

Research Article

Assessment of Drug Utilization Pattern, Prescription Appropriateness and Glycaemic Control Among Patients with Type 2 Diabetes Mellitus in a Tertiary Care Teaching Hospital: A Prospective Observational

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic progressive disorder that requires long-term, multi-drug therapy. Periodic evaluation of prescribing patterns and their appropriateness is essential to promote rational drug use and achieve optimal glycaemic control.

Objectives: To evaluate the drug utilization pattern, assess the appropriateness of prescriptions and determine the glycaemic control among patients with T2DM attending a tertiary care teaching hospital.

Materials and Methods: A prospective observational study was conducted for 12 months in the medicine outpatient and inpatient departments of a tertiary care teaching hospital. Three hundred adult patients with T2DM were enrolled and followed for six months. Prescriptions were analysed using the WHO prescribing indicators, the Anatomical Therapeutic Chemical (ATC) classification and a guideline-based appropriateness checklist (ADA 2021, RSSDI 2018 and ICMR 2018). Glycaemic control was assessed by fasting blood sugar (FBS), post-prandial blood sugar (PPBS) and glycated haemoglobin (HbA1c) at baseline, 3 months and 6 months. Data were analysed with SPSS version 26; $p < 0.05$ was considered significant.

Results: The mean age was 56.4 ± 11.2 years and 56.0% were men. A total of 1,842 drugs were prescribed (6.14 per prescription), of which 848 (2.83 per patient) were antidiabetic agents. Metformin was the most frequently prescribed drug (82.3% of patients), followed by sulfonylureas (66.0%) and DPP-4 inhibitors (48.3%). Fixed-dose combinations were used in 47.3% of patients and only 33.2% of drugs were prescribed by generic name. Overall, 211 prescriptions (70.3%) were appropriate, while 89 (29.7%) had at least one inappropriate element; the commonest were non-use of an indicated SGLT2 inhibitor/GLP-1 receptor agonist (7.3%) and omission of metformin without contraindication (9.7%). Potential drug-drug interactions were seen in 44.7% of patients. Among 268 patients who completed follow-up, mean HbA1c fell from $8.38 \pm 1.68\%$ to $7.46 \pm 1.44\%$ ($p < 0.001$), and the proportion achieving HbA1c $< 7\%$ rose from 16.0% to 36.6%. Target attainment was higher with appropriate prescriptions (43.2% vs 20.5%; $p = 0.001$). Adverse drug events occurred in 31.3% of patients; hypoglycaemia (12.7%) was the commonest serious event.

Conclusion: Prescribing in this hospital was largely guideline-concordant with metformin-based therapy as the cornerstone; however, low generic prescribing, polypharmacy, under-use of cardio-renal protective agents and suboptimal glycaemic control highlight areas for intervention through prescriber education, clinical pharmacist involvement and periodic prescription audit.

Keywords: Type 2 Diabetes Mellitus, Drug Utilization, Prescribing Pattern, Appropriateness, Glycaemic Control, HbA1c, Tertiary Care Hospital, India.

INTRODUCTION

Diabetes mellitus is one of the fastest-growing non-communicable diseases of the twenty-first century. The International Diabetes Federation estimated that 463 million adults aged 20–79 years were living with diabetes worldwide in 2019, a number projected to reach 700 million

by 2045, with more than three-quarters of affected adults residing in low- and middle-income countries.[1] India, often described as the diabetes capital of the world, carries a particularly large share of this burden. The ICMR-INDIAB study, covering 15 states, estimated that about 7.3% of Indian adults had

diabetes and a further 10.3% had prediabetes, with striking variation between states and between urban and rural areas.[2] The Global Burden of Disease analysis for 1990–2016 likewise showed a rising diabetes burden in every Indian state,[3] and the disease now affects younger, leaner individuals earlier than in Western populations, which prolongs the exposure to hyperglycaemia and increases the risk of complications.[4,5]

Sustained hyperglycaemia is the principal modifiable determinant of microvascular and macrovascular complications. In the UK Prospective Diabetes Study, intensive glucose control reduced the risk of microvascular endpoints,[6] and the observational analysis (UKPDS 35) showed that every 1% reduction in HbA1c was associated with a 37% decrease in microvascular complications and a 14% decrease in myocardial infarction.[7] Achieving and maintaining glycaemic targets therefore depends largely on the timely selection and appropriate use of pharmacotherapy.

