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COMPARATIVE ASSESSMENT OF ADVERSE DRUG REACTIONS IN TYPE 2 DIABETES MELLITUS PATIENTS RECEIVING MONOTHERAPY VERSUS COMBINATION THERAPY: A PROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder that almost always demands lifelong pharmacotherapy, and as the disease advances patients are frequently escalated from single-agent to multi-agent regimens. Both approaches carry a risk of adverse drug reactions (ADRs), yet real-world comparative safety data remain limited. **Objectives:** To compare the pattern, severity and outcome of ADRs in T2DM patients receiving monotherapy versus combination therapy in a tertiary care hospital. **Methods:** A prospective, comparative, observational study was carried out over four months in the general medicine and surgery wards of a tertiary care teaching hospital. Forty consenting adults with T2DM were enrolled by universal sampling and divided equally into a monotherapy group (n=20) and a combination therapy group (n=20). ADRs were captured through case-sheet review, patient interview and treatment-chart analysis, and were graded for severity using the modified Hartwig and Siegel scale. Data were summarised as frequencies and percentages, and the two groups were compared using the chi-square (or Fisher exact) test, with $p<0.05$ taken as

significant. **Results:** The cohort was predominantly elderly (50% aged 60 years or above) with a slight male preponderance (52.5%). A total of 43 ADRs were recorded among the 40 patients. Hypoglycaemia was by far the commonest reaction (90.70%), occurring in 46.51% of events in the monotherapy group and 44.19% in the combination group. Seizure and hypokalaemia (2.33% each) were confined to monotherapy, whereas dizziness and vomiting (2.33% each) occurred only with combination therapy. Overall, monotherapy accounted for a marginally higher share of ADRs (51.16% versus 48.84%). Most reactions were moderate in severity (95.3%), and every reaction resolved completely (100% recovery). **Conclusion:** Hypoglycaemia dominated the safety profile of antidiabetic therapy and was somewhat more frequent with single-agent regimens, underscoring the need for individualised dosing, structured glucose monitoring and pharmacist-led counselling. Combination therapy produced a slightly wider but milder spectrum of reactions, supporting its rational use when tighter glycaemic control is required.

KEYWORDS: Adverse drug reactions, Antidiabetic agents, Combination therapy, Hypoglycaemia, Monotherapy, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder that arises from a defect in insulin secretion, insulin action, or both, and the resulting insulin deficiency produces sustained hyperglycaemia together with disturbances of carbohydrate, fat and protein metabolism.[1,2] As the disease runs its course, persistent hyperglycaemia inflicts progressive tissue and vascular damage, giving rise to the familiar spectrum of complications such as retinopathy, neuropathy, nephropathy, cardiovascular disease and non-healing ulceration.[3,4,5] Diabetes is therefore best understood not as a single illness but as a group of heterogeneous disorders united by chronic elevation of blood glucose.

Broadly, diabetes is classified into type 1 (insulin-dependent) and type 2 (non-insulin-dependent) disease, with gestational diabetes representing hyperglycaemia first recognised during pregnancy.[6] Type 2 diabetes mellitus (T2DM) accounts for more than ninety per cent of all cases and stems from a combination of progressively impaired insulin secretion by the pancreatic beta-cells against a background of insulin resistance in skeletal muscle, liver and adipose tissue.[7,8] Overt hyperglycaemia is typically preceded by a prediabetic phase characterised by impaired fasting glucose, impaired glucose tolerance, or a glycated

haemoglobin between 5.7 and 6.4 per cent, and annual conversion from prediabetes to frank diabetes ranges from three to eleven per cent.[9,10]

The pathophysiology of T2DM is multifactorial. At least eight distinct abnormalities, collectively described as the 'ominous octet', contribute to impaired glucose homeostasis: reduced insulin secretion, increased glucagon secretion, heightened hepatic glucose output, neurotransmitter dysfunction, increased renal glucose reabsorption, reduced peripheral glucose uptake, accelerated lipolysis and diminished incretin effect.[11,12] Vascular insulin resistance and chronic low-grade inflammation are now added to this framework, further widening the therapeutic target set.

