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Impact Of Medication Adherence On Depression And Quality Of Life Among South Indian Rural Type 2 Diabetes Mellitus Patients

Mohammed Azhar Hussain Ph.D. Scholar[1], Gooty Shanaz Pharm D Student[2], Abhirup Bhusan Nandi Pharm D Student[3], Sannik Chakraborty Pharm D Student[3], Mudigubba Manoj Kumar Pharm.D[5], Ph.D, Mahadevamma Lingaiah Ph.D[6], Shashikumar N MBBS, MD[7].

[1,2,3,4,5]Department of Pharmacy Practice, College of Pharmaceutical Sciences, Dayananda Sagar University, Bangalore, Karnataka, India.

[7]Department of General Medicine, CDSIMER, Dayananda Sagar University, Bangalore Karnataka, India.

[6]Department of Pharmacy Practice, Raghavendra Institute of Pharmaceutical Education and Research-Autonomous, Anantapur, Andhra Pradesh, India.

Correspondence: **Mahadevamma Lingaiah**

Associate professor & HOD, Department of Pharmacy Practice, College of Pharmaceutical Sciences, Dayananda Sagar University, Bangalore Karnataka, India, savipharma@gmail.com, ORCID: 0000-0002-2152-8627

ABSTRACT

Introduction: *Diabetes Mellitus poses a significant global challenge, notably increasing the risk of comorbidities and complications. Medication adherence, a significant modifiable factor plays a vital role in the effective management of diabetes. Promoting medication adherence can delay the progression of depressive symptoms, as poor adherence is associated with diminished quality of life. The study aims to evaluate the Quality of Life in individuals with Type 2 Diabetes Mellitus and to explore the connection between the severity of depressive symptoms and medication adherence.*

Methodology: *In this cross-sectional study, a total of 101 individuals diagnosed with Type 2 Diabetes Mellitus were recruited. Medication Adherence was assessed using Medication Adherence Rating Scale (MARS). Quality of Life was evaluated using the WHOQOL-BREF Questionnaire, while the severity of depressive symptoms was assessed with the Hamilton Depression Rating Scale (HDRS).*

Results: *Patients with lower MARS scores demonstrated significantly higher HDRS scores ($r = -0.270$, $p = 0.006$), indicating an inverse relationship between medication adherence and depressive symptoms. Regression analysis revealed that medication adherence accounted for 7.3% for the variance in depressive symptoms ($F(1,99) = 7.805$, $p = 0.006$). Higher HDRS scores were significantly associated with lower physical and psychological domain scores on the WHOQOL-BREF ($r = -0.522$ and $r = -0.566$ respectively, both $p < 0.001$).*

Conclusion: *Implementing strategies to enhance medication adherence will effectively delay the progression of depressive symptoms among Type 2 diabetes patients. Better management of depressive symptoms can lead to improved quality of life for this population.*

Keywords: *Diabetes Mellitus, Medication Adherence, Depression, Quality of Life*

1. INTRODUCTION

Diabetes Mellitus (DM), a progressive metabolic condition marked by sustained hyperglycemia, is associated with both macrovascular and microvascular complications. In the past three decades, there has been a notable increase in the rate of Type-2 Diabetes Mellitus (T2DM) among all socioeconomic categories, resulting in 1.5 million deaths annually. The number of deaths related to diabetes is expected to increase with projections suggesting it could reach 592 million by 2035 [1]. From 2% in the 1970s to over 20% today, the prevalence of diabetes has risen in urban India, with large cities setting the trend and rural areas quickly following [2]. The expected prevalence rate can increase to 12.8% by 2045 [3]. Nonetheless, the prevalence of diabetes in India, Southeast Asia, and the rest of the world was 10.5%, 8.8%, and 9.6% in 2021, respectively, and might rise to 12.5%, 11.5%, and 10.9% by 2045 [3].