The pharmacological armamentarium for T2DM has expanded enormously over the last decade. Besides metformin, sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors and insulin, newer classes such as dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RA) are now available. International guidelines recommend a patient-centred approach in which metformin remains the usual first-line drug, and agents with proven cardiovascular or renal benefit are preferred in patients with established atherosclerotic cardiovascular disease, heart failure or chronic kidney disease irrespective of HbA1c.[8,9] In India, the Research Society for the Study of Diabetes in India (RSSDI) and the Indian Council of Medical Research (ICMR) have issued country-specific recommendations that take into account cost, availability and the clinical profile of Indian patients.[10,11] However, the wide choice of drugs, the frequent coexistence of hypertension, dyslipidaemia and renal disease, and the common use of fixed-dose combinations (FDCs) make prescribing in diabetes complex and prone to irrational practices.

Drug utilization research, defined by the World Health Organization as the study of the marketing, distribution, prescription and use of drugs in society with special emphasis on the resulting medical, social and economic consequences, provides a systematic method to

describe prescribing habits and to identify opportunities for improvement.[12] Despite the availability of effective drugs, nationwide data from India indicate that a considerable proportion of patients do not achieve glycaemic targets,[13,14] and similar gaps between guideline recommendations and real-world control have been described globally.[15] Prescription audit combined with outcome assessment can therefore reveal whether the observed therapeutic gaps arise from inappropriate drug selection, dosing errors, drug interactions, or other factors such as adherence and lifestyle.

Most published drug-utilization studies in diabetes are cross-sectional and describe only what is prescribed, without linking prescribing quality to clinical outcome. A prospective design that follows the same patients and correlates appropriateness of therapy with HbA1c response is more informative for clinicians and hospital drug and therapeutics committees. Hence, the present study was undertaken to assess the drug utilization pattern, evaluate the appropriateness of prescriptions and determine the glycaemic control among patients with T2DM in a tertiary care teaching hospital.

Aim and Objectives

Primary Objectives: (i) to analyse the drug utilization pattern in T2DM patients using WHO prescribing indicators and ATC classification; (ii) to evaluate the appropriateness of prescriptions against standard guidelines; and (iii) to assess glycaemic control (FBS, PPBS and HbA1c) over six months.

Secondary Objectives: to identify potential drug-drug interactions, to document adverse drug events, and to correlate the appropriateness of prescribing with glycaemic outcome.

MATERIALS AND METHODS

Study design, setting and duration

This was a prospective, observational, hospital-based study carried out in the outpatient department (OPD) and inpatient wards of the Department of General Medicine of a tertiary care teaching hospital in India over a period of 12 months, with each participant followed up for six months after enrolment. The study was initiated after approval from the Institutional Ethics Committee (Approval No. [2026/192]) and was conducted in accordance with the Declaration of Helsinki and the National Ethical Guidelines for Biomedical and Health Research Involving Human Participants issued by

ICMR.[16] Written informed consent was obtained from every participant in a language understood by them, and patient identity was kept confidential.

Study Population and Sample Size

Adult patients (≥ 18 years) of either sex with a diagnosis of T2DM according to ADA criteria, who were receiving at least one antidiabetic drug and who consented to participate, were included. Patients with type 1 diabetes, gestational diabetes or secondary diabetes, pregnant or lactating women, patients admitted to intensive care units with acute diabetic emergencies, and those with incomplete records or unwilling to give consent were excluded. The sample size was calculated using the formula $n = Z^2pq/d^2$, assuming an expected proportion of inappropriate prescriptions of 25%, 95% confidence and an absolute precision of 5%, which gave 288; this was rounded off to 300 patients. Participants were recruited consecutively by convenience sampling.

Data Collection

A pre-designed, pre-validated case record form was used to capture (i) socio-demographic data (age, sex, residence, body mass index [BMI], family history); (ii) clinical data (duration of diabetes, comorbidities, complications, serum creatinine and estimated glomerular filtration rate [eGFR] calculated by the CKD-EPI equation);[17] (iii) prescription details (drug name, class, dose, frequency, route, FDC use, generic/brand name, concomitant medicines); and (iv) laboratory data (FBS, PPBS and HbA1c). Patients were enrolled at baseline (visit 1) and reassessed at 3 months (visit 2) and 6 months (visit 3), coinciding with their routine follow-up visits. FBS and PPBS were measured by the glucose oxidase–peroxidase method and HbA1c by high-performance liquid chromatography (NGSP-certified).

