Prevalence and Associated Risk Factors of Metformin Use in the Treatment of Type-2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a progressive, lifelong metabolic disease characterized by insulin resistance and elevated blood glucose levels. Metformin is the most common initial therapy of choice for T2DM due to its antihyperglycemic activity, safety, and cardiovascular benefits. However, there is a need to explore the prevalence of metformin use and its associated risk factors, given its widespread use and prescription in diverse populations.

Objective: To assess the proportion and risk factors of metformin use among patients with T2DM attending Jinnah Hospital, Lahore, Pakistan, from March 2024 to October 2024.

Methods: This cross-sectional study employed an observational approach. Data was obtained through patient interviews and hospital record searches. A total of 1,729 patients with T2DM who were receiving metformin participated in the study by answering structured questions.

Results: The findings showed a significant association between smoking and metformin use, with smokers accounting for 45.0% and non-smokers 29.7% of users (OR = 1.45, 95% CI: 1.25–1.69). Patients with a body mass index (BMI) ≥30 (53.5%) had higher metformin use compared to those with a BMI <30 (25.7%) (OR = 1.85, 95% CI: 1.45–2.23). Additionally, older patients exhibited higher odds of belonging to the obese category (OR = 1.53, 95% CI: 1.25–1.89).

Conclusions: This study highlights that metformin, the first-line treatment for T2DM, is widely used and more frequently prescribed to older, obese individuals and smokers. These findings raise important questions for future research, particularly regarding lifestyle modification interventions to improve medication compliance, reduce potential harms, and evaluate the long-term effects of treatment among different patient groups, thereby promoting equitable and effective diabetes management.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a group of metabolic diseases characterized by hyperglycemia. General symptoms include polyuria, polydipsia, weight loss, tiredness, fatigue, and a higher susceptibility to infections (1). Diabetes Mellitus is recognized as a growing global health concern, with the number of patients projected to rise from 360 million in 2011 to an estimated 550 million by 2030 (2). The disease is associated with complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy, which are major causes of morbidity and mortality among affected individuals.

Metformin, a drug derived from Galega officinalis (commonly known as goat's rue), belongs to the biguanide class of medications and is widely employed in the treatment of T2DM (3). Metformin was first synthesized in the 1920s and subsequently reformulated for clinical use in the 1950s. It received FDA approval in the United States in 1994. Metformin is now considered a first-line treatment for T2DM, as it effectively controls blood glucose levels without significant risk of hypoglycemia, particularly in overweight or obese patients (4).

As an insulin-sensitizing agent, metformin is the preferred pharmacological treatment for T2DM (5). Its primary mechanism of action involves suppressing hepatic glucose production by reducing gluconeogenesis and glycogenolysis while enhancing glucose uptake in peripheral tissues such as skeletal muscles and adipose tissue. Metformin also improves insulin sensitivity (6). These actions decrease hepatic glucose output and enhance insulin-mediated glucose uptake (7). Its effectiveness, safety, and ability to reduce cardiovascular risks associated with diabetes have established metformin as a cornerstone of T2DM management since its introduction in the 1950s (8). However, the use of metformin among outpatient diabetic patients and the factors predicting its usage remain underexplored.

Approximately 80% of diabetic patients are diagnosed with non-insulin-dependent diabetes mellitus (NIDDM). These individuals often have pancreatic or upper abdominal conditions, reduced capacity of the islets of Langerhans to secrete insulin after glucose loading, and insulin

insensitivity in peripheral tissues (9). Diagnostic abnormalities include impaired insulin-stimulated glucose uptake in muscle and other tissues and insufficient suppression of hepatic glucose production (10).

Understanding the epidemiology and determinants of metformin use in diabetes patients is critical. Metformin is cost-effective and delivers satisfactory outcomes for long-term diabetes therapy (11). However, knowledge gaps persist regarding its use and its relationship with specific demographic and clinical characteristics, potentially leading to suboptimal patient management. Improved comprehension of metformin utilization can enable healthcare practitioners to develop strategies that promote its use and address associated challenges, ultimately improving the quality of life for diabetic patients (12).

In the United States, metformin is a widely used medication for type 2 diabetes. According to recent data, more than one in five adults with diabetes take metformin as part of their antidiabetic therapy, often alongside other drugs (13). Diabetes affects approximately 8.9% of the U.S. population, with 30–40% of these individuals using metformin as a first-line treatment (14).

