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Medicine

IMPACT OF POLYPHARMACY ON GLYCEMIC CONTROL IN DIABETES: A STUDY ON PHARMACOLOGICAL PERSPECTIVE

Dr. Deepak Kavhar Junior Resident, Department of Pharmacology, Government Medical College Jalgaon, Maharashtra, India.

Dr. Pravin Lohar Professor, Department of Pharmacology, Government Medical College Jalgaon, Maharashtra, India.

Dr. Sakshi Kamble Junior Resident, Department of Pharmacology, Government Medical College Jalgaon, Maharashtra, India.

ABSTRACT **Introduction:** Diabetes mellitus (DM) is a chronic condition characterized by hyperglycemia due to impaired insulin secretion, insulin resistance, or both. Glycemic control is vital to prevent complications such as cardiovascular diseases and neuropathy. Polypharmacy, defined as the use of five or more medications, is common in type 2 diabetes mellitus (T2DM) due to associated comorbidities. However, it can lead to nonadherence, drug-drug interactions, and adverse effects, potentially worsening glycemic outcomes. **Materials And Methods:** This prospective study included 100 T2DM patients categorized into polypharmacy (≥5 medications) and non-polypharmacy (<5 medications) groups. Glycemic control was assessed using fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated hemoglobin (HbA1c). Medication adherence was measured using the Medication Adherence Rating Scale (MARS), and drug-drug interactions and complications were documented. **Results:** Patients in the polypharmacy group had higher FBG (150 ± 20 vs. 140 ± 18 mg/dL, p=0.04), PPBG (200 ± 30 vs. 180 ± 25 mg/dL, p=0.01), and HbA1c levels (8.5 ± 1.0 vs. 7.8 ± 0.8%, p=0.02). Medication adherence was lower in the polypharmacy group (6.5 ± 1.2 vs. 8.2 ± 0.9, p=0.003), with more frequent drug-drug interactions (60% vs. 20%, p<0.001). Complications, including hypoglycemia (20% vs. 10%), hyperglycemia (15% vs. 8%), and cardiovascular events (25% vs. 15%), were significantly higher in this group. **Discussion:** Polypharmacy negatively impacts glycemic control, adherence, and safety. The complexity of managing multiple medications contributes to medication mismanagement, highlighting the need for regular reviews and patient education to optimize treatment regimens. **Conclusion:** Polypharmacy in T2DM patients is linked to poorer glycemic control, lower adherence, and increased complications. Optimizing medication regimens, regular reviews, and adherence strategies are essential to improve outcomes and reduce risks.

KEYWORDS : Type 2 diabetes mellitus, polypharmacy, glycemic control, fasting blood glucose, postprandial blood glucose, glycated hemoglobin

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin resistance, or a combination of both. Effective glycemic control is crucial in preventing the progression of diabetes-related complications, including cardiovascular diseases, neuropathy, nephropathy, and retinopathy.[1] Achieving optimal blood glucose levels requires a combination of lifestyle modifications and pharmacological interventions. However, the complexity of diabetes management often leads to polypharmacy, which refers to the use of five or more medications concurrently.[2]

Polypharmacy is particularly prevalent among individuals with type 2 diabetes mellitus (T2DM) due to the frequent coexistence of multiple comorbidities such as hypertension, dyslipidemia, and cardiovascular disease.[3] While the use of multiple medications may be necessary for comprehensive disease management, it also presents challenges, including increased risks of medication nonadherence, drug-drug interactions, and adverse drug reactions. These factors can contribute to poor glycemic control and unfavorable clinical outcomes.[4,5]

Despite the widespread occurrence of polypharmacy in T2DM, its direct impact on glycemic control and patient adherence remains an area of concern. Understanding the relationship between polypharmacy and diabetes outcomes can help in optimizing treatment regimens, minimizing adverse effects, and improving medication adherence. [6-8] This study aims to assess the impact of polypharmacy on glycemic control in T2DM patients by evaluating fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated hemoglobin (HbA1c) levels. Additionally, the study explores medication adherence and the incidence of drug-related complications to provide insights into potential strategies for improving diabetes management.