Improving glycaemic control is central to preventing diabetes-related complications, and a range of anti-hyperglycaemic agents is available to achieve this goal. However, roughly sixty per cent of patients fail to reach their therapeutic targets on a single agent, making dual or triple therapy a practical necessity for many.[13] Escalation to multiple drugs, while often essential, increases the likelihood of adverse drug reactions (ADRs) through pharmacokinetic interaction, pharmacodynamic overlap and cumulative toxicity. Monotherapy generally presents a leaner safety profile, yet certain single agents—particularly sulfonylureas and insulin—carry a substantial hypoglycaemic risk when doses are not carefully individualised.

Despite the widespread use of both strategies, comparative real-world data that quantify and characterise the ADR profiles of these regimens remain sparse, which hampers evidence-based, patient-specific decision-making. The present study was therefore designed to compare the frequency, pattern, severity and outcome of ADRs in T2DM patients receiving monotherapy versus combination therapy in a tertiary care setting, with the aim of strengthening rational prescribing and pharmacovigilance practice.

Review of literature

Mukadam and colleagues, in a retrospective analysis of 282 ADR reports at a monitoring centre, found that most reactions were linked to the oral route (79.43%), were minor in severity (68.44%) and were of probable causality (91.84%), with antimicrobials the most frequently implicated class; vomiting and rash were the commonest symptoms.[14] Ramnath and co-workers, reviewing 634 ADRs over three years in South Kerala, reported skin and appendages as the most affected system and antimicrobials—especially beta-lactams—as the leading culprits, with a median time to onset of four days.[15] Sen and colleagues analysed

sixty reported ADRs at a tertiary care hospital and observed that patients aged 41–50 years were most often affected, that cutaneous reactions predominated, and that the majority of reactions were non-serious, moderate and treatable with early intervention, while under-reporting remained the principal limitation.[16]

These reports consistently identify under-reporting and the need for active surveillance as recurring themes, and they establish hypoglycaemia and antimicrobial-related reactions as prominent contributors to the ADR burden. What is less well characterised is a direct, prospective comparison of monotherapy and combination therapy within a single T2DM cohort—the gap the present study seeks to address.

AIM AND OBJECTIVES

The aim of this study was to evaluate and compare the adverse drug reactions occurring in type 2 diabetic patients on monotherapy versus combination therapy in a tertiary care teaching hospital. The specific objectives were: (i) to compare the pattern and frequency of ADRs between the two treatment groups; and (ii) to evaluate the severity and outcomes of the ADRs recorded in each group.

MATERIALS AND METHODS

Study design and setting

A prospective, comparative, observational study was conducted over a period of four months in the departments of general medicine and surgery of S. N. Medical College and H. S. K. Hospital and Research Centre, Bagalkot, a tertiary care teaching hospital.

Sampling method and sample size

A universal (total enumeration) sampling technique was employed. A total of forty patients who satisfied the eligibility criteria and provided written informed consent were enrolled during the study period. Of these, twenty patients were receiving monotherapy and twenty were receiving combination therapy.

Eligibility criteria

Patients were included if they had a confirmed diagnosis of T2DM, were between 20 and 95 years of age, were currently maintained on stable monotherapy or combination therapy, and were willing to provide informed consent. Patients with type 1 diabetes, those with a terminal illness or severe psychiatric condition, and pregnant or lactating women were excluded.

Sources of data

Information was drawn from case sheets, direct patient interviews, laboratory data and patient treatment charts. Data were documented using a purpose-designed patient profile form, an adverse drug reaction reporting form, the patient consent form, the yellow card, and the modified Hartwig and Siegel scale for severity assessment.

Study procedure

After ethics committee approval, patients admitted to the medicine and surgery wards were prospectively identified. For each enrolled patient a detailed review of the complete medication record was carried out on the first day and followed until discharge. Case records—comprising history, diagnosis, physician order sheets, nursing administration records, progress notes, laboratory investigations and other diagnostic reports—were reviewed for drug interactions, therapeutic duplication, adverse reactions and medication errors. Suspected interactions and reactions were verified against the CIMS database (cimsasia.com) and cross-checked with MICROMEDEX (version 2), the Drug Today handbook and the Drug Digest resource. Whenever a pharmacist intervention was identified, the relevant details were transferred from the patient profile form to the pharmacist intervention form.

