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# Association Between Diabetic Control And Anti-Diabetic Medication Adherence Using 8-Point Morisky Medication Adherence Scale In Local Population Of Khyber Pakhtunkhwa

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## Abstract

**Objective:** To assess the correlation between medication adherence and control of diabetes.
**Materials & Methods:** This research was conducted as a cross-sectional study. It was scheduled between July 2022 to December 2022 in the medical outpatient department of Combined Military Hospital, Peshawar.
**Results:** 110 individuals were inducted in this study. The mean age across the study sample was 50.25 ± 11.97 years with 58 (52.73%) males and 52 (47.27%) females. The average duration of diabetes across the sample was 6.1 ± 3.69 years. The most common comorbidity among the study population was hypertension, seen in 59 (53.94%) diabetic patients. Among all 110 individuals, only 29 (26.36%) had good glycemic control (HbA1c <7%) with an average glycosylated haemoglobin percentage measuring 8.29% ± 1.59%. According to the MMAS-8 score, 25 (22.73%) patients reported good adherence, 31 (28.18%) reported fair adherence, and the remaining 54 (49.09%) were found to have poor adherence. The average MMAS-8 score was 5.17. A rise of 1 point of MMAS-8 was correlated with a fall of HbA1c by 0.247%.
**Conclusion:** A negative correlation exists between poor anti-diabetic medication adherence and MMAS-8 score
**Keywords:** Drug adherence, Morisky Medication Adherence Scale, Diabetes, Non-diabetes, diabetic medications

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## 1. Introduction

Diabetes Mellitus is one of the most prevalent chronic diseases. World Health Organization (WHO) estimates 2 million deaths each year due to diabetes and its complications[1]. Not only is it a major cause of morbidity and mortality, but also it is the second most expensive disease in terms of healthcare costs in the United States wan with estimated costs surpassing $300 billion per year[2]. The reason for its high health cost is not only the disease itself but also a myriad of microvascular and macrovascular complications associated with its chronicity and control.

Microvascular complications such as retinopathy, nephropathy and neuropathy appear earlier as compared to macrovascular complications such as cardiovascular issues and therefore with optimal control of diabetes, the benefit in the form of delayed appearance is most noticeable and seen earlier for microvascular complications as well. Several landmark trials that include VADT, ADVANCE and ACCORD have shown a decrease in microvascular complications with good control of diabetes in terms of low HbA1c levels[3–5]. A similar reduction in macrovascular complications with lower HbA1c levels hahasot been proven although UKPDS, which followed its cohort for more than a decade has provided some evidence of a reduction in myocardial deaths with optimal control of diabetes and/or blood pressure[6].

Diabetes control is based on its management which depending on its pathogenesis, type, health status and chronicity includes a variety of non-pharmacological and pharmacological strategies revolving around diet control, exercise, weight control, hypoglycemic medication, insulin therapy and control of co-morbid conditions. As the duration of diabetes increases, especially in type 2 diabetes, due to depletion of insulin secretion and increase in insulin resistance, the requirement and dosage of insulin and non-insulin antidiabetic drugs increases. Therefore, adherence to antidiabetic medication can be postulated to be one of the most important factors affecting diabetic control.

Although medication adherence is pivotal to diabetes management, still various studies across the globe have revealed suboptimal levels of self-care behaviour in patients from all backgrounds with slight variation[7,8]. Similar evidence of the low level of

adherence has been seen in Pakistan and has been postulated to be secondary to factors such as low literacy, increasing age, presence of comorbidities, polypharmacy, fear of needles, use of unorthodox medications and misconceptions about diabetes[9]. It can be reasonably deduced that lower adherence is linked with raised fasting glucose and HbA1c, studies to investigate such an effect are lacking in Pakistan[10]. This study aims to quantify such effect using already available tools in a tertiary care setup the in Khyber Pakhtunkhwa region of Pakistan.

## 2. Materials & Methods

This research was conducted as a cross-sectional study. It was scheduled between July 2022 to December 2022 in the medical outpatient department of Combined Military Hospital, Peshawar. Permission to conduct of this study was taken from the ethical committee ex Combined Military Hospital, Peshawar via letter no __N/Q16/22 dated 25TH May 2022, and guidelines set forth by the Helsinki Declaration were followed. Participants were inducted into this study after detailed verbal and written consent.

Sample size calculations were done using the OpenEPI toolkit keeping the level of significance at 95%, power of study at 80%, and the expected 1:1 ratio between individuals with good compliance and poor compliance to antidiabetic medicine. We used a value of 60% for compliant individuals with poor glycemic control and an odds ratio of 4.0 as odds of individuals with poor glycemic control and poor compliance, a sample size of 96 individuals was calculated10. We aimed to induct 20% above the minimal sample size to counter failure to follow-up by individual patients. Nonprobability convenience sampling was used to induct patients who followed inclusion and exclusion criteria.