Assessment of drug utilization

Antidiabetic and concomitant drugs were classified according to the WHO ATC classification system.[18] Core prescribing indicators were calculated as recommended by the WHO: average number of drugs per prescription, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic, percentage of encounters with an injection, and percentage of drugs prescribed from the National List of Essential Medicines (NLEM) 2015.[19,20] Polypharmacy was defined as the concurrent use of five or more

drugs.[21] The therapy pattern was described as mono-, dual, triple or $\geq$ four-drug therapy, and the use of FDCs was recorded separately.

Assessment Of Prescription Appropriateness

Appropriateness was assessed with a guideline-based checklist developed from the ADA Standards of Medical Care 2021, the RSSDI 2017 recommendations and the ICMR 2018 guidelines,[8,10,11] the AGS Beers Criteria for patients aged 65 years and above,[22] and the concept of drug-therapy problems described by Hepler and Strand.[23] A prescription was labelled “inappropriate” if it had one or more of the following: (a) omission of metformin in the absence of a contraindication or intolerance; (b) metformin use with $\text{eGFR} < 30 \text{ mL/min/1.73 m}^2$; (c) use of glibenclamide in elderly or renal-impaired patients; (d) therapeutic duplication within the same class; (e) pioglitazone in patients with heart failure or oedema; (f) non-use of an SGLT2 inhibitor or GLP-1 RA in patients with established atherosclerotic cardiovascular disease or chronic kidney disease; (g) dose or frequency outside the recommended range; (h) incorrect timing of administration with respect to meals; and (i) failure to intensify therapy (e.g. initiate insulin) when HbA1c remained above 10% on dual oral therapy. Two investigators independently reviewed each prescription, and disagreements were resolved by a third reviewer (inter-rater agreement, Cohen's kappa = 0.82).

Drug Interactions and Adverse Drug Events

Potential drug-drug interactions (DDIs) were screened using a standard interaction database and categorised as major, moderate or minor. Adverse drug events were recorded during every visit by direct interview and review of records; causality was assessed with the Naranjo algorithm.[24] Hypoglycaemia was defined as a blood glucose level $< 70 \text{ mg/dL}$ with or without symptoms.

Assessment of Glycaemic Control

Glycaemic control was assessed by the change in mean FBS, PPBS and HbA1c from baseline to 3 and 6 months. In line with ADA recommendations, an $\text{HbA1c} < 7\%$ was taken as the general treatment target.[8] Patients were further classified into four HbA1c categories ($< 7\%$, 7–8%, 8.1–9% and $> 9\%$).

Statistical analysis

Data were entered in Microsoft Excel and analysed with IBM SPSS Statistics version 26.

Categorical variables are expressed as numbers and percentages, and continuous variables as mean $\pm$ standard deviation (SD). Changes in glycaemic parameters at three time points were compared using repeated-measures ANOVA with Bonferroni post-hoc correction; independent groups were compared with the unpaired t-test or one-way ANOVA, and proportions with the Chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 318 patients were screened, of whom 300 met the eligibility criteria and were enrolled. Follow-up data up to six months were available for 268 patients (89.3%); 32 patients were lost to follow-up ($n = 21$), withdrew consent ($n = 6$) or died of unrelated causes ($n = 5$). Prescription analysis was based on all 300

patients at enrolment, while glycaemic outcomes were analysed for the 268 completers.

Socio-Demographic and Clinical Characteristics

The mean age of the patients was 56.4 ± 11.2 years, and the largest proportion (32.0%) belonged to the 50–59 year group. There was a male predominance (56.0%). More than half of the patients (51.7%) were obese by the Asia-Pacific BMI criteria ($\geq 25 \text{ kg/m}^2$), and 39.7% had had diabetes for 5–10 years (Table 1). At least one comorbid condition was present in 79.3% of patients, hypertension (57.0%) and dyslipidaemia (32.7%) being the most common, and neuropathy was the most frequent diabetic complication (29.3%) (Table 2).

Table 1: Socio-Demographic and Clinical Characteristics of the Study Population (N = 300)

Characteristic	Number of patients (n)	Percentage (%)
Age group (years); mean $\pm$ SD = 56.4 ± 11.2		
30–39	18	6.0
40–49	62	20.7
50–59	96	32.0
60–69	83	27.7
≥ 70	41	13.7
Sex		
Male	168	56.0
Female	132	44.0
Residence		
Urban	163	54.3
Rural	137	45.7
Duration of diabetes (years)		
< 5	112	37.3
5–10	119	39.7
> 10	69	23.0
BMI (kg/m^2); mean $\pm$ SD = 25.9 ± 4.3		
18.5–22.9 (normal)	74	24.7
23.0–24.9 (overweight)	71	23.7
≥ 25.0 (obese)	155	51.7
Other characteristics		
Family history of diabetes	129	43.0
Outpatients / Inpatients	218 / 82	72.7 / 27.3

