**Original Article**

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# Frequency of Missing Dose of Anti-Diabetic Medications and its Impact on Blood Glucose Levels Among Patients of Diabetes Mellitus

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Author`s Contribution

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**ABSTRACT**

**Objective:** To determine the frequency of missed medications and its association with glycemic control among patients of diabetes mellitus.

**Methodology**: This cross-sectional study was conducted at the Outpatient Department of Medicine, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from January 2022 to June 2022. Patients with type-1 or type-2 diabetes mellitus who visited the outpatient department and had a disease duration of at least six months were included in the study. Participants might be either gender and ranged in age from 18 to 70. Along with sociodemographic information, characteristics of diabetes mellitus were recorded including fasting and postprandial blood glucose levels, kinds of DM, drugs used, and family history of DM. All patients' frequency of missing diabetic mellitus prescription doses was also assessed.

**Results:** In a total of 230 patients of DM, 148 (64.3%) were male. The mean age was a 45.00±12.48 year. Family history of diabetes was present in 113 (49.1%) patients. There were 215 (93.5%) patients who had type 2 DM while remaining 15 (6.5%) were type-1 DM. Mean duration of DM was 7.63±7.6 years. It was found that 105 (45.7%) patients were using both oral and insulin. It was noted that 30 (13.0%) patients were missing their DM medications daily, 43 (18.7%) most frequently, 21 (9.1%) frequently and 54 (23.5%) missed their DM medications/dosages occasionally. It was observed that statistically significant differences existed for blood glucose parameters and frequency of missed medications ($p<0.0001$).

**Conclusion:** Vast majority of diabetes mellitus patients were found to miss their anti-diabetic medications. Missed medication frequency was significantly linked with higher blood glucose levels.

**Keywords:** Anti-diabetic medications, blood glucose, diabetes mellitus, fasting, postprandial.

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## Introduction

Diabetes mellitus (DM) is estimated to directly influence at least 1.6 million deaths annually while global estimates have shown that beyond 690 million individuals will have DM by year 2045.[1,2] DM is considered to be one of the major contributor to financial burden in health systems all across the globe as DM related morbidity and mortality is high in all geographies.[3,4] Future estimates have shown that cost burden related to DM is expected to rise significantly in the coming decades.[5,6]

In medical disorders that require long term management course, World Health Organization has highlighted low adherence to medications as one of the major issues in achieving expected outcomes.[7] Researchers have shown that adherence to oral anti-hyperglycemic drugs among patients of type-1 DM (T1DM) and type-2 DM (T2DM) is estimated to be between 36-93% while it is calculated to be around 63% among patients using insulin.8 Medication adherence is described as "voluntary cooperation of the patients in taking drugs or medicine as prescribed".[9] Researchers have nominated various demographical, disease related and medication related factors to be associated with non-adherence to DM medications.[10,11]

Researchers in the past have shown direct relationship between adherence to DM related medications and glycemic control.[12-14]

Recent literature reviews have provided additional information on the frequency of missed anti-diabetic drug doses and their effects on blood glucose levels in patients with diabetes mellitus. The relationship between medication non-adherence and glycemic control in type 2 diabetes patients was investigated in a comprehensive review and meta-analysis. The analysis examined a number of trials and identified a strong correlation between higher rates of medication non-adherence and inferior glycemic control and a higher risk of complications. It also highlighted the necessity for medication adherence initiatives and the possible benefits to better glycemic outcomes.[15]

Recent research has also concentrated on the frequency and causes of medication non-adherence in diabetic patients. The analysis summarised findings from numerous research and identified common reasons for missed doses, such as forgetfulness, side effects from medications, complicated treatment plans, and a lack of awareness of the significance of adherence. The authors emphasised the significance of specific strategies that are specifically designed to address these characteristics in order to increase medication adherence and, as a result, improve glycemic control in people with diabetes mellitus.[16]

To the best of our knowledge, not much work is seen analyzing frequency of missed medications among patients of DM and its effect on the glycemic control so the present study was planned. The objective of this study was to determine the frequency of missed medications and its association with glycemic control among patients of DM. The findings of the present study were thought to help us in measuring the burden of adherence to medications among DM patients.