Severity assessment

The severity of each documented ADR was graded as mild, moderate or severe using the modified Hartwig and Siegel scale, and the eventual outcome of every reaction was recorded as recovered, continuing, unknown or other.

Statistical analysis

Data were entered and analysed using IBM SPSS Statistics. Demographic and clinical variables were summarised using descriptive statistics and expressed as frequencies and percentages. Because all study variables were categorical, between-group comparisons of ADR pattern and severity were performed using the Pearson chi-square test, with the Fisher exact test applied where expected cell counts were small. A two-tailed p-value of less than 0.05 was regarded as statistically significant. Given the modest sample size, these inferential results are reported as exploratory and are interpreted alongside the descriptive findings.

Ethical approval

Sl.	Age	Gender	Drug(s)	Dose	ADR	Therapy

No.						type
1	50	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
2	46	F	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
3	68	M	Sitagliptin, Metformin, Glimepiride	50 mg, 500 mg, 2 mg	Hypoglycaemia	Combination
4	93	F	Metformin, Glimepiride	500 mg, 2 mg	Hypoglycaemia	Combination
5	35	F	Glimepiride, Voglibose, Metformin	2 mg, 0.2 mg, 500 mg	Hypoglycaemia	Combination
6	30	M	Linagliptin	5 mg	Hypoglycaemia	Combination
7	62	M	Gliclazide, Metformin	50 mg, 500 mg	Hypoglycaemia, dizziness	Combination
8	52	M	Insugen 30% regular + 70% NPH	A/S/S	Hypoglycaemia	Combination
9	70	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
10	84	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
11	55	F	Injection Isophane	A/S/S	Hypoglycaemia	Monotherapy
12	40	M	Pioglitazone, Glimepiride	15 mg, 2 mg	Hypoglycaemia	Combination
13	21	F	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
14	54	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
15	67	M	Injection X Sulin	A/S/S	Hypoglycaemia	Monotherapy
16	66	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
17	75	M	Injection X Sulin; Injection Basalog	A/S/S	Hypoglycaemia	Combination
18	50	M	Injection X Sulin	A/S/S	Hypoglycaemia	Monotherapy
19	59	F	Gliclazide, Metformin	50 mg, 500 mg	Vomiting	Combination
20	55	F	Injection Mixtard	A/S/S	Hypoglycaemia	Combination
21	76	F	Metformin, Glimepiride	500 mg, 2 mg	Hypoglycaemia	Combination
22	73	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
23	60	M	Insugen 30% regular + 70% NPH	A/S/S	Hypoglycaemia, seizure	Combination
24	70	F	Linagliptin	1 mg, 5 mg	Hypoglycaemia	Combination
25	78	M	Metformin, Glimepiride	500 mg, 0.5 mg	Hypoglycaemia	Combination
26	47	F	Metformin, Glimepiride	500 mg, 1 mg	Hypoglycaemia	Combination
27	37	F	Injection X Sulin	A/S/S	Hypoglycaemia	Monotherapy
28	85	F	Metformin, Glimepiride	500 mg, 1 mg	Hypoglycaemia	Combination
29	38	F	Injection X Sulin	A/S/S	Hypoglycaemia	Monotherapy
30	57	F	Glimepiride, Pioglitazone, Metformin	2 mg, 15 mg, 500 mg	Hypoglycaemia	Combination

31	55	M	Injection Basalog	A/S/S	Hypoglycaemia	Monotherapy
32	70	F	Glimepiride, Metformin	1 mg, 500 mg	Hypoglycaemia	Combination
33	78	M	Injection Basalog	A/S/S	Hypoglycaemia	Monotherapy
34	56	M	Injection X Sulin	A/S/S	Hypoglycaemia	Monotherapy
35	73	M	Injection H Actrapid	A/S/S	Hypoglycaemia	Monotherapy
36	74	F	Injection Lantus	A/S/S	Hypoglycaemia	Monotherapy
37	39	F	Injection Mixtard	A/S/S	Hypoglycaemia	Monotherapy
38	24	M	Injection X Sulin	A/S/S	Hypoglycaemia	Monotherapy
39	65	F	Linagliptin, Dapagliflozin	5 mg, 10 mg	Hypoglycaemia	Combination
40	67	F	Glimepiride, Metformin	1 mg, 500 mg	Hypoglycaemia	Combination

The study protocol was reviewed and approved by the Institutional Ethics Committee of B. V. V. Sangha's Hanagal Shri Kumareshwar College of Pharmacy, Bagalkot (Reference No. HSKCOP/IEC/25/2, dated 17 June 2025). Written informed consent was obtained from every participant before enrolment, and the investigation was conducted in accordance with the ethical principles laid down by the committee.