Table 2: Comorbidities and Diabetic Complications among Study Participants (N = 300)

Condition	Number of patients (n)	Percentage (%)
Comorbid conditions*		
Hypertension	171	57.0
Dyslipidaemia	98	32.7
Coronary artery disease	54	18.0
Chronic kidney disease (eGFR < 60)	31	10.3

Hypothyroidism	27	9.0
Others	22	7.3
No comorbidity	62	20.7
Diabetic complications*		
Peripheral neuropathy	88	29.3
Nephropathy	61	20.3
Retinopathy	52	17.3
Diabetic foot	19	6.3

Drug Utilization Pattern

The 300 prescriptions contained 1,842 drugs, giving a mean of 6.14 drugs per prescription; 221 patients (73.7%) were on five or more drugs (polypharmacy). Of these, 848 (46.0%) were antidiabetic agents (mean 2.83 per patient) and 994 (54.0%) were drugs for comorbidities and supportive care. Metformin was the commonest antidiabetic drug (29.1%

of antidiabetic prescriptions; 82.3% of patients), followed by sulfonylureas (23.3%), DPP-4 inhibitors (17.1%) and insulins (13.2%). Among sulfonylureas, glimepiride was dominant (64.6%), and among DPP-4 inhibitors vildagliptin (51.0%) was preferred. SGLT2 inhibitors were prescribed in only 15.0% of patients and GLP-1 RA in two (Table 3, Figure 1).

Table 3: Pattern of Antidiabetic Drug Prescriptions (Total Antidiabetic Prescriptions = 848)

Drug class / drug	Number (n)	% of antidiabetic prescriptions
Biguanide	247	29.1
Metformin	247	29.1
Sulfonylureas	198	23.3
Glimepiride	128	15.1
Gliclazide	61	7.2
Glibenclamide	9	1.1
DPP-4 inhibitors	145	17.1
Vildagliptin	74	8.7
Teneligliptin	33	3.9
Sitagliptin	28	3.3
Linagliptin	10	1.2
Insulins	112	13.2
Premixed human insulin (30/70)	41	4.8
Insulin glargine	29	3.4
Regular human insulin	22	2.6
Premixed insulin analogues	12	1.4
Insulin degludec	8	0.9
Thiazolidinedione (pioglitazone)	61	7.2
SGLT2 inhibitors	45	5.3
Dapagliflozin	31	3.7
Empagliflozin	14	1.7
Alpha-glucosidase inhibitor (voglibose)	38	4.5
GLP-1 receptor agonist (liraglutide)	2	0.2
Total	848	100.0

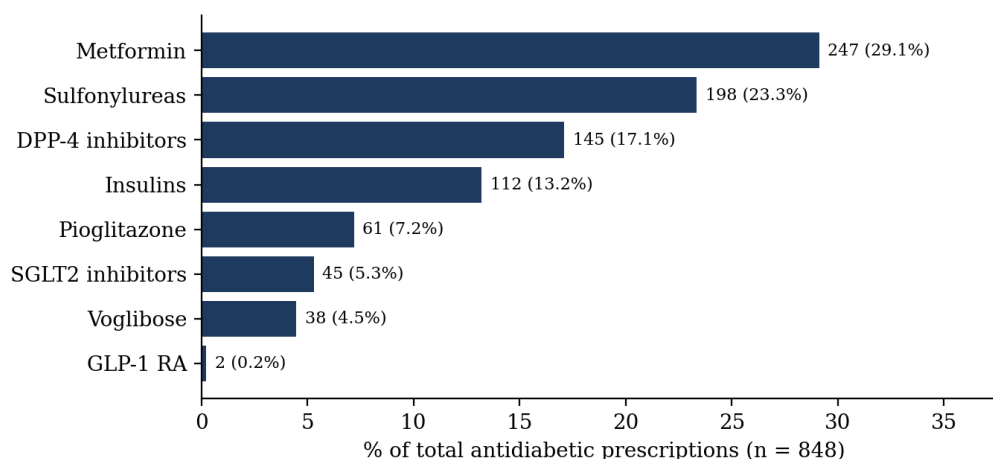


Figure 1: Utilization of Antidiabetic Drug Classes

Monotherapy was prescribed to only 10.0% of patients, whereas dual (26.0%) and triple therapy (39.3%) predominated; 20.7% received four drugs and 4.0% five antidiabetic drugs (Table 4). Fixed-dose combinations accounted for 187 antidiabetic items (22.1%) and were used in 142 patients (47.3%);

metformin + glimepiride was the most frequent FDC (Table 5). Among the 994 non-antidiabetic drugs, antihypertensives (24.2%), lipid-lowering agents (16.5%) and vitamins/nutritional supplements (14.8%) were most common (Table 6).