A low quality of life among diabetes patients is associated with factors such as education, marital status, occupation, complications, social support, depression, anxiety, and stress [4–6]. Assessing health-

related quality of life (HRQOL) provides essential information on diabetes care. It serves as a screening and monitoring measure, providing insights into patients' health perception and wellbeing and serving as an indicator of mortality risk. HRQOL assessment provides valuable insights for optimizing patient care by identifying modifiable factors that can be targeted with timely interventions [7]. Medication adherence, a broader term encompassing factors beyond simple compliance, refers to a patient's behaviour regarding their medication regimen [8]. Patients who stick to their treatment plans have better glycemic control and use fewer medical resources [9]. Effective management of Type-2 Diabetes relies heavily on patients adhering to their prescribed medications [10]. Diabetic patients with higher medication adherence, influenced by regular exercise, psychological traits, social support, self-efficacy, gender and disease duration, demonstrate better glycemic control [11–13]. Medication adherence in the newly diagnosed can maximize the efficacy of pharmacotherapeutic regimens with higher medical resource use [14]. Medication adherence rates differ among treatment regimens for T2DM, indicating that treatment choices may impact compliance [15]. In elderly individuals with chronic illnesses, there is an inverse relationship between depression and medication adherence [9,16]. The likelihood of acquiring comorbid depression is markedly increased in individuals with type-2 diabetes mellitus [17]. Because comorbid depression is so common in diabetes patients, early detection and intervention techniques in specialized healthcare settings are essential for the best possible outcomes for patients[18,19]. Patients with depressive symptoms had a higher level of hyperglycemia and cognitive impairment among diabetic patients [17,20]. Among diabetic older persons with poor sleep quality driven by cognitive impairment, depressive symptoms negatively affected their quality of life [21]. Medication adherence, a crucial modifiable factor in managing blood glucose levels, is highly correlated with HRQOL [10]. Research suggests that medication adherence and depression among diabetic patients are essential factors affecting their Quality of Life (QOL) [22]. The association between medication adherence and QOL is inversely proportional [23,24]. The factors responsible for the development of depression among diabetic adults remain unclear. It is crucial to comprehend how medication adherence, depression symptoms, and quality of life are related. Existing studies indicate that depressive symptoms among diabetic patients can lead to medication non-adherence, thereby decreasing their quality of life [25–27]. However, the contributing factors for depression among diabetic patients need further evaluation. This study aims to evaluate the effects of medication non-adherence on quality of life and the intensity of depressive symptoms among T2DM patients. We hypothesized that "Increased medication non-adherence is positively correlation with the severity of depressive symptoms, which in turn leads to a negative impact on quality of life."

The Medication Rating Scale (MARS) was used in this study to evaluate medication adherence[28], and the severity of depressive symptoms was assessed utilizing the 17-item Hamilton Depression Rating Scale (HDRS-17)[29]. The WHOQOL-BREF, a 26-item scale with a rating on a 1–5 ordinal scale transformed to a 0–100 scale to produce an overall QOL score, was used to assess quality of life[30].

Using these three scales, this study's goal was to determine the role of medication adherence in development of depressive symptoms and how these symptoms pertain to the standard of living of type-2 diabetic patients in rural South India. By establishing these relationships, we hope this study contributes to a better understanding of managing comorbid depression among T2DM patients.

2. MATERIALS AND METHODS:

2.1 Study Design and Population:

A cross-sectional study with 101 patients was conducted at Chandramma Dayananda Sagar Institute of Medical Education Research between November 2023 and April 2024. The inclusion criteria required participants diagnosed with Type-2 Diabetes Mellitus for a minimum of 3 months and to be receiving treatment. The study included patients aged 18 to 75, of any gender, inpatients and outpatients from the General Medicine department. Eligibility criteria required a confirmed diagnosis of diabetes mellitus with a minimum disease duration of three months. This study got approval from the Institutional Human Ethics Committee, CDSIMER, with wide reference No. CDSIMER/MR/0110/IEC/2024.

2.2 Variable and Outcome Analysis:

In this study, medication adherence was considered as the independent variable, depression was the dependent variable, and QOL was designated as the outcome. Patients were initially selected based on specific inclusion and exclusion criteria, with their treatment records and Hba1c levels reviewed.