RESULTS AND DISCUSSION

A total of forty T2DM patients were studied, equally distributed between monotherapy and combination therapy. The demographic and clinical details of the patients who experienced ADRs, together with their prescribed drugs, doses, therapy type and the observed reaction, are presented in Table 1.

A/S/S = as per sliding scale; NPH = neutral protamine Hagedorn insulin.

Age-wise distribution of the study population

The distribution of patients across age bands revealed clear trends in prescribing. In the monotherapy group the largest share of patients (20%) were aged 60 years or above, followed by the 40–59 year band (17.5%), the 30–39 year band (7.5%) and the 19–29 year band (5%). A comparable gradient was seen in the combination group, where patients aged 60 years or above again predominated (30%), followed by the 40–59 (15%) and 30–39 (5%) bands; no patient in the youngest band received combination therapy. Although both regimens contributed equally to the total sample (50% each), combination therapy was concentrated in the elderly, consistent with the intensified management that longer-standing or poorly controlled disease demands, whereas monotherapy was relatively more common among middle-aged adults (Table 2, Figure 1).

Age group (years)	Monotherapy	Combination therapy	Total
19–29	5% (2)	0% (0)	5% (2)
30–39	7.5% (3)	5% (2)	12.5% (5)
40–59	17.5% (7)	15% (6)	32.5% (13)
≥60	20% (8)	30% (12)	50% (20)
Total	**50% (20)**	**50% (20)**	**100% (40)**

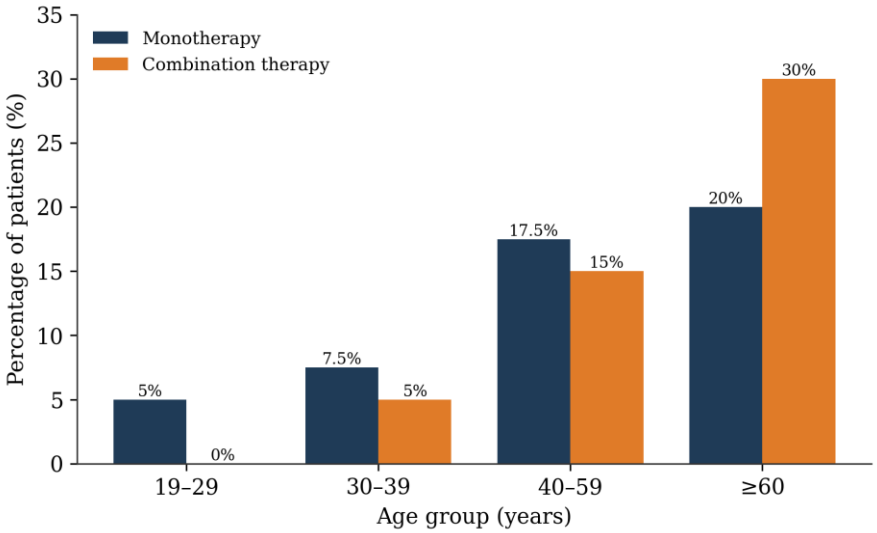

Figure 1: Age group-wise categorisation of the study population.

Gender-wise distribution of the study population

Gender analysis showed that males formed a larger proportion of the monotherapy group (32.5%) than females (22.5%), whereas the combination group contained relatively more females (25%) than males (20%). Across the whole cohort, more patients received monotherapy (55%) than combination therapy (45%), and males slightly outnumbered females overall (52.5% versus 47.5%). The marginally greater use of combination therapy among women may reflect more variable glycaemic control or a physician preference for tighter regimens in this subgroup, although the small numbers preclude firm inference (Table 3, Figure 2).