Table 4: Pattern of Antidiabetic Therapy (N = 300)

Regimen	Number of patients (n)	Percentage (%)
Monotherapy	30	10.0
Dual therapy	78	26.0
Triple therapy	118	39.3
Four-drug therapy	62	20.7
Five-drug therapy	12	4.0
Total	300	100.0

Table 5: Fixed-Dose Combinations (Fdc's) Prescribed (Total FDC Items = 187)

Fixed-dose combination	Number (n)	Percentage (%)
Metformin + glimepiride	74	39.6
Metformin + vildagliptin	41	21.9
Metformin + glimepiride + pioglitazone	22	11.8
Metformin + sitagliptin	17	9.1
Metformin + pioglitazone	15	8.0
Metformin + dapagliflozin	10	5.3
Teneligliptin + metformin	8	4.3
Total	187	100.0

Table 6: Non-Antidiabetic Drugs Prescribed (Total = 994)

Drug group	Number (n)	Percentage (%)
Antihypertensives (ARBs, ACE inhibitors, CCBs, beta-blockers, diuretics)	241	24.2
Lipid-lowering agents (statins, fibrates)	164	16.5
Vitamins and nutritional supplements	147	14.8
Proton pump inhibitors / antacids	118	11.9
Antiplatelet drugs	96	9.7
Analgesics / NSAIDs	62	6.2
Neuropathic pain agents	49	4.9
Antibiotics	34	3.4

Others	83	8.4
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WHO Prescribing Indicators

Only one-third of the drugs (33.2%) were prescribed by generic name, while 61.3% of

drugs belonged to the NLEM 2015. An antibiotic was prescribed in 11.3% of encounters and an injectable (insulin) in 37.3% (Table 7).

Table 7: WHO Core Prescribing Indicators

Indicator	Observed value	Reference / remark
Average number of drugs per prescription	6.14 (1842/300)	Ideal: as low as possible (WHO: 1.6–1.8)
Average number of antidiabetic drugs per patient	2.83 (848/300)	—
Drugs prescribed by generic name	33.2% (612/1842)	Ideal: 100%
Encounters with an antibiotic	11.3% (34/300)	WHO: 20.0–26.8%
Encounters with an injection	37.3% (112/300)	Insulin only
Drugs prescribed from NLEM 2015	61.3% (1129/1842)	Ideal: 100%
Prescriptions with polypharmacy (≥ 5 drugs)	73.7% (221/300)	—

Appropriateness of Prescriptions

Of the 300 prescriptions, 211 (70.3%) were considered fully appropriate and 89 (29.7%) had at least one inappropriate element, with a total of 121 instances of inappropriateness. The commonest problems were non-use of SGLT2 inhibitors/GLP-1 RA in patients with a

compelling cardio-renal indication (7.3%), omission of metformin without a documented contraindication (9.7%), and dose or frequency errors (5.7%). Glibenclamide was prescribed to nine patients, all aged above 65 years or with CKD (Table 8).

Table 8: Types of Inappropriate Prescribing (N = 300; 121 Instances In 89 Patients)

Type of inappropriateness	Instances (n)	% of patients
Metformin omitted without contraindication	29	9.7
SGLT2 inhibitor / GLP-1 RA not used despite ASCVD or CKD	22	7.3
Dose or frequency outside recommended range	17	5.7
Failure to intensify therapy (HbA1c > 10% on dual therapy)	12	4.0
Incorrect timing with respect to meals	11	3.7
Glibenclamide in elderly / CKD patients	9	3.0
Therapeutic duplication within a class	8	2.7
Pioglitazone in heart failure / oedema	7	2.3
Metformin with eGFR < 30 mL/min/1.73 m ²	6	2.0
Total instances	121	—

A patient could have more than one type of inappropriateness.

Potential Drug-Drug Interactions and Adverse Drug Events

Potential DDIs were identified in 134 patients (44.7%), with 207 interacting pairs in total: 18 (8.7%) major, 141 (68.1%) moderate and 48 (23.2%) minor. The most frequent moderate interaction was between sulfonylureas/insulin and beta-blockers, which may mask the

warning symptoms of hypoglycaemia (Table 9). Adverse drug events were noted in 94 patients (31.3%), with 126 events in all. Gastrointestinal intolerance (14.0%) and hypoglycaemia (12.7%) were most frequent; seven patients (2.3%) had hypoglycaemia needing assistance (Table 10).