MATERIALS AND METHODS

Study Design And Setting

This prospective observational study was carried out in the Department of Pharmacology at Government Medical College, Jalgaon, Maharashtra, India. The objective was to evaluate the impact of polypharmacy on glycemic control among patients diagnosed with type 2 diabetes mellitus (T2DM).

Study Population

A total of 100 patients with T2DM attending the outpatient department were recruited for the study. Participants were divided into two groups based on the number of medications they were taking. The *polypharmacy group* consisted of patients who were prescribed five or more medications, whereas the *non-polypharmacy group* included those taking fewer than five medications.

Inclusion Criteria

Patients aged 18 years or above, with a confirmed diagnosis of T2DM for at least one year, and currently receiving oral hypoglycemic agents (OHAs) and/or insulin therapy were included in the study.

Exclusion Criteria

Patients diagnosed with Type 1 diabetes mellitus, pregnant or lactating women, and those suffering from end-stage renal disease, malignancies, or severe hepatic dysfunction were excluded. Additionally, patients who were unwilling to participate or were lost to follow-up were also not considered for the study.

Data Collection And Outcome Measures

Participants were evaluated for glycemic control, medication adherence, and drug-related complications. Glycemic control was assessed using fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated hemoglobin (HbA1c) levels. FBG was measured after an overnight fast, PPBG was recorded two hours after a meal, and HbA1c levels provided an estimate of long-term glycemic control. Medication adherence was evaluated using the Medication Adherence Rating Scale (MARS), a validated tool for assessing patient compliance with prescribed treatments. Drug-drug interactions and complications were identified by reviewing patient prescriptions and medical records, focusing on adverse effects such as hypoglycemia, hyperglycemia, and cardiovascular events.

Statistical Analysis

Continuous variables, including FBG, PPBG, HbA1c, and adherence scores, were expressed as mean ± standard deviation (SD) and compared between the polypharmacy and non-polypharmacy groups using the Student's t-test. Categorical variables such as the presence of drug-drug interactions and adverse events were analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically

significant for all comparisons.

RESULTS

The demographic data indicate that the mean age of participants in the polypharmacy group was significantly higher (62 ± 8 years) compared to the non-polypharmacy group (58 ± 7 years), with a p-value of 0.03, suggesting that polypharmacy is more common among older individuals. However, there were no significant differences in gender distribution between the groups. The proportion of males was 55% in the polypharmacy group versus 52% in the non-polypharmacy group (p = 0.42), while females constituted 45% and 48%, respectively (p = 0.56). These findings suggest that age, but not gender, may play a role in the prevalence of polypharmacy among patients with type 2 diabetes mellitus.

Analysis of clinical characteristics revealed that the polypharmacy group had a significantly longer duration of diabetes (12 ± 4 years) compared to the non-polypharmacy group (10 ± 3 years), with a p-value of 0.04. The body mass index (BMI) was also higher in the polypharmacy group (27.5 ± 3.2 kg/m²) than in the non-polypharmacy group (26.0 ± 2.8 kg/m²), with a borderline significant difference (p = 0.05). The prevalence of comorbid conditions was markedly higher in the polypharmacy group, including hypertension (70% vs. 50%, p = 0.02), dyslipidemia (65% vs. 45%, p = 0.01), and cardiovascular disease (50% vs. 30%, p = 0.003). These findings underscore the association between polypharmacy and the presence of multiple comorbidities, which may contribute to the increased medication burden in this group.