Gender	Monotherapy	Combination therapy	Total
Male	32.5% (13)	20% (8)	52.5% (21)
Female	22.5% (9)	25% (10)	47.5% (19)
Total	**55% (22)**	**45% (18)**	**100% (40)**

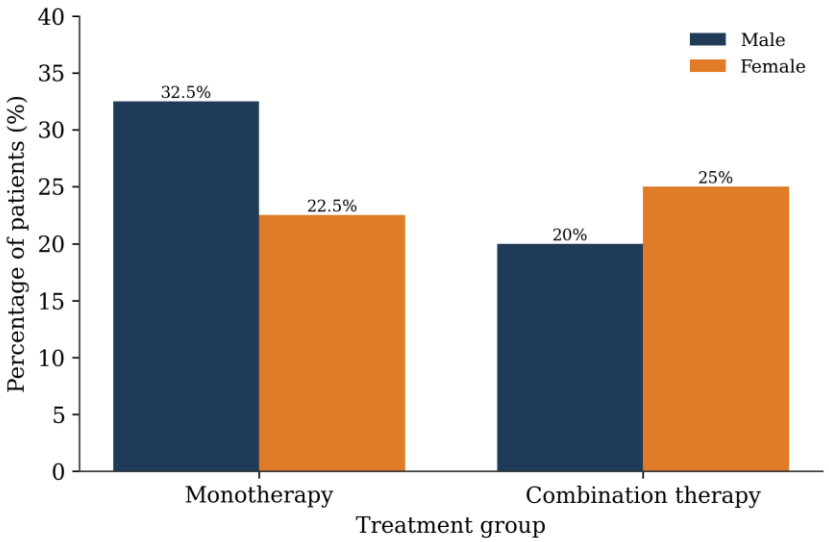

Figure 2: Gender-wise categorisation of the study population.

Oral hypoglycaemic drugs prescribed

Oral antidiabetic agents formed the cornerstone of therapy. Among the oral drugs prescribed, the biguanide metformin and the sulfonylurea glimepiride were used most often, each accounting for 35.29% of oral prescriptions, followed by the dipeptidyl peptidase-4 inhibitor linagliptin (8.82%), the thiazolidinedione pioglitazone (5.88%) and the sulfonylurea gliclazide (5.88%); sitagliptin, voglibose and dapagliflozin each contributed 2.94%. The most frequently prescribed dual combination was metformin plus glimepiride, seen in six patients (15%), which is fully consistent with guideline recommendations positioning metformin as first-line therapy and a sulfonylurea as a common second agent. The prominence of metformin-centred regimens reflects its established efficacy, favourable safety profile and cost-effectiveness (Table 4, Figure 3).

Class of oral agent	Drug prescribed	Number of times prescribed	Percentage (%)
Enhance insulin secretion – Sulfonylureas	Glimepiride	12	35.29
	Gliclazide	2	5.88
Enhance insulin secretion – DPP-4 inhibitors	Linagliptin	3	8.82
	Sitagliptin	1	2.94
Overcome insulin resistance – Biguanides	Metformin	12	35.29
Overcome insulin resistance – Thiazolidinediones	Pioglitazone	2	5.88
Delay carbohydrate absorption – Alpha-glucosidase inhibitors	Voglibose	1	2.94

Promote glucose excretion – SGLT-2 inhibitors	Dapagliflozin	1	2.94
Total		**34**	**100**