The Medication Adherence Rating Scale (MARS) was used to assess adherence, consisting of ten items that evaluated the respondents' level of adherence. Items 7 and 8 were scored as "No=0 and "Yes=1", while items 1 to 6, 9 and 10 were scored as "No=1" and "Yes=0". The overall score indicates the level of adherence; A higher score indicates more adherence, while a lower number denotes non-adherence. Patients are likely to be adherent if they respond "Yes" to questions 7 and 8 and "No" to questions 1, 6, 9, and 10. A perfect score of 10 indicates adherence, whereas a score below 10 indicates non-adherence[28]. The Hamilton Depression Rating Scale (HDRS) was implemented to evaluate depression symptoms. This 17-item questionnaire classifies depression severity based on the aggregate score: A score of 0-7 is considered normal, while moderate depression is defined as 8-16, major depression as 17-23, and severe depression as a score of 24 or higher[29]. Quality of Life (QOL) was assessed utilizing the WHOQOL-BREF scale, a 26-item instrument covering four domains: social relationships, physical health, psychological wellbeing, and environmental health. Each item is scored on a five-point ordinal scale, ranging from 1 to 5. These responses are then converted to a scale from 0 to 100, assessing the patient's perceived quality of life [30].

2.3 Data Collection and Statistical Analysis:

Once entered into a pre-designed data collection form, the data were compiled using Microsoft Excel 2010. The data was summarised using descriptive statistics like proportions and frequencies. The chi-square test, Karl Pearson's correlation method, and ANOVA were used for inferential statistical analysis. The probabilities of elevated depressive symptoms in the three treatment groups (oral monotherapy, insulin monotherapy, and combination therapy) were estimated using logistic regression.

They computed the mean and standard deviation for the Medication Adherence Rating Scale (MARS), Hamilton Depression Scale (HDRS), and WHOQOL-BREF scores. The p-value criterion for statistical significance was less than 0.05. The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 27 and Microsoft Excel.

3. RESULTS:

Table 1 included information on the patient's demographics, clinical features, and coexisting conditions. The current study included 101 participants with type 2 diabetes; 75 patients were adhere to medication, and 26 were not. The adherent group exhibited higher mean values in age (59.28 ± 10.65 years vs 50.96 ± 11.91 years), hospitalization (9.97 days ± 7 vs 8.80 ± 5.377 days), weight (58.25 kg ± 11.55 vs 57.52 kg ± 13.95), BMI (24.07 kg/m^2 ± 3.84 vs 22.42 kg/m^2 ± 12.70) and diabetes duration (7.966 years ± 5.929 vs 6.630 years ± 4.796) compared to the non-adherent group. Conversely, the mean height (155.33 cms ± 8.04 vs 157.6 cms ± 11.14), frequency of insulin administration (1.75 ± 1.361 vs 2.20 ± 1.08), and pulse rate (89.67 bpm ± 13.6 vs 91.96 bpm ± 16.33) were lower in the adherent group. Additionally, the mean Hba1c level was lower in the adherent group (9.78 % ± 2.47 vs 10.36 % ± 2.96), compared to the non-adherent group, suggesting a possible relationship between glycaemic control and medication adherence.

Table 1: Comparison of characteristics of the patients with Medication Adherence and Non-Adherence:

Variables	Adherence	Non Adherence	P

Age	Female 30-50 50-70 >70 Male 30-50 50-70 >70	 13 39 13 13 22 1	0.038
Social habits Smoker Alcoholic Smoker and Alcoholic Tobacco Chewer Nil	 2 0 1 0 72	 3 2 2 18 1	0.0032
Blood Pressure Systolic <80 81-100 101-120 121-140 141-160 >160 Diastolic ≤ 60 61-80 81-100 >100	 1 2 31 31 8 2 2 61 11 1	 0 1 10 12 3 0 3 16 7 0	 0.33 0.65
Pulse rate Normal (60-100) Tachycardia (>100)	 64 11	 19 7	 0.158
Diabetes duration Newly diagnosed (<1 year) Short duration (1-5 years) Moderate duration (6-10 years) Long duration (>10 years)	 3 27 26 19	 1 13 7 5	 0.6563
HbA1c 6.5 6.6-8 8.1-10 >10	 7 16 19 33	 3 3 4 16	 0.3701
Type of Therapy Oral Insulin Both	 22 23 31	 3 6 6	 0.994

Combination			
Monotherapy	17	5	0.1039
Dual therapy	27	4	
Triple or more	31	16	
Comorbidities			
Present	48	17	0.8989
Absent	27	9	
Hospitalization			
OPD	11	3	0.1150
Short stay (1-3)	4	0	
Moderate stay (4-7)	30	9	
Long stay (8-14)	16	12	
Extended (≥ 15)	14	2	