The glycemic control parameters showed statistically significant differences between the two groups. The polypharmacy group exhibited higher fasting blood glucose levels (150 ± 20 mg/dL) compared to the non-polypharmacy group (140 ± 18 mg/dL, p = 0.04), as well as higher postprandial blood glucose levels (200 ± 30 mg/dL vs. 180 ± 25 mg/dL, p = 0.01). Similarly, mean HbA1c levels were significantly elevated in the polypharmacy group (8.5 ± 1.0%) compared to the non-polypharmacy group (7.8 ± 0.8%), with a p-value of 0.02, indicating poorer long-term glycemic control. Furthermore, medication adherence scores were significantly lower in the polypharmacy group (6.5 ± 1.2) compared to the non-polypharmacy group (8.2 ± 0.9), with a highly significant p-value of 0.003, suggesting reduced adherence among patients on multiple medications. The incidence of drug-drug interactions was also substantially higher in the polypharmacy group (60% vs. 20%, p < 0.001). In terms of glycemic events, the polypharmacy group showed a higher frequency of hypoglycemia (20% vs. 10%, p = 0.05) and hyperglycemia (15% vs. 8%, p = 0.08), though the latter did not reach statistical significance. Cardiovascular events were also more frequent in the polypharmacy group (25% vs. 15%, p = 0.04). Overall, these results highlight that polypharmacy is associated with poorer glycemic control, lower medication adherence, increased drug-related risks, and greater cardiovascular morbidity.

General Demographic Characteristics

Characteristic	Polypharmacy Group (≥5 medications) (Mean ± SD)	Non-Polypharmacy Group (<5 medications) (Mean ± SD)	p-value
Age (years)	62 ± 8	58 ± 7	0.03
Male (%)	55	52	0.42
Female (%)	45	48	0.56

Clinical Characteristics Of Study Participants

Characteristic	Polypharmacy Group (≥5 medications) (Mean ± SD)	Non-Polypharmacy Group (<5 medications) (Mean ± SD)	p-value
Duration of Diabetes (years)	12 ± 4	10 ± 3	0.04
BMI (kg/m²)	27.5 ± 3.2	26.0 ± 2.8	0.05
Hypertension (%)	70	50	0.02
Dyslipidemia (%)	65	45	0.01
Cardiovascular Disease (%)	50	30	0.003

Study Results On Polypharmacy And Glycemic Control

Parameter	Polypharmacy Group (≥5 medications) (Mean ± SD)	Non-Polypharmacy Group (<5 medications) (Mean ± SD)	p-value
Fasting Blood Glucose (mg/dL)	150 ± 20	140 ± 18	0.04
Postprandial Blood Glucose (mg/dL)	200 ± 30	180 ± 25	0.01
HbA1c (%)	8.5 ± 1.0	7.8 ± 0.8	0.02
Medication Adherence Score	6.5 ± 1.2	8.2 ± 0.9	0.003
Drug-Drug Interactions (%)	60	20	<0.001
Hypoglycemia (%)	20	10	0.05
Hyperglycemia (%)	15	8	0.08
Cardiovascular Events (%)	25	15	0.04

DISCUSSION

In our study, the mean age in the polypharmacy group was significantly higher (62 ± 8 years) compared to the non-polypharmacy group (58 ± 7 years, $p = 0.03$), indicating that advancing age may be a contributing factor to polypharmacy in patients with type 2 diabetes mellitus (T2DM). These findings are in line with the results of Alwhaibi et al. (2019)[8], who reported that polypharmacy was more prevalent in older adults, with the majority of polypharmacy cases observed in patients aged ≥60 years . Similarly, Wimmer et al. (2017) [9] noted an increasing trend of medication use with age, especially in elderly diabetic populations. Gender distribution, however, did not differ significantly between groups in our study (Male: 55% vs. 52%, Female: 45% vs. 48%; $p > 0.05$), which corroborates findings by Sinnott et al. (2015) [10], who observed no significant sex-based disparity in the prevalence of polypharmacy.