Table 9: Potential Drug-Drug Interactions (Total = 207)

Severity / interacting pair	Number (n)	Percentage (%)
Major	18	8.7

Spironolactone + ACE inhibitor / ARB (hyperkalaemia)	11	5.3
Ciprofloxacin + glimepiride (dysglycaemia)	7	3.4
Moderate	141	68.1
Sulfonylurea / insulin + beta-blocker (masked hypoglycaemia)	41	19.8
Metformin + furosemide (altered metformin levels)	29	14.0
Sulfonylurea + aspirin (potentiated hypoglycaemia)	22	10.6
Clopidogrel + proton pump inhibitor	18	8.7
Other moderate interactions	31	15.0
Minor	48	23.2

Table 10: Adverse Drug Events Observed (94 Patients; 126 Events)

Adverse event	Number of events (n)	% of patients (n = 300)
Gastrointestinal intolerance (metformin, voglibose)	42	14.0
Hypoglycaemia (sulfonylurea / insulin)	38	12.7
Weight gain	17	5.7
Peripheral oedema (pioglitazone)	14	4.7
Genital mycotic infection / UTI (SGLT2 inhibitors)	9	3.0
Others	6	2.0

Glycaemic Control

Among the 268 patients who completed follow-up, there was a significant, progressive improvement in all glycaemic parameters (Table 11, Figure 2). Mean HbA1c decreased from $8.38 \pm 1.68\%$ at baseline to $7.78 \pm 1.52\%$ at 3 months and $7.46 \pm 1.44\%$ at 6 months

(absolute reduction 0.92%; $p < 0.001$). Mean FBS and PPBS declined by 31.6 mg/dL and 50.5 mg/dL, respectively. The proportion of patients with HbA1c $< 7\%$ increased from 16.0% to 36.6%, while the proportion with HbA1c $> 9\%$ decreased from 31.7% to 14.6% (Table 12).

Table 11: Changes in Glycaemic Parameters During Follow-Up (N = 268; Mean $\pm$ SD)

Parameter	Baseline	3 months	6 months	p-value*
FBS (mg/dL)	164.8 ± 47.3	142.6 ± 38.9	133.2 ± 34.5	< 0.001
PPBS (mg/dL)	238.4 ± 63.1	201.5 ± 52.7	187.9 ± 47.2	< 0.001
HbA1c (%)	8.38 ± 1.68	7.78 ± 1.52	7.46 ± 1.44	< 0.001

*Repeated-measures ANOVA; Bonferroni post-hoc test showed significant differences between all pairs of time points ($p < 0.05$).

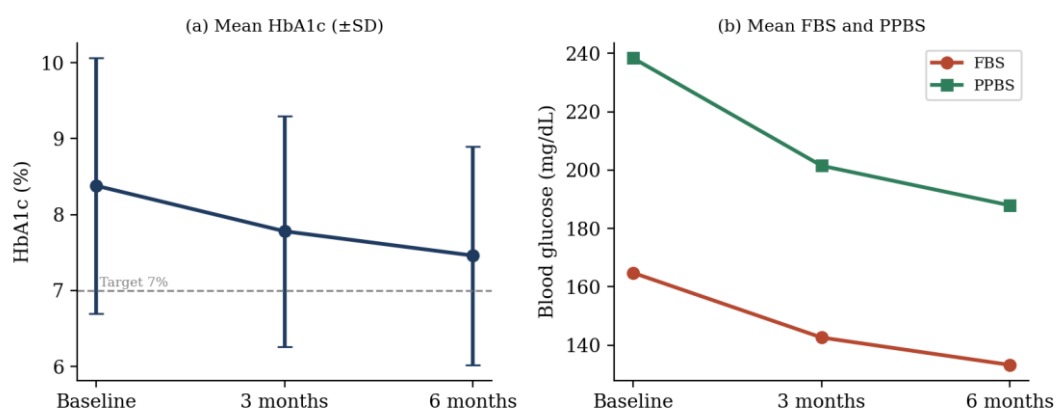


Figure 2: Trend of glycaemic parameters over six months

Table 12: Distribution of HbA1c categories at baseline and at six months (n = 268)

HbA1c category	Baseline n (%)	6 months n (%)
$< 7.0\%$	43 (16.0)	98 (36.6)
7.0–8.0%	72 (26.9)	79 (29.5)

8.1–9.0%	68 (25.4)	52 (19.4)
> 9.0%	85 (31.7)	39 (14.6)

Chi-square for trend, $p < 0.001$.