The table presents a comparison of demographic and clinical variables between medication adherence and non-adherence groups. Adherence status was assessed using the Medication Adherence Rating Scale (MARS). Categorical data are expressed as frequencies. The p-values were calculated using Chi-square test or Fisher's exact test, as appropriate. A p-value < 0.05 was considered statistically significant.
P-value <0.05 is considered significant, P value>0.05 is not significant
HbA1c - Hemoglobin A1c, OPD - Outpatient department

3.1 Association of medication adherence with depressive symptoms in adults with T2DM

Using Simple Linear Regression analysis, the correlation between MARS score and the HDRS score was analyzed. The overall model was statistically significant, F(1,99) =7.805 (p=0.006). The regression model accounted for approximately 7.3% of the variance in the HDRS scores (R^2 = 0.073) (Supplementary Table 1). Specifically, the predictor MARS score explained a significant proportion of the variance in the dependent variable, HDRS score, with a sum of squares of 175.151. The residual sum of squares was 2221.76, based on 99 degrees of freedom, yielding a mean square error of 22.442 (Table 2).

Table 2: Regression Analysis summary of the predictive model

Model		Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	175.151	1	175.151	7.805	.006[b]
	Residual	2221.760	99	22.442		
	Total	2396.911	100			

a. Dependent Variable: HDRS SCORE
b. Predictors: (Constant), MARS SCORE

3.2 Impact of depressive symptoms on Quality of Life among Type-2 Diabetes Mellitus adults:

By comparing four categories (Physical, psychological, social, and environmental health), the correlation between WHOQOL and HDRS was examined based on the severity of depression (mild, moderate, and normal). Participants with normal depression scores consistently showed higher mean scores across physical and psychological (69.06% ± 7.656 and 69.42 ± 8.635 respectively) compared to those with mild (60.94% ± 10.341 and 59.11% ± 9.823 respectively) and moderate depression (57.20% ± 10.001 and 59.73% ± 8.598 respectively) (Table 3).

Table 3: Presents descriptive statistics, including mean and standard deviation, along with 95% confidence intervals for each measure.

WHO-QOL	HDRS	N	Mean	Std. Deviation	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
PHYSICAL HEALTH (%)	Mild	53	60.94	10.341	58.09	63.79
	Moderate	15	57.20	10.001	51.66	62.74
	Normal	33	69.06	7.656	66.35	71.78
	Total	101	63.04	10.382	60.99	65.09
PSYCHOLOGICAL HEALTH (%)	Mild	53	59.11	9.823	56.41	61.82
	Moderate	15	59.73	8.598	54.97	64.49
	Normal	33	69.42	8.635	66.36	72.49
	Total	101	62.57	10.365	60.53	64.62
SOCIAL RELATIONSHIPS (%)	Mild	53	73.23	7.800	71.08	75.38
	Moderate	15	73.33	6.842	69.54	77.12
	Normal	33	72.52	9.770	69.05	75.98
	Total	101	73.01	8.298	71.37	74.65
ENVIRONMENTAL HEALTH (%)	Mild	53	67.55	8.142	65.30	69.79
	Moderate	15	66.47	6.221	63.02	69.91
	Normal	33	69.09	7.800	66.33	71.86
	Total	101	67.89	7.75 9	66.36	69.42

Values are presented as mean ± standard deviation with 95% confidence intervals. WHO-QOL scores are reported as percentages across four domains: Physical Health, Psychological Health, Social Relationships, and Environmental Health. HDRS classification: *Mild* (HDRS score 8–13), *Moderate* (14–18), and *Normal* (HDRS score <8).

3.3 Interaction Effect of Medication Adherence and Depressive Symptoms on Quality of Life among Individuals with Type 2 Diabetes:

A considerable negative correlation existed between MARS and HDRS scores. ($r = -0.270$, $p = 0.006$). Additionally, a substantial negative correlation existed between the HDRS score and the psychological and physical health domains of the WHOQOL ($r = -0.566$, $p < 0.001$ and $r = -0.522$, $p < 0.001$, respectively). Furthermore, a notable positive correlation was seen between the psychological health domain and the MARS score ($r = 0.292$, $p = 0.003$). A significant negative correlation was observed between environmental health and the HDRS score ($r=-0.021$, $p=0.044$), while the correlation between social relationships and HDRS was not statistically significant (see Table 4).