Our study revealed a significantly longer duration of diabetes in the polypharmacy group (12 ± 4 years) than in the non-polypharmacy group (10 ± 3 years, $p = 0.04$). This aligns with the study by Guisado-Clavero et al. (2018), [11] which found that patients with longer diabetes duration tend to develop more complications, leading to the use of multiple medications. Furthermore, the mean BMI was higher in the polypharmacy group (27.5 ± 3.2 kg/m²) compared to the non-polypharmacy group (26.0 ± 2.8 kg/m²; $p = 0.05$). Similarly, the study by Hovstadius et al. (2010) [12] reported that obesity was significantly associated with increased medication use in patients with T2DM.Our study also demonstrated significantly higher rates of comorbidities in the polypharmacy group: hypertension (70% vs. 50%, $p = 0.02$), dyslipidemia (65% vs. 45%, $p = 0.01$), and cardiovascular disease (50% vs. 30%, $p = 0.003$). These findings mirror those of Rajendiran et al. (2020),[13] who observed that patients with multiple chronic conditions such as hypertension and dyslipidemia had a higher probability of being on five or more medications .

Our study found that glycemic control was poorer among polypharmacy patients. Fasting blood glucose was significantly higher in the polypharmacy group (150 ± 20 mg/dL) compared to the non-polypharmacy group (140 ± 18 mg/dL, $p = 0.04$). Similarly, postprandial glucose levels were also higher (200 ± 30 mg/dL vs. 180 ± 25 mg/dL, $p = 0.01$). HbA1c levels were significantly elevated in the polypharmacy group (8.5 ± 1.0%) versus the non-polypharmacy group (7.8 ± 0.8%, $p = 0.02$). These findings are consistent with the study by Kalogianni et al. (2021),[14] which demonstrated that polypharmacy was associated with suboptimal glycemic control, with mean HbA1c levels of 8.6% in the polypharmacy group compared to 7.7% in those taking fewer medications .

Medication adherence was significantly lower in the polypharmacy group (6.5 ± 1.2) than in the non-polypharmacy group (8.2 ± 0.9, $p = 0.003$). This supports the findings of Jin et al. (2008),[15] who reported that medication adherence declines with an increasing number of prescribed drugs due to complex regimens and pill burden . Additionally, Vimalananda et al. (2015)1 [16] observed lower adherence scores among diabetic patients on multiple therapies, further substantiating our results.

Our data also revealed a significantly higher incidence of drug-drug interactions in the polypharmacy group (60% vs. 20%, $p < 0.001$). These findings are consistent with those of Weng et al. (2013),[17] who

reported a drug-drug interaction rate of 55% in polypharmacy patients with T2DM . In terms of adverse glycemic events, the polypharmacy group had higher rates of hypoglycemia (20% vs. 10%, $p = 0.05$) and hyperglycemia (15% vs. 8%, $p = 0.08$). These observations are similar to the findings of Inzucchi et al. (2012), [18]who emphasized the increased risk of both hyper- and hypoglycemic events with polypharmacy, especially when multiple antidiabetic agents are used .

A higher proportion of cardiovascular events was seen in the polypharmacy group (25% vs. 15%, $p = 0.04$). This concurs with the study by Mangin et al. (2018),[19] who highlighted that polypharmacy, particularly involving cardiovascular and antidiabetic medications, may be associated with increased cardiac morbidity due to drug interactions and cumulative toxicity .

CONCLUSION

In summary, our findings support the growing evidence that polypharmacy is more prevalent in older patients with T2DM, especially those with a longer disease duration and multiple comorbidities. It is associated with poorer glycemic control, lower medication adherence, increased risk of drug-drug interactions, and higher rates of adverse events and cardiovascular complications. These observations emphasize the need for regular medication reviews, patient education, and individualized treatment planning to minimize the risks associated with polypharmacy in diabetic patients.

Limitations Of The Study

This study was limited by its small sample size and single-center design, which may affect generalizability. The short follow-up period restricted assessment of long-term outcomes. Medication adherence was self-reported, introducing possible bias. The study did not account for specific drug classes or confounding lifestyle factors such as diet and physical activity. Additionally, patient-reported outcomes like quality of life were not evaluated.

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