In contrast, diabetes prevalence in China is estimated at 11.2%, and in India, it is 8.9%. Metformin is a preferred first-line oral hypoglycemic agent in these countries due to its efficacy and affordability, with 40–50% of type 2 diabetes patients using it (15). In Pakistan, the prevalence of diabetes has reached an alarming rate of 16.9%, translating to approximately 33 million adults living with the disease. Of these patients, 60–70% are prescribed metformin as part of their management plan (16).

Metformin's benefits extend beyond glycemic control. It lowers triglyceride and cholesterol levels, improves fibrinolytic activity, and reduces cardiovascular risks (17). For example, metformin has been shown to reduce HbA1c levels by 1.5% and is associated with a low risk of hypoglycemia, making it a mainstay for managing T2DM (18). The UK Prospective Diabetes Study (UKPDS) demonstrated that metformin reduced the risk of myocardial infarction by 39%, underscoring its role as a first-line therapy (19). However, gastrointestinal side effects occur in 20–30% of patients and may lead to discontinuation in 5% of cases. Factors such as dosage, patient age, and concomitant medications influence its tolerability (20).

Metformin is the most widely prescribed oral antidiabetic medication for T2DM, used by approximately 85% of patients on pharmacotherapy. In addition to lowering blood glucose, it reduces all-cause mortality and cardiovascular events compared to agents like sulfonylureas (21). Nevertheless, evidence suggests that metformin is underprescribed, with only 50–70% of patients on second- or third-line therapies also using metformin (22).

MATERIAL AND METHODS

Study Design: This study was a cross-sectional observational study aimed at assessing the prevalence and risk factors of metformin usage among outpatients with T2DM at Jinnah Hospital, Lahore, from March 2024 to October 2024. To analyze the effect of age on metformin use and associated risk factors, patients were divided into four age groups: 20–30 years, 30–40 years, 40–50 years, and 50–60 years. Samples were obtained, ensuring comprehensive documentation of features that determine metformin consumption within a large population of T2DM patients.

Data Collection: Data collection was conducted from March to October 2024 through patient interviews combined with a review of hospital records at Jinnah Hospital, Lahore, Pakistan. Semi-structured questionnaires were used to interview 1,729 T2DM patients prescribed metformin. Face-to-face interviews conducted by qualified healthcare workers effectively gathered demographic data, lifestyle practices, and health histories.

The questionnaire encompassed several key variables, including patient-related data such as age, gender, socioeconomic status (SES), and BMI; dietary patterns, physical activity levels, and smoking status; and disease history, including the duration of T2DM, metformin dosage and frequency of use, and concomitant medications. In addition to the demographic questionnaire, clinical details were collected from hospital records to enhance validity and broaden the scope of analysis.

This clinical data included measures of blood glucose control such as glycated hemoglobin (HbA1c), blood pressure, and lipid profiles, including total cholesterol and triglycerides, as well as liver and renal function tests to assess potential side effects or contraindications to metformin therapy. All collected data were meticulously checked for accuracy and completeness to prepare a detailed profile for each participant. This combined use of self-reported and clinical data allowed for a comprehensive approach to analyzing the prevalence of metformin use and its associated risk factors within the T2DM patient population.

Ethical Considerations: Before conducting the research, approval was obtained from the Institutional Review Board of Jinnah Hospital. The principles of informed consent and ethical standards for research involving human subjects were strictly adhered to.

Inclusion Criteria: Patients aged 20 years or older, diagnosed with T2DM, and currently using metformin to manage their condition were included in the study.

Exclusion Criteria: The exclusion criteria included patients with Type 1 DM, those on other oral antidiabetic drugs only, patients who had discontinued metformin, pregnant patients, and individuals with incomplete data.

Biochemical Tests: Biochemical tests were conducted on T2DM patients using metformin to evaluate the effectiveness of therapy and potential side effects. The tests included:

- Fasting Plasma Glucose (FPG): To assess blood glucose levels.
- HbA1c: To evaluate long-term glycemic control.
- LDL Cholesterol: To assess cardiovascular risk.
- Serum Creatinine: To evaluate kidney function.
- Vitamin B12 Levels: To assess for deficiency profiles.

These tests provided critical insights into glucose metabolism, renal function, and side effects, contributing to

an improved understanding of T2DM management and the safety of long-term metformin therapy.

Statistical Analysis: Data analysis was performed using the Statistical Package for Social Sciences (SPSS) software, version 26. Demographic and clinical characteristics were described using frequency distributions and measures of central tendency. The proportion of metformin use was estimated as a percentage of the overall population. Logistic regression models were applied to identify key risk indicators for metformin usage while controlling for influential covariates.