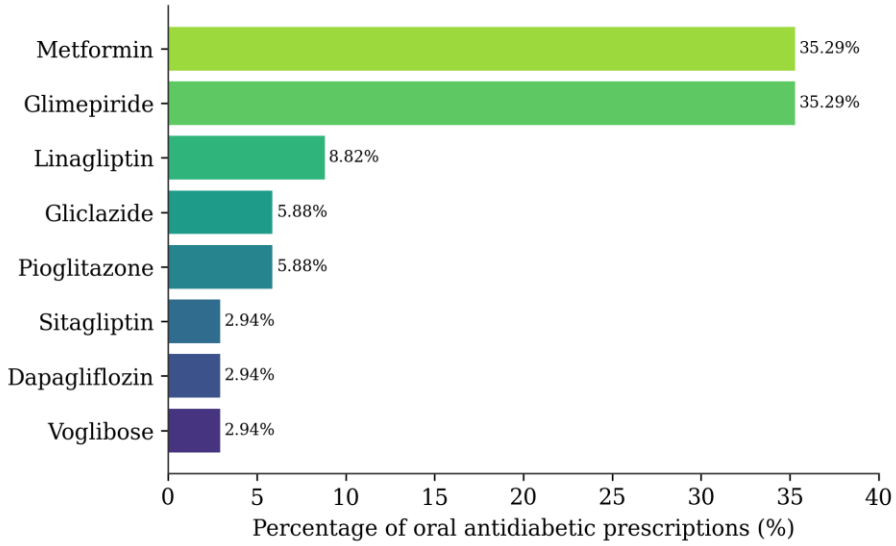

Figure 3: Oral hypoglycaemic drugs prescribed among the study population.

Types of insulin used

In addition to oral agents, a sizeable proportion of patients required insulin. Human Actrapid was the most frequently used preparation (36%), followed by Basalog (12%), Insugen and Mixtard (8% each), and Isophane and Lantus (4% each). The clear preference for premixed and combination insulin regimens indicates that, in many patients—particularly elderly individuals with long-standing disease—oral therapy alone was insufficient, and mixed regimens were chosen to provide both basal and prandial coverage in a simplified manner (Table 5, Figure 4).

Insulin preparation	Number of times prescribed	Percentage (%)
H Actrapid	9	36
Injection Basalog	3	12
Injection Insugen	2	8
Injection Mixtard	2	8
Injection Isophane	1	4
Injection Lantus	1	4
Total	**25**	**100**

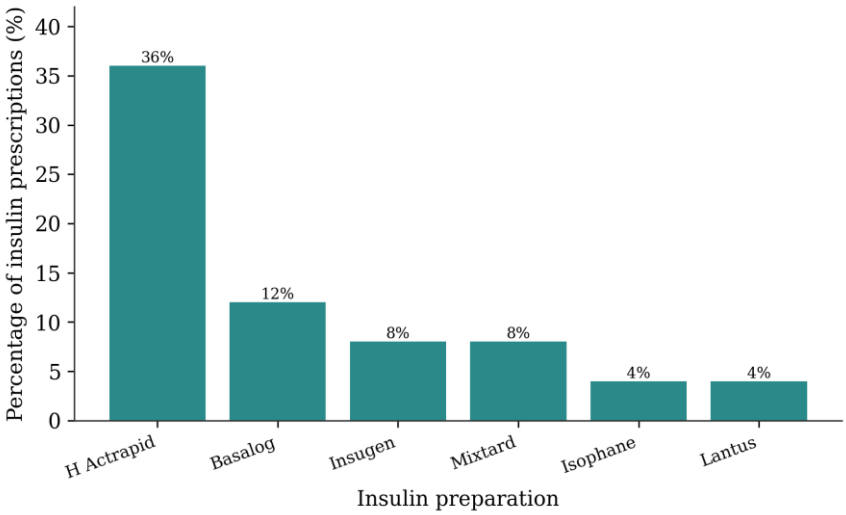

Figure 4: Percentage distribution of insulin preparations used in the study population.

Comparison of adverse effects between monotherapy and combination therapy

A total of 43 adverse drug reactions were documented among the 40 patients, since a few patients experienced more than one reaction. Monotherapy accounted for a marginally higher share of the overall ADR burden (51.16%) than combination therapy (48.84%). Hypoglycaemia was overwhelmingly the most frequent reaction, constituting 90.70% of all events, and was slightly more common in the monotherapy group (46.51%) than in the combination group (44.19%), indicating that patients on a single antidiabetic agent were somewhat more prone to hypoglycaemic episodes. Seizure and hypokalaemia (2.33% each) were observed exclusively with monotherapy, while dizziness and vomiting (2.33% each) occurred only with combination therapy. The predominance of hypoglycaemia in the monotherapy group is best explained by the direct action of single agents such as insulin or sulfonylureas, which can drive a sharp fall in blood glucose when used without careful dose adjustment (Table 6, Figure 5).

A chi-square comparison of the overall ADR distribution between the two regimens did not reach statistical significance ($p>0.05$), which is unsurprising given the small sample and the strong dominance of a single reaction type; the difference between groups is therefore best regarded as a clinically meaningful trend rather than a statistically established effect.