Table 4: Correlation analysis between MARS and HDRS scores with Quality of Life Domains (Physical, Psychological, Social and Environmental Health)

		MARS SCORE	HDRS SCORE
MARS SCORE	Pearson Correlation	1	-.270**
	p-value	----	.006
	N	101	101
HDRS SCORE	Pearson Correlation	-.270**	1
	p-value	.006	----
	N	101	101
PHYSICAL HEALTH (%)	Pearson Correlation	.033	-.522**
	p-value	.742	.000
	N	101	101
PSYCHOLOGICAL HEALTH (%)	Pearson Correlation	.292**	-.566**
	p-value	.003	.000
	N	101	101
SOCIAL RELATIONSHIPS (%)	Pearson Correlation	-.004	-.051
	p-value	.968	.613
	N	101	101
ENVIRONMENTAL HEALTH (%)	Pearson Correlation	.071	-.201*
	p-value	.482	.044
	N	101	101

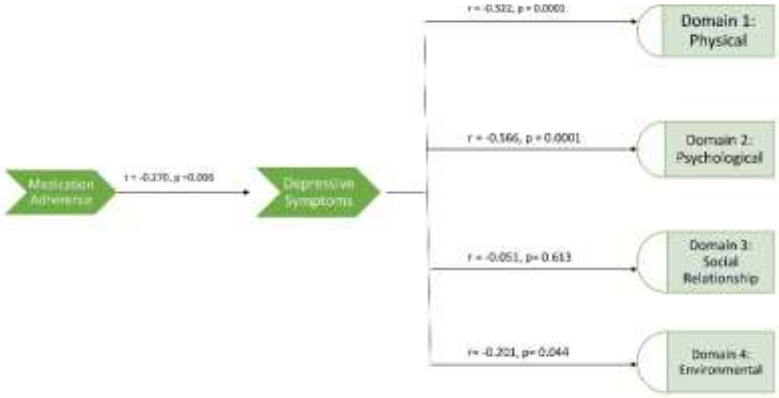
Pearson correlation coefficients (r) are reported to assess the strength and direction of relationships between variables. MARS = Medication Adherence Rating Scale; HDRS = Hamilton Depression Scale. WHO-QOL domains (Physical Health, Psychological Health, Social Relationships, and Environmental Health) are expressed as percentage scores. Significance levels: *$p < 0.01$, $p < 0.05$. Negative correlations between HDRS scores and WHO-QOL domains indicate that higher depression severity is associated with poorer quality of life.

DISCUSSION:

This observational study involved 101 patients with T2DM to examine the influence of medication adherence on the development of depressive symptoms and Quality of Life. Our findings indicate that medication adherence is negatively correlated with increased severity of depressive symptoms.

Additionally, individuals exhibiting depressive symptoms demonstrated a diminished quality of life (Figure 1). This study offers valuable insight for patients and healthcare professionals, presenting strategies to enhance the Quality of Life in diabetes management. This study represents a novel investigation into the role of medication adherence as a predictor of depressive symptoms within the South Indian population.

Figure 1



A study in Indian urban areas revealed that women had a greater lifetime risk of diabetes; these findings were supported by our investigation, which indicates a growing prevalence with an advancing age (Supplementary Table 2) [31]. According to MARS scores, 74.3% of subjects demonstrated adherence to the treatment regimen. The adherence level observed in our study was higher than that reported in a previous study in India [32]. This study indicated that women are likely to adhere to their treatment, contrary to a prior study that found men to be more adherent [31,33]. Patients receiving oral therapy alone have higher levels of adherence than those receiving insulin therapy alone or oral therapy in combination with insulin (Table 1).

Individuals diagnosed with T2DM demonstrate a higher rate of depressive disorders, indicating the necessity to assess the factors associated with the onset of depression [34]. Improved adherence levels correlated with a decrease in the advancement of depressive symptoms. The results indicate notable differences in the average scores among various age groups (p=0.011), whereas gender did not exhibit a significant impact (Supplementary Tables 3 and 4). The findings were observed to be inconsistent with prior research indicating that females exhibit elevated levels of depression, and that advancing age correlates with increased depression levels among patients with diabetes [35,36]. Although previous research suggests that individuals using insulin have more depressive symptoms than those receiving oral medications, our analysis did not find a significant difference in HDRS score changes with route of administration [33].

