events between visits, reliance on patient recall for some symptoms and absence of pharmacogenomics data that could explain inter-individual susceptibility. Results may therefore underestimate true adverse event incidence and should be generalised cautiously beyond similar tertiary-care settings.

Conclusion

This study reinforces that adverse events remain a frequent and partly preventable threat to optimal diabetes care. Hypoglycaemia with insulin or sulfonylureas, GI intolerance caused by metformin and genitourinary tract infections due to SGLT-2 inhibitors account for most events. Systematic medication review, renal-function-guided dosing and a culture of proactive ADR reporting are pragmatic steps to enhance patient safety in routine practice. Future multi centric studies incorporating real-time electronic pharmacovigilance and pharmacogenomics profiling are warranted to tailor therapy and minimise harm further.

Ethics

The protocol was approved by the Institutional Ethics Committee of Malwanchal University decision No: MU/Research/EC/Ph.D./2021/93a, dated 23 November 2021. Written informed consent was acquired from all subjects. Confidentiality was maintained. The study conformed to the Declaration of Helsinki (2013) and ICH-GCP guidelines.

Acknowledgement

We sincerely thank all the study participants for their valuable time and efforts.

Conflicts of interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data access

The datasets generated and analysed during the current study are not publicly available due to institutional regulations and confidentiality agreements with the participating patients. All data were anonymised prior to analysis to ensure participant privacy and compliance with ethical standards.

Author ORCID numbers

Rajveer Singh Rathore (RSR):
0000-0003-3903-2600
Akash Vishwe (AV):
0000-0003-4873-8226
Susheel Kumar (SK):
0000-0003-3560-718X
Lokendra Sharma (LS):
0000-0001-8949-9079
Alka Bansal (AB):
0000-0002-0289-5640

Punam Jakhar (PJ):
0000-0002-5050-8473

Author contributions

Conceptualisation: RSR, AV, SK
Methodology: RSR, AV, SK
Formal analysis: RSR, SK, LS, PJ
Investigation: RSR, SK, LS, PJ
Data curation: RSR, AV, AB
Writing - original draft: RSR, AV, AB, PJ
Writing - review and editing: RSR, SK, LS.

References

1. Kumari N, Motghare VM, Dash K, Sen S. Women with diabetes in South East Asia and associated risk factors: a review. In: Shiomi N, Ed. Advances in metabolic syndrome and hypoglycemia. London, UK: IntechOpen, 2025; doi: 10.5772/intechopen.1009484.
2. Johansson KS, Jimenez-Solem E, Petersen TS, Christensen MB. Increasing medication use and polypharmacy in type 2 diabetes: the Danish experience from 2000 to 2020. Diabetes Care. 2024;47(12):2120-7. doi: 10.2337/dc24-0011.
3. Sahoo J, Mohanty S, Kundu A, Epari V. Medication adherence among patients of type II diabetes mellitus and its associated risk factors: a cross-sectional study in a tertiary care hospital of eastern India. Cureus. 2022 Dec 29;14(12). doi: 10.7759/cureus.33074.
4. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR, Pirmohamed M. Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. PLoS one. 2009 Feb 11;4(2):e4439. doi: 10.1371/journal.pone.0004439.
5. Kumaraswamy M, Mohan A, Chonari TA, Dahim M. Adverse drug reaction tools used in causality assessment. Indian J Pharm Pract. 2023;16(4):281–8. doi: 10.5530/ijopp.16.4.50.
6. Khan Z, Karataş Y, Kıroğlu O. Evaluation of adverse drug reactions in pediatric patients: a retrospective study in Turkish hospital. Front Pharmacol. 2021 Nov 12;12:786182. doi: 10.3389/fphar.2021.786182.
7. Inamdar SZ, Kulkarni RV. Drug related problems in elderly patients with type 2 diabetes mellitus. J Diabetol. 2016 Jan 1;7(1):1. doi: 10.4103/2078-7685.198422.
8. Reghunath SR, Chackochan A, Thunga G, Acharya DU, Shivashankara KN, Ravindra Prabhu A, et al. Prevalence and predictors of adverse events associated with dipeptidyl peptidase-4 (DPP-4) inhibitors in type 2 diabetic patients: a cross-sectional Study. Clin Med Insights Endocrinol Diabetes. 2024 Oct 23;17:11795514241288645. doi: 10.1177/11795514241288645.
9. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45. doi:10.1038/clpt.1981.154.
10. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49(9):2229-32. doi: 10.1093/ajhp/49.9.2229.
11. Patel SR, Gupta SD, Patel KP, Malhotra SD, Patel PR. Analysis of adverse drug reactions in a tertiary care emergency medicine department: prevalence, preventability and reporting. Int J Basic Clin Pharmacol. 2018;7(9):1787–93. doi: 10.18203/2319-2003.ijbcp20183490.
12. 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. doi: 10.4103/ijmr.IJMR_109_16.
13. Aravind SR, Ismail SB, Balamurugan R, Gupta JB, Wadhwa T, Loh SM, et al. Hypoglycemia in patients with type 2 diabetes from India and Malaysia treated with sitagliptin or a sulfonylurea during Ramadan: a randomized, pragmatic study. Curr Med Res Opin. 2012 Aug;28(8):1289-96. doi: 10.1185/03007995.2012.707119.
14. Unnikrishnan AG, Kalra S, Purandare V, Vasnawala H. Genital infections with sodium glucose cotransporter-2 inhibitors: occurrence and management in patients with type 2 diabetes mellitus. Indian J Endocrinol Metab. 2018 Nov-Dec;22(6):837-842. doi: 10.4103/ijem.IJEM_159_17.
15. Harris GA, Hirschfeld LR, Gonzalez MI, Pritchard MC, May PC. Revisiting the therapeutic landscape of tauopathies: assessing the current pipeline and clinical trials. Alzheimers Res Ther. 2025 Jun 4;17(1):129. doi: 10.1186/s13195-025-01775-x.
16. Baye AM, Fanta TG, Siddiqui MK, Dawed AY. The genetics of adverse drug outcomes in type 2 diabetes: a systematic review. Front Genet. 2021 Jun 14;12:675053. doi: 10.3389/fgene.2021.675053.
17. Kalaiselvan V, Srivastava S, Singh A, Gupta SK. Pharmacovigilance in India: present scenario and future challenges. Drug Safety. 2019 Mar 7;42(3):339-46. doi: 10.1007/s40264-018-0730-7.