When glycaemic outcome was related to prescription quality, patients whose prescriptions were appropriate ($n = 190$ completers) had a significantly lower mean HbA1c at six months than those with inappropriate prescriptions ($n = 78$): $7.31 \pm 1.35\%$ versus $7.83 \pm 1.58\%$ ($p = 0.004$). The target HbA1c $< 7\%$ was attained by 43.2% of

the former and 20.5% of the latter ($p = 0.001$) (Table 13). Six-month HbA1c values were higher in patients on triple therapy and on four or more drugs than in those on mono- or dual therapy ($p = 0.008$), reflecting the greater baseline severity and longer disease duration of patients who needed more drugs.

Table 13: Glycaemic Control at Six Months in Relation to Appropriateness of Prescription and Number of Antidiabetic Drugs ($N = 268$)

Group	n	HbA1c at 6 months (mean $\pm$ SD)	HbA1c $< 7\%$ n (%)	p-value
Appropriateness of prescription				
Appropriate	190	7.31 ± 1.35	82 (43.2)	0.004 / 0.001†
Inappropriate	78	7.83 ± 1.58	16 (20.5)	
Number of antidiabetic drugs				
Monotherapy	27	7.12 ± 1.05	—	0.008‡
Dual therapy	70	7.31 ± 1.32	—	
Triple therapy	106	7.52 ± 1.41	—	
$\geq$ Four drugs	65	7.81 ± 1.62	—	

†Unpaired *t*-test for HbA1c / Chi-square test for target attainment. ‡One-way ANOVA.

DISCUSSION

Diabetes care in a tertiary teaching hospital is complex because patients frequently present with long-standing disease, multiple comorbidities and complications, and receive several drugs concurrently. This prospective study evaluated what was prescribed, whether it was appropriate, and how well glycaemia was controlled during follow-up. The principal findings were that metformin-based therapy was the backbone of treatment, one in three prescriptions had at least one inappropriate component, generic prescribing was low, and HbA1c improved significantly but target attainment remained modest.

The mean age of 56.4 years and the peak in the sixth decade are consistent with the typical Indian presentation of T2DM, which tends to occur about a decade earlier than in Western populations.[4,25] The slight male predominance may reflect better access to tertiary care for men. More than half of our patients were obese by Asia-Pacific criteria and 57.0% were hypertensive, confirming the clustering of cardiometabolic risk factors noted in earlier Indian surveys, including the CURES and INDIAB reports.[2,26,27] The high

prevalence of neuropathy, nephropathy and retinopathy points to late diagnosis and prolonged poor control, as also highlighted in the DiabCare India study.[13]

Metformin was prescribed to 82.3% of patients, in agreement with global and Indian guidelines that endorse it as the first-line agent because of its efficacy, safety, weight neutrality, low cost and potential cardiovascular benefit.[8,11,28] Metformin dose is related to the magnitude of HbA1c reduction,[29] and metformin-based combinations have been shown to be superior to monotherapy.[30] The continued high use of sulfonylureas (66.0% of patients) mirrors the Indian practice in which these inexpensive drugs are widely used as second-line agents, although they carry a risk of hypoglycaemia and weight gain. We also observed substantial use of DPP-4 inhibitors (48.3%), especially vildagliptin and teneligliptin; their popularity in India can be attributed to oral administration, weight neutrality, low hypoglycaemia risk and the availability of low-cost generics and FDCs with metformin, although their cardiovascular benefit has not been shown in outcome trials.[31]

Insulin was used in 37.3% of patients, a figure compatible with the long disease duration and high baseline HbA1c of tertiary-care referrals. Premixed human insulin was the commonest preparation, probably for reasons of cost and convenience. By contrast, SGLT2 inhibitors (15.0%) and GLP-1 RA (0.7%) were under-used even though several outcome trials have shown cardiovascular and renal protection with empagliflozin, canagliflozin and liraglutide in high-risk patients.[32,33,34] Cost, limited insurance coverage and prescriber unfamiliarity are plausible barriers in the Indian setting. Dual and triple therapy accounted for 65.3% of regimens, reflecting the progressive nature of the disease and the need for early combination therapy.[9]

The mean number of 6.14 drugs per prescription and the 73.7% polypharmacy rate are high, but largely explained by the need to treat concurrent hypertension, dyslipidaemia and cardiovascular risk, along with the use of supplements and gastroprotective drugs. Nevertheless, polypharmacy increases the risk of interactions, nonadherence and adverse events.[21,35] Fixed-dose combinations were prescribed to nearly half of the patients; while FDCs may simplify regimens and improve adherence, rational selection and monitoring are necessary because some combinations lack evidence-based justification.