Adverse drug reaction	Monotherapy	Combination therapy	Total
Hypoglycaemia	46.51% (20)	44.19% (19)	90.70% (39)
Seizure	2.33% (1)	0.00% (0)	2.33% (1)
Hypokalaemia	2.33% (1)	0.00% (0)	2.33% (1)
Dizziness	0.00% (0)	2.33% (1)	2.33% (1)

Vomiting	0.00% (0)	2.33% (1)	2.33% (1)
Total	**51.16% (22)**	**48.84% (21)**	**100% (43)**

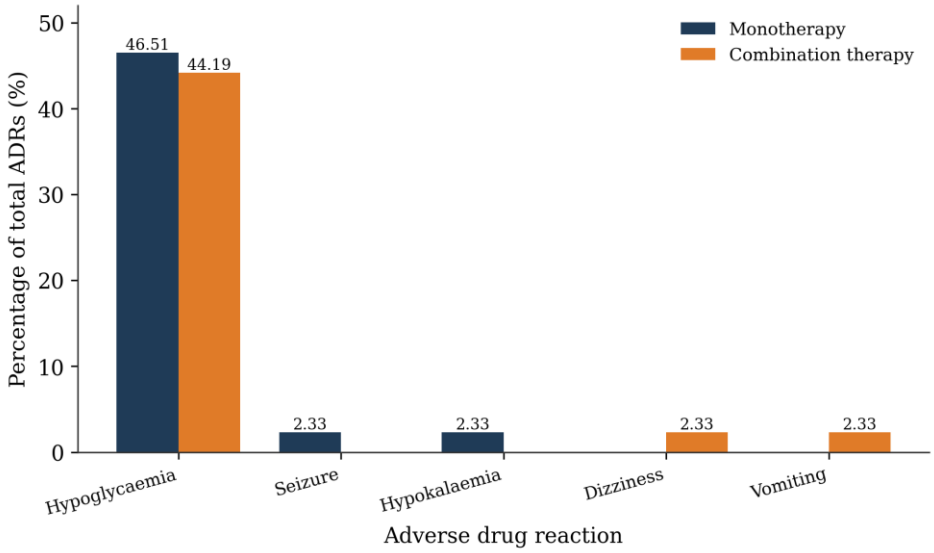

Figure 5: Comparison of adverse effects between monotherapy and combination therapy.

Severity and outcome of adverse drug reactions

Severity grading on the modified Hartwig and Siegel scale showed that the great majority of reactions were moderate in intensity (95.3%), with mild and severe reactions each accounting for only 2.3%. The predominance of moderate reactions indicates that most patients required some medical intervention or a temporary modification of therapy but recovered fully without lasting harm. Outcome assessment was uniformly favourable: all 43 reactions resolved completely, giving a 100% recovery rate with no ongoing, unknown or fatal cases. Together these findings confirm that the adverse reactions associated with antidiabetic therapy in this cohort were largely manageable and fully reversible following appropriate management (Tables 7 and 8, Figure 6).

Severity grade	**Number of ADRs**	**Percentage (%)**
Mild	1	2.3
Moderate	41	95.3
Severe	1	2.3
Outcome	**Number of ADRs**	**Percentage (%)**
Recovered	43	100
Unknown	0	0
Continuing	0	0
Other	0	0

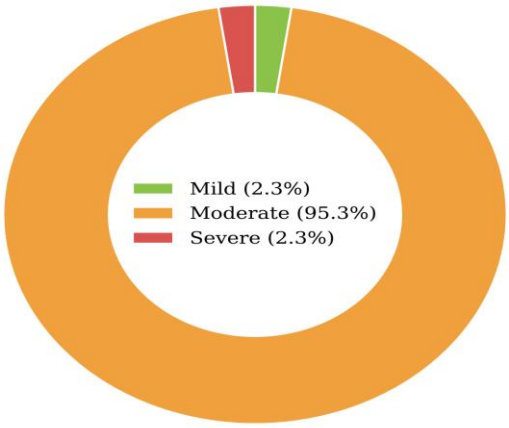

Figure 6: Severity distribution of adverse drug reactions.