Among the WHO-QOL domains, only the physical health component differed significantly between males and females (p=0.001). The results are consistent with existing literature suggesting that females experience a lower QOL than males [32,35]. This could be explained by the fact that women experience depression at higher rates. The study also discovered that people over 70 years of age had the lowest mean QOL scores in physical health.

A study by Mohammed Reza Abedini et al in Brijain supports these findings, that a patients under 50 had higher mean QOL scores than patients in older age groups [32]. In a study conducted by Andrzej M Fal et al., it was observed that patients receiving oral hypoglycemic agents exhibited a superior quality of life compared to those undergoing insulin treatments [36]. However, statistical significance is absent across different age cohorts within all the domains examined. The route of administration of anti-diabetic therapy is expected to have minimal impact on the quality of life (Supplementary Table 5).

With a weak positive association (R=0.270) between MARS and HDRS scores, our study revealed that reduced medication adherence is associated with greater depression scores, which is in line with findings by David P Nau et. al [37]. About 7.3% of the variation in depression scores can be attributed

to differences in medication adherence. This correlation might not be established because the MARS questionnaire is subjective and only classifies as adherence or non-adherence rather than using specific subcategories. The objective data utilized to assess medication adherence can aid in determining the relationship between medication adherence and depression [37].

Multiple studies indicate that anxiety and depressive symptoms negatively impact HRQOL in diabetes patients, with depression directly affecting both physical and psychological health [34,38,39]. By previous findings, the study's results suggest that depression significantly impacts only physical and psychological health. Declining mean scores in the physical and psychological health domain of the WHO-QOL indicate the correlation between poor quality of life and the severity of depressive symptoms. In contrast, the mean scores for Environmental health and Social relationships exhibit minimal variation or remain relatively consistent (Table 2).

Our findings indicate that medication non-adherence is associated with depressive symptoms, subsequently diminishing the QOL, similar to the findings of Hao Yang's study [33]. We computed a single average for all WHOQOL domains to determine the overall quality of life. Using MARS and HDRS scores as predictors showed a substantial correlation with overall quality of life ($R=0.528$, $P<0.05$). Our study's regression analysis investigating the correlation between medication adherence and HDRS score with overall QOL yields numerous significant findings. The model exhibited a multiple correlation coefficient of 0.528, signifying a moderate association between the predictors (MARS and HDRS score) and overall QOL (Supplementary Table 6). Approximately 27.9% (Supplementary Table NO. 7) of the difference in overall QOL can be attributed to the combined effects of MARS and HDRS scores. The coefficient for the MARS score is 0.203, indicating that a one-unit reduction in the MARS score correlates with a 0.203 unit decline in the overall quality of life score. This connection was not statistically significant ($t = 0.143$, $p > 0.05$) (Supplementary Table no. 8), indicating that variations in MARS scores do not consistently predict changes in QOL. Furthermore, we discovered that the HDRS score significantly influenced overall QOL. The coefficient for the HDRS score is -2.692. This is a robust negative correlation ($t = -5.882$, $p < 0.001$) between the HDRS score and QOL, suggesting that elevated HDRS values, indicative of deteriorating health conditions, are significantly linked to diminished quality of life. Medication adherence has been shown in our study to improve quality of life by delaying or preventing the progression of depressive symptoms. This association highlights the importance of patient counselling, simplifying drug regimens where possible, using reminder systems and regularly adjusting regimens to improve medication adherence. The clinicians should emphasize the significance of medication adherence in diabetes management. This may enhance the quality of life for diabetic people. The research has multiple limitations. The evidence gathered from patients via various questionnaires is inherently subjective and may be biased. Questionnaires do not facilitate the determination of causal relationships or temporal associations. Evaluating the relationship between the variables was difficult due to limited time and sample size constraints.

CONCLUSION

Elevated depressive symptoms were associated with poor drug adherence, which adversely impacted quality of life. While there is no direct association between medication non-adherence and QOL, the indirect effects via depression are significant. The study emphasizes the need for strategies to enhance medication adherence, such as patient counselling, streamlined regimens, and reminder systems, to improve the overall treatment outcomes. In conclusion, healthcare providers should encourage adherence in treating diabetes mellitus to improve patients' quality of life.

Conflict of Interest: No conflict of Interest

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