RESULTS

A total of 1,704 patients with T2DM who initiated active metformin treatment were enrolled in the study. Patients were divided into four age groups: young adults, middle-aged adults, and older adults, categorized as 20–30 years, 30–40 years, 40–50 years, and 50–60 years, respectively. Demographic characteristics such as gender, BMI, and lifestyle factors were analyzed according to these age groups.

Table 1: Demographic Characteristics of Study Population (N = 1,729)

Age Group (years)	Male (%)	Female (%)	Average BMI (kg/m²)	Smokers (%)	Family History of T2DM (%)
20–30 (n = 340)	45% (153)	55% (187)	27.3 ± 3.4	30% (102)	25% (85)
30–40 (n = 450)	48% (216)	52% (234)	29.5 ± 3.7	35% (158)	33% (149)
40–50 (n = 520)	50% (260)	50% (260)	30.2 ± 3.5	40% (208)	40% (208)
50–60 (n = 419)	52% (218)	48% (201)	30.8 ± 3.9	42% (176)	45% (189)

The study population (N = 1,729) was evenly divided between males and females. However, the proportion of males increased with age, peaking at 52% in the 50–60 years category. Average BMI also increased across age groups, from 27.3 kg/m^2 among 20–30-year-olds to 30.8 kg/m^2 among 50–60-year-olds. Smoking prevalence rose with age, from 30% in the youngest group to 42% in the oldest group. Similarly, a family history of T2DM increased from 25% in the youngest group to 45% in the oldest group.

Table 2: Gender-Specific Prevalence of Metformin Use

Age Group (years)	Male Patients Using Metformin (n, %)	Female Patients Using Metformin (n, %)	Total Patients Using Metformin (n)	Total Patients in Age Group	Prevalence (%)
20–30	33 (21.6%)	42 (22.5%)	75	340	22.1%
30–40	58 (26.9%)	62 (26.5%)	120	450	26.7%
40–50	92 (35.4%)	88 (33.8%)	180	520	34.6%
50–60	80 (36.7%)	70 (34.8%)	150	419	35.8%

Metformin usage increased with age, with the highest prevalence (35.8%) observed in the 50–60 years category. Male and female usage rates were similar across all age groups. The highest total number of users (180) belonged to the 40–50 years group, while the lowest prevalence (22.1%) and number of users (75) were found in the 20–30 years category.

Table 3: Biochemical Test Results by Age Group

Biochemical Test	Reference Range	20–30 (n = 340)	30–40 (n = 450)	40–50 (n = 520)	50–60 (n = 419)
Fasting Plasma Glucose	Normal: 70–99 mg/dL; Abnormal: ≥100 mg/dL	125 ± 20 (80% abnormal)	130 ± 25 (85% abnormal)	140 ± 30 (90% abnormal)	145 ± 32 (95% abnormal)
HbA1c (%)	Normal: ≤5.7%; Diabetes: ≥6.5%	7.2 ± 0.5 (75% abnormal)	7.5 ± 0.7 (80% abnormal)	7.8 ± 1.0 (85% abnormal)	8.0 ± 1.2 (90% abnormal)
LDL Cholesterol (mg/dL)	Optimal: <100 mg/dL; High: ≥130 mg/dL	102 ± 15 (65% borderline)	110 ± 18 (70% borderline)	118 ± 20 (80% borderline)	120 ± 25 (85% borderline/high)
Serum Creatinine (mg/dL)	Normal: 0.6–1.3 mg/dL	0.90 ± 0.20 (normal)	0.95 ± 0.30 (normal)	1.00 ± 0.30 (normal)	1.10 ± 0.40 (10% borderline)
Vitamin B12 (pg/mL)	Normal: 200–900 pg/mL; Deficiency: <200 pg/mL	420 ± 80 (normal)	400 ± 75 (normal)	380 ± 70 (normal)	350 ± 65 (15% deficiency)

Biochemical test results showed worsening glycemic control with increasing age. HbA1c levels rose from 7.2% in the youngest group to 8.0% in the oldest. LDL cholesterol and serum creatinine levels also showed age-related trends, with borderline or high values increasing among older patients. Vitamin B12 deficiency was observed in 15% of the oldest group.