# Methodology

This cross-sectional study was carried out at the Outpatient Department of Medicine, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from January 2022 to June 2022. Informed consent was obtained from all patients, ensuring the secrecy of their data . Patients with a history of type 1 or type 2 diabetes mellitus for at least six months who were attending the outpatient department were included in the study. They ranged in age from 18 to 70 and were of both genders. The study did not include patients with dependence, acute illness, severe illness, or memory difficulties. Patients whose prescriptions had changed within the previous month were also excluded.

During the study period, a total of 230 patients who met the inclusion and exclusion criteria were enrolled using a non-probability convenient sampling technique. Socio-demographic data and diabetes mellitus (DM) related characteristics, including family history of DM, types of DM, types of medications being used, and fasting/postprandial blood glucose levels, were recorded. All patients were evaluated for their frequency of missed medications for DM. "Daily miss" was labeled as missing more than 50% of doses daily. "Most frequently" was termed as missing 50% of doses at least 2 days a week. "Frequently" was labeled as missing 50% of medications less than 1 day a week. "Occasionally" was named if a patient missed 2-4 doses per month.

Proforma was designed to record study data. "Statistical Package for Social Sciences" version 26.0 was used for data analysis. Descriptive statistics were applied, with categorical variables shown as frequency and percentages, while numeric variables were calculated for mean and standard deviation. Analysis of variance (ANOVA) was applied to compare differences between fasting blood glucose, postprandial blood glucose, and frequency of missed medications for DM, in order to find any statistically significant differences. The chi-square test was employed to compare gender and age groups with respect to the frequency of missed medications. $P<0.05$ was considered statistically significant.

# Results

In a total of 230 patients of DM, 148 (64.3%) were male. The mean age was a 45.00±12.48 years ranging between 20-68 year. The educational status of 120 (52.2%) patients was illiterate. Mean BMI was 23.32±4.75 kg/m2 while 170

(73.9%) patients had BMI below 25 kg/m2. Family history of diabetes was present in 113 (49.1%) patients. There were 215 (93.5%) patients who had type 2 DM, while the remaining 15 (6.5%) were type-1 DM. Mean duration of DM was 7.63±7.6 years. It was found that 97 (42.2%) patients were using oral hypoglycemic agents, injectable/insulin were being used by 28 (12.2%) whereas remaining 105 (45.7%) patients were using both oral and injectable/insulin. Exercise or walk daily for a minimum of 20 minutes 36 (15.7%) Table I is showing details about the characteristics of patients with diabetes.

Evaluation about frequency of missed medications revealed that 148 (64.3%) patients were missing their medications for some sort of frequency. Further it was noted that 30 (13.0%) patients were missing their DM medications daily, 43 (18.7%) most frequently, 21 (9.1%) frequently and 54 (23.5%) missed their DM medications/dosages occasionally as shown in figure-1.

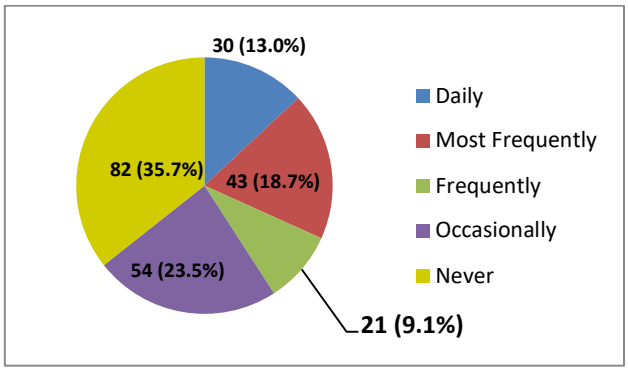


**Figure 1. Frequency of Missed Medications for Patients of Diabetes (n=230)**

The mean fasting blood glucose and mean postprandial blood glucose were noted to be was 148.50±49.15 mg/dl and 234.89±58.76 mg/dl respectively. Comparison of fasting blood glucose and postprandial blood glucose with respect to frequency of missed medications for DM are shown in table II and it was found that statistically significant differences existed for blood glucose parameters (p<0.0001).