DISCUSSION

This prospective comparative study set out to characterise and contrast the ADR profiles of monotherapy and combination therapy in patients with T2DM. The demographic pattern—with half the cohort aged 60 years or above and the next largest share in the 40–59 year band—mirrors the well-established rise in T2DM prevalence with advancing age, driven by progressive beta-cell dysfunction and worsening insulin resistance. Combination therapy clustered in the elderly, whereas monotherapy was relatively more frequent among middle-aged adults, a distribution that reflects the natural progression of the disease from single-agent control toward multi-drug management as glycaemic targets become harder to maintain.

The prescribing pattern was rational and guideline-concordant. Metformin emerged as the backbone of therapy, used both alone and, most commonly, in combination with glimepiride, in keeping with recommendations that place metformin first-line and a sulfonylurea as a frequent add-on. Insulin—particularly Human Actrapid and premixed preparations—was reserved for elderly or more advanced cases in whom oral therapy alone could not achieve control, signalling judicious escalation rather than reflexive polypharmacy.

The safety findings are the heart of the study. Hypoglycaemia dominated the ADR landscape and was marginally more prevalent with monotherapy, suggesting that single-agent regimens—especially those built on insulin or sulfonylureas—may carry a higher risk of hypoglycaemic complications when doses are not individualised or monitored closely.

Combination therapy, by contrast, produced a slightly wider but milder spectrum of reactions (dizziness and vomiting) that most likely reflect additive tolerability effects rather than severe glycaemic instability. These observations are consistent with earlier reports that identify hypoglycaemia as a leading ADR in diabetic patients treated with insulin or sulfonylureas,[14,15,16] while adding a focused head-to-head comparison within a single cohort.

The outcome data were reassuring. The overwhelming majority of reactions were moderate in severity and every reaction resolved completely, indicating that the ADRs were identified, treated and monitored effectively through sound pharmacovigilance. The near-absence of severe or life-threatening events underscores the manageability of antidiabetic-related reactions when timely dose titration, blood glucose monitoring and patient counselling are in place.

Several clinical implications follow. Patients should be counselled to recognise the early warning signs of hypoglycaemia—sweating, tremor, dizziness and confusion—and instructed in immediate corrective action. Regular self-monitoring of blood glucose, especially after any dose change, is essential to reduce hypoglycaemic risk. In elderly or otherwise high-risk patients, clinicians should favour agents with a lower hypoglycaemic potential or adjust dosing schedules to smooth glucose peaks and troughs. Throughout, the clinical pharmacist has a pivotal role in dose optimisation, interaction screening and structured patient education, all of which can help temper the ADR burden observed with monotherapy.

The strengths of this work include its prospective design, which improved the accuracy of ADR detection, and its focus on a specific high-risk population, which allowed disease-relevant patterns to be identified. Its limitations must, however, be acknowledged. The modest sample size (n=40) limits generalisability and constrains the power of statistical comparison; the single-centre setting may limit external validity; and some mild reactions may have gone unreported during interviews or chart review. Future research should therefore pursue multi-centre studies with larger, matched cohorts, apply more robust statistical methods to compare ADR frequency and severity between regimens, and evaluate the impact of structured pharmacist-led counselling and dose-titration protocols on reducing hypoglycaemia.

CONCLUSION

This study concludes that monotherapy accounted for a marginally higher overall ADR occurrence in T2DM patients, driven chiefly by hypoglycaemia. Hypoglycaemia was the commonest reaction in both regimens but was slightly more frequent and clinically significant with single-agent therapy, and seizure and hypokalaemia were confined to the monotherapy group—further highlighting its greater susceptibility to hypoglycaemic complications. Combination therapy was associated with fewer hypoglycaemic episodes but a somewhat wider range of mild gastrointestinal and neurological effects such as dizziness and vomiting. Reassuringly, the majority of reactions were moderate in severity and every reaction was fully reversible, with all patients recovering after appropriate management. Combination therapy thus offers tighter glycaemic control with a slightly safer hypoglycaemic profile, while monotherapy remains valuable but higher-risk and demands careful dose adjustment, frequent glucose monitoring and patient counselling. Strengthening pharmacovigilance, rational prescribing, individualised therapy selection and interdisciplinary follow-up can substantially reduce the ADR burden and improve the overall quality of diabetes care.

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Conflict of interest

The authors declare that they have no conflict of interest.

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