Table 4: Smoking and BMI Impact on Metformin Use (N = 1,729)

Category	Patients Using Metformin (n, %)	Total Patients in Category (n)	Prevalence (%)	Odds Ratio (OR)	95% CI for OR
Smoking Status					
Smokers	290 (45.0%)	644	45.0%	1.45	1.25–1.69
Non-Smokers	235 (29.7%)	1,085	29.7%	Reference	N/A
Body Mass Index (BMI)					
BMI ≥ 30	250 (53.5%)	467	53.5%	1.85	1.53–2.23
BMI < 30	275 (25.7%)	1,262	25.7%	Reference	N/A

Smokers were more likely to use metformin than non-smokers, with an odds ratio (OR) of 1.45 (95% CI: 1.25–1.69). Patients with BMI ≥ 30 were significantly more likely to use metformin (53.5%) compared to those with BMI < 30 (25.7%), with an OR of 1.85 (95% CI: 1.53–2.23).

Table 5: Risk Factors Associated with Metformin Use Among Patients with T2DM (N = 1,729)

Risk Factor	Category	Patients Using Metformin (n, %)	Total Patients in Category (n)	Prevalence (%)	Odds Ratio (OR)	95% CI for OR
Smoking Status	Smokers	290 (45.0%)	644	45.0%	1.45	1.25–1.69
	Non-Smokers	235 (29.7%)	1,085	29.7%	Reference	N/A
Body Mass Index (BMI)	BMI ≥ 30	250 (53.5%)	467	53.5%	1.85	1.53–2.23
	BMI < 30	275 (25.7%)	1,262	25.7%	Reference	N/A
Age Group (years)	20–30	75 (22.1%)	340	22.1%	Reference	N/A
	30–40	120 (26.7%)	450	26.7%	1.25	0.93–1.68
	40–50	180 (34.6%)	520	34.6%	1.87	1.45–2.40
	50–60	150 (35.8%)	419	35.8%	1.95	1.51–2.53
Gender	Male	425 (34.7%)	1,220	34.7%	1.22	1.03–1.44
	Female	300 (30.6%)	509	30.6%	Reference	N/A
Family History of T2DM	Yes	360 (42.4%)	849	42.4%	1.76	1.48–2.08
	No	365 (28.3%)	880	28.3%	Reference	N/A

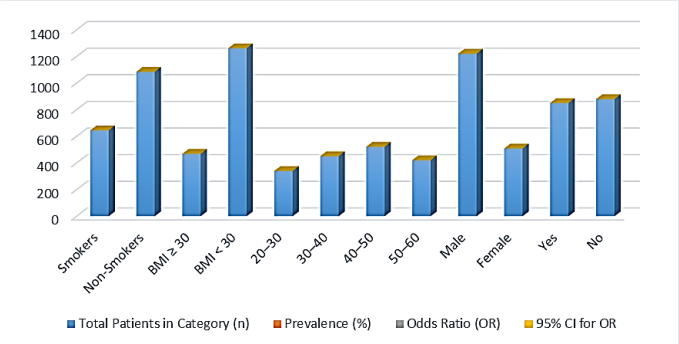

Figure 1 Risk Factors Associated with Metformin Use Among Patients with T2DM

Risk factors associated with metformin use included smoking, obesity (BMI ≥ 30), older age, male gender, and a family history of T2DM. Smoking and obesity were particularly strong predictors of metformin use.

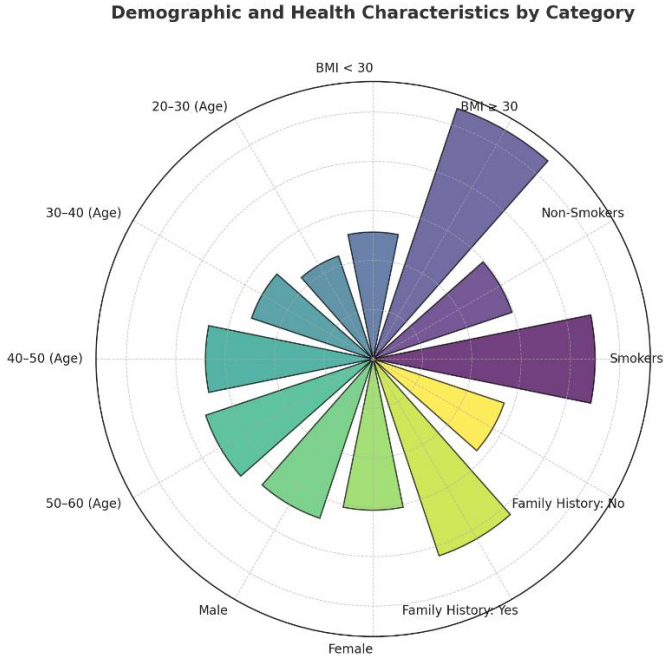

Figure 2 Category wise Demographic and Health Characteristics

The radial bar chart visualizes the prevalence percentages of various demographic and health characteristics, including smoking status, BMI categories, age groups, gender, and family history of T2DM. Each bar's length represents the prevalence percentage, with categories arranged circularly to highlight distribution patterns and facilitate comparison across groups in an engaging and unconventional layout.