Table III is showing Comparison of gender, age and types of medication with frequency of missed medications frequency. Male gender was found to have signification association with frequency of missed medications (p<0.0001). Increasing age was also found to have significant association with increasing frequency of missed medications (p<0.0001). It was found that significant association existed between frequency of missed medications and current medication types (p<0.0001). Patients using orals or insulin reported higher frequency of daily missed medications while patients using both insulin and oral drugs were missing doses less frequently.

**Table I: Characteristics of Patients with DM (n=230)**

| Characteristics | | Number (%) |
|---|---|---|
| Gender | Male | 148 (64.3%) |
| | Female | 82 (35.7%) |
| Age in Years | 18-30 | 22 (9.6%) |
| | 31-45 | 105 (45.7%) |
| | 46-60 | 88 (38.3%) |
| | 61-70 | 15 (6.5%) |
| Residential Status | Rural | 84 (36.5%) |
| | Urban | 146 (63.5%) |
| BMI | <25 | 170 (73.9%) |
| | 25-30 | 37 (16.1%) |
| | >30 | 23 (10.0%) |
| Educational Status | Illiterate | 120 (52.2%) |
| | Primary | 43 (18.7%) |
| | Secondary to Intermediate | 53 (23.0%) |
| | Graduation or Above | 14 (6.1%) |
| Marital Status | Married | 194 (84.3%) |
| | Unmarried | 36 (15.7%) |
| Occupation | Laborer | 38 (16.5%) |
| | Housewives | 59 (25.7%) |
| | Shopkeeper | 45 (19.6%) |
| | Machine Operator | 8 (3.5%) |
| | Fruit Stall | 20 (8.7%) |
| | Sanitary Worker | 22 (9.6%) |
| | Toll Booth Operator | 7 (3.0%) |
| | None | 31 (13.5%) |
| Monthly Income (PKR) | <25,000 | 177 (77.0%) |
| | 25,000 to 45,000 | 8 (3.5%) |
| | >45,000 | 14 (6.1%) |
| Family History of Diabetes | Yes | 113 (49.1%) |
| | No | 73 (31.7%) |
| | Don't Know | 44 (19.1%) |
| Diabetes Type | Type-1 | 15 (6.5%) |
| | Type-2 | 215 (93.5%) |
| Duration of Diabetes | 6 months to 1 years | 54 (23.5%) |
| | >1 year to 5 years | 74 (32.2%) |
| | >5 to 10 years | 14 (6.1%) |
| | 10 years | 88 (38.3%) |
| Medications for Diabetes | Oral | 97 (42.2%) |
| | Injectable/Insulin | 28 (12.2%) |
| | Oral & Injectable/Insulin | 105 (45.7%) |

**Table II: Comparison of Fasting Blood Glucose and Postprandial Blood Glucose With Respect To Frequency of Missed Medications for Diabetes**

| Blood Glucose Parameters | Frequency of Missed Medications for Diabetes | | | | | P-Value |
|---|---|---|---|---|---|---|
| | Daily | Most Frequently | Frequently | Occasionally | Never | |
| Fasting Blood Glucose | 191.8±68.7 | 153.5±29.7 | 156.7±33.8 | 112.8±59.8 | 144.5±30.9 | <0.0001 |
| Postprandial Blood Glucose | 281.7±94.9 | 289.5±14.4 | 213.3±29.3 | 207.4±30.6 | 207.4±38.3 | <0.0001 |