Only 33.2% of drugs were prescribed by generic name, far from the WHO target of 100%, though 61.3% of the drugs were listed in the NLEM 2015. Low generic prescribing is a known problem in Indian hospitals, where brand prescribing by clinicians persists despite policy directives, and it increases the cost of lifelong therapy in a country where out-of-pocket expenditure is high.[5,20] The antibiotic encounter rate (11.3%) was lower than the WHO reference range and acceptable in a chronic-disease population.[19]

About 70% of prescriptions were fully appropriate. The leading problem was the omission of metformin without a documented reason, followed by non-use of SGLT2 inhibitors or GLP-1 RA in patients with ASCVD or CKD, which current ADA/EASD recommendations advise irrespective of HbA1c.[8,9] Glibenclamide use in older and renal-impaired patients (3.0%) is of concern, since this long-acting sulfonylurea is listed among potentially inappropriate medications in the Beers Criteria and carries a high risk of prolonged hypoglycaemia.[22,36] The therapeutic duplication within the same class and the use

of pioglitazone in patients with oedema or heart failure were uncommon but clinically important and entirely avoidable. Delayed intensification of therapy in patients with HbA1c above 10% on dual therapy (4.0%) represents clinical inertia, which has repeatedly been identified as a barrier to glycaemic control.[15]

Almost half of the patients had at least one potential DDI, the commonest being the combination of insulin or sulfonylurea with beta-blockers; although these drugs are often essential in patients with coexisting coronary disease, patients need to be counselled regarding masked hypoglycaemia. The overall adverse event rate of 31.3% was largely due to metformin-related gastrointestinal symptoms and hypoglycaemia, which are the well-recognised adverse effects of these drugs.[6,28] Hypoglycaemia in 12.7% of patients underscores the importance of individualised targets, particularly in the elderly, in whom hypoglycaemia is associated with falls, cognitive decline and cardiovascular events.[36]

Mean HbA1c improved from 8.38% to 7.46% during six months of follow-up, an absolute reduction of 0.92%. Given the UKPDS relationship between HbA1c reduction and complication risk,[7] such a reduction is clinically meaningful. Nevertheless, only 36.6% of patients achieved the target of < 7%, which is similar to the modest control reported in other Indian and international real-world data.[13,14,15] The probable contributors are long disease duration with progressive beta-cell failure, delayed treatment intensification, dietary and lifestyle factors, poor medication adherence and inappropriate prescribing.[35] Importantly, our study linked prescribing quality with outcome: patients with appropriate prescriptions had lower HbA1c and were more than twice as likely to attain the target as those with inappropriate prescriptions. The inverse relation between the number of drugs and glycaemic control should be interpreted cautiously, since patients with more advanced disease receive more drugs (confounding by indication).

Implications

The findings support several practical measures: (i) promoting generic prescribing and adherence to the essential medicines list; (ii) circulating a concise institutional diabetes prescribing protocol based on ICMR/RSSDI guidance, with explicit criteria for SGLT2 inhibitors/GLP-1 RA, renal dose adjustment,

and avoidance of glibenclamide in the elderly; (iii) integration of clinical pharmacists in diabetes clinics for interaction screening, hypoglycaemia counselling and adherence support; and (iv) periodic prescription audit with feedback to prescribers through the Drug and Therapeutics Committee.

Strengths and limitations

The strengths of the study are its prospective design, six-month follow-up with objective HbA1c measurement, the use of standard WHO indicators and a structured appropriateness checklist applied by two independent reviewers. The limitations include a single-centre setting and convenience sampling, which limit generalisability; a short follow-up; the lack of a direct measure of adherence, diet and physical activity; reliance on a checklist that may not capture clinical judgement in individual patients; and the inability to infer causality from an observational design. Multi-centre studies with longer follow-up are recommended.

CONCLUSION

Metformin-based combination therapy formed the cornerstone of T2DM management in this tertiary care hospital, in keeping with national and international guidelines. Nevertheless, about 30% of prescriptions had at least one inappropriate element, generic prescribing was low, polypharmacy and potential drug interactions were common, and newer cardio-renal protective agents were under-used. Glycaemic control improved significantly over six months but fewer than four in ten patients reached the HbA1c target, and appropriate prescribing was associated with better control. Regular prescription audit, development of an institutional treatment protocol, promotion of generic prescribing and the involvement of clinical pharmacists can improve rational use of antidiabetic drugs and clinical outcomes.

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