DISCUSSION

T2DM is the most common type of diabetes and requires lifelong treatment to properly manage blood glucose levels and reduce the risk of complications. However, compliance rates among patients often decrease over time, particularly for those on chronic medication, which significantly reduces treatment effectiveness (23).

Oral metformin is regarded as the first-line pharmacologic therapy for T2DM due to its proven ability to reduce blood glucose levels, its favorable risk profile, and additional beneficial effects. Metformin monotherapy is common among T2DM patients, and research shows that it is prescribed to the majority of such individuals. This discussion considers the current knowledge of metformin use, the factors associated with its utilization, and comparisons with other management options for T2DM.

The utilization of metformin in the management of T2DM is substantial, with a significant proportion of patients prescribed the medication. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) clinical guidelines recommend metformin as the initial treatment for T2DM. Based on its efficacy, it is suggested that metformin, either as monotherapy or in combination with other drugs, can effectively lower HbA1c levels by approximately 1.12% as monotherapy or 0.95% when combined with other medications (24).

Mazumder and Sing (2021) explained that metformin commonly causes gastrointestinal (GI) side effects, which have a prevalence of 20–30%. These symptoms include nausea, vomiting, diarrhea, dyspepsia, bloating, a metallic taste, and cramp-like abdominal pain.

Changes in GI motility can sometimes become uncontrollable, and approximately 5% of diabetic patients discontinue therapy prematurely due to these side effects (25).

Dutta et al. (2023) highlighted that metformin has been recognized for its ability to attenuate hyperglycemia and obesity, lower triglyceride and cholesterol levels, and increase fibrinolytic activity in both diabetic and non-diabetic individuals for more than two decades (26).

Recent reports by Masson et al. (2021) indicated that metformin is beneficial in preventing cardiac events in T2DM patients, delaying the onset of T2DM in non-diabetic individuals, modifying impaired glucose tolerance (IGT) in patients with metabolic syndrome, and controlling weight gain caused by atypical antipsychotics. Despite its minimal side effects and relative safety for use in T2DM patients, metformin often provokes adverse drug reactions (ADRs), particularly gastrointestinal symptoms such as diarrhea (27).

According to Bouchi et al. (2022), a possible concern is the rate of serious ADRs triggered by metformin. A retrospective cohort study in Japan identified factors associated with ADR development in T2DM patients initiating metformin therapy. These risk factors can guide clinicians in predicting and mitigating potential ADRs, ultimately improving treatment processes (27).

While metformin offers numerous benefits, its underdosing in appropriate populations with T2DM remains a significant issue. Future efforts should focus on better understanding the antecedents of metformin utilization and enhancing its implementation in clinical practice. This includes addressing clinicians' concerns about ADRs and contraindications, as well as educating patients about the potential benefits and risks of metformin therapy.

Smoking status emerged as another determinant of metformin use in this study. Metformin therapy was more prevalent among smokers than non-smokers, likely due to the impact of smoking on metabolism and glycemic control. This finding underscores the need for comprehensive intervention strategies that combine smoking cessation with pharmacologic treatment to improve outcomes (23-27).

CONCLUSION

This research emphasizes the importance of metformin in treating T2DM, as reflected by its widespread use in real-world data, particularly among the elderly, obese, and smokers. Metformin provides effective glycemic control without significant cardiovascular hazards, but chronic use can lead to side effects such as vitamin B12 deficiency and gastrointestinal issues.

It is recommended that future care incorporate biochemical monitoring to optimize therapy and tailor educational materials. Behavior modification programs, including smoking cessation and weight loss campaigns, should be integral to patient management. Additionally, barriers to metformin use among special patient groups should be addressed.

Further studies should explore the factors influencing adherence to metformin regimens, investigate side effects systematically and objectively, and assess the long-term impact of metformin therapy across diverse patient groups. These efforts are essential to improving diabetes management for all.

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