**Table III: Comparison of Gender, Age and Types of Medications with Frequency of Missed Medications for DM (n=230)**

| Parameters | | Frequency of Missed Medications for Diabetes | | | | | P-Value |
|---|---|---|---|---|---|---|---|
| | | Daily (n=30) | Most Frequently (n=43) | Frequently (n=21) | Occasionally (n=54) | Never (n=82) | |
| Gender | Male | 23 (76.7%) | 20 (46.5%) | 21 (00%) | 47 (87.0%) | 37 (45.1%) | <0.0001 |
| | Female | 7 (23.3%) | 23 (53.5%) | - | 7 (13.0%) | 45 (54.9%) | |
| Age Groups | 18-30 | - | - | 7 (33.3%) | 15 (27.8%) | - | <0.0001 |
| | 31-45 | 15 (50.0%) | 7 (16.3%) | 7 (33.3%) | 23 (42.6%) | 53 (64.6%) | |
| | 46-60 | | 29 (67.4%) | 7 (33.3%) | 16 (29.6%) | 21 (25.6%) | |
| | 61-70 | 15 (50.0%) | 7 (16.3%) | - | - | 8 (9.8%) | |
| Types of Medications | Oral | 15 (50.0%) | 15 (34.9%) | 21 (100%) | 16 (29.6%) | 30 (36.6%) | <0.0001 |
| | Insulin | 15 (50.0%) | 13 (30.2%) | - | - | - | |
| | Oral and Insulin | - | 15 (34.9%) | - | 38 (70.4%) | 52 (63.4%) | |

# Discussion

The main goal of diabetes mellitus (DM) management revolves around achieving satisfactory glycemic control to prevent microvascular and macrovascular complications throughout the course of the disease. Poor glycemic control is perceived to be significantly associated with non-adherence to anti-diabetic drugs. The present study was the first of its kind in Punjab, Pakistan, where we revealed that the vast majority of DM patients (64.3%) were missing their medications. It was noted that 13.0% of patients were missing their DM medications daily, 18.7% most frequently, 9.1% frequently, and 23.5% occasionally. A study conducted by Ranjbaran S et al. from Iran found that only 17.7% of DM patients had proper adherence to medications, highlighting the vast majority of patients with poor adherence. [17] Another study by Martinez YV et al. from Mexico reported 82.8% of DM patients to have poor adherence to medications.[18] Another study by Alatawi noted that 60% of DM patients were not following the proper dosage administration of DM-related medications.[19] It has been shown that poor adherence to DM-related medications leads to poor outcomes, deteriorating the quality of life for the affected patients and their families, as well as significantly increasing health-related costs. [7] We found a significant association between gender (female) and increasing age with non-adherence to anti-diabetic medications. Similar findings have been reported by other researchers, where gender (either male or female) was associated with non-adherence to anti-diabetic medicines. Differences could be due to variations in socio-demographic factors.

We noted that non-adherence to anti-diabetic medication was impacting fasting blood glucose as well as postprandial blood glucose levels in the patients. We observed that blood glucose levels were significantly higher among patients who had an increased frequency of missed medications. Researchers have argued that some DM patients miss medications when they feel that their glucose levels are under control.[17] Devin and colleagues revealed that 23% of DM patients thought that their glucose levels were under control, so they skipped their medications. [20] As hyperglycemia is often asymptomatic, DM patients taking anti-diabetic drugs should be advised to strictly adhere to the prescribed plan for their medications.[21] A study from the UK revealed that poor medication adherence and missed clinical appointments were independently linked to mortality among patients with type 2 diabetes mellitus (T2DM).[5] Ho et al. also reported that poor medication adherence in DM was significantly related to all-cause deaths. [22] Efforts must be made to design and implement easy-to-understand tools for patients that will motivate them to adhere to anti-diabetic medications, which are thought to improve DM-related outcomes in these patients. Future research should also be planned to identify patient-related, prescriber-related, and medication-related factors that might hinder proper adherence to anti-diabetic medications.

Being a cross-sectional study conducted at a single study center, our findings should be further verified in future studies. We were unable to measure HbA1c levels among the studied population, which would have given us better insights into glycemic control.

# Conclusion

Vast majority of diabetes mellitus patients were found to miss their anti-diabetic medications. Missed medication frequency was significantly linked with higher blood glucose levels. Female gender and rising age had significant relationship with missed medication frequency.

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