Inclusion Criteria: Patients, (1) both males and females, (2) above 18 years of age, with a (3) diagnosis of type I or type II diabetes (4) on either oral hypoglycemic or insulin therapy (5) able to communicate and fill 8-item, Urdu translated and verified, Morisky medication adherence scale (MMAS-8) score directly or through interview with physician/data collector were inducted in this study.11

Exclusion Criteria: Patients excluded from this study were (1) diagnosed with psychiatric illnesses that may hamper patients adherence, including but not limited to depression, sleep disorders, and psychosis (2) diagnosed with dementia, (3) patients on medications that may cause sedation (4) bedridden individuals (5) individuals who do not have the physical or mental capacity to self-medicate (6) patients on 5 or more than 5 medications (polypharmacy), or (7) a score of 19 or more in Beck's depression index (BDI) to rule out patients with depression.

Patients who fulfilled the inclusion criteria were screened for the abovementioned exclusion criteria followed by a request to fill out BDI Questionnaire to rule out clinical depression. This was deemed necessary as not only depression has a higher incidence and prevalence in diabetes but also it is independently linked with a lack of medication adherence12. The BDI questionnaire was chosen as it is self-administer able, available in both English and Urdu language and has been independently verified in the local population.13 This questionnaire has 21 individual statements with a minimum score of 0 and a maximum of 3, giving a theoretical maximum of 63 points. We used a cutoff of ≥20 points in the BDI questionnaire to diagnose and exclude patients with moderate to severe depression.14

Following the BDI questionnaire all inducted participants were interviewed to elicit detailed demographic and medical history. Demographic details inquired included age, gender, education, marital status, height in meters, and weight in kilograms. A detailed history of diabetes mellitus was taken which included the duration of illness, details of medication (oral drugs and insulin), adherence to medication and details of associated conditions and complications.

Medication adherence was assessed using the Morisky medication adherence scale (MMAS-8). An Urdu version of this scale has been validated to be used in Pakistan in 2020 by Naqvi et al. 11 This simple scale consists of eight validated questions to inquire about patients' compliance and medication adherence. Each question has been given 1 point with a theoretical maximum of 8 points indicating "good" adherence. A score of 6 or less indicates "poor" adherence and a score of 7 indicates "fair" adherence.

This study used HbA1c levels to calculate the correlation between adherence and diabetic control. 1 blood sample from each patient was collected to measure HbA1c. HbA1c >7% was considered inappropriate control. Patients' BMI was also calculated from provided height and weight. Patients who fail to submit the identification number of HbA1c or failed to

communicate blood results were considered in 'failure to follow-up' and were excluded from the study.

Collected data were entered and further processed in Microsoft Excel 365. Categorical data was expressed as frequencies with percentages while nominal data was expressed as mean with standard deviation. The chi-square test was used to assess the relationship amongst categorical variables while the independent sample t-test was used to compare means between groups. We used Pearson's correlation coefficient to calculate the relationship between normally distributed variables. Simple logarithmic regression analysis was calculated to determine the effects of BMI, MMAS-8 score, age and gender on HbA1c and to calculate the p-value.

## 3. Results

In this study, 115 individuals were inducted over a period of 6 months from medical OPD ex Combined Military Hospital Peshawar. Five patients failed to follow -up with the research team resulting in a total of 110 participants included in the results. The average age across the study sample was 50.25 ± 11.97 years with 58 (52.73%) males and 52 (47.27%) females. Most participants in our study sample were educated up to matriculation with BMI <25kg/m2 (details in Table 1).

**Table-1** Characteristics of the study population

| Characteristics | | n ± SD, n(%) |
|---|---|---|
| **Age (years)** | | 50.25±11.97 |
| **Gender** | Male | 58 (52.73%) |
| | Female | 52 (47.27%) |
| **Education** | Less than Matric | 18 (16.36%) |
| | Up to Matric | 44 (40%) |
| | Intermediate | 34 (30.91%) |
| | Bachelor or higher | 14 (12.73%) |
| **Duration of Diabetes** | | 6.1 ± 3.69 |
| **HbA1c (%)** | | 8.29±1.59 |
| **Diabetes Control** | Good | 29 (26.36%) |
| | Bad | 81 (73.64%) |
| **MMAS Score** | | 5.17±2.759 |
| **Adherence** | Good | 25 (22.73%) |
| | Borderline | 31 (28.18%) |
| | Bad | 25 (22.73%) |
| **Sleep Quality** | Good | 50 (45.45%) |
| | Bad | 60 (54.55%) |
| **BMI (kg/m²)** | <18 | 31 (28.18%) |
| | 18-24.9 | 48 (43.64%) |
| | 25-29.9 | 16 (14.55%) |
| | ≥30 | 15 (13.64%) |
| **Treatment** | Oral Hypoglycemic only | 53 (48.18%) |
| | Insulin Only | 16 (14.55%) |
| | Both | 41 (37.27%) |
| **Comorbid** | Chronic Kidney Disease | 24 (21.82%) |
| | Hypertension | 59 (53.64%) |
| | Ischemic Heart Disease | 33 (30.00%) |
| | Cataract | 41 (37.27%) |
| | Cerebrovascular Accident | 23 (20.91%) |
| | ≥3 Comorbid | 19 (17.27%) |

The mean duration of diabetes across the sample was 6.1 ± 3.69 years. In treatment options, 53 (48.18%) individuals were only managed with oral therapy, 16 (14.55%) on insulin only while 41 (37.27%) were prescribed with both oral hypoglycemic drugs and insulin. The most common comorbid across the study population was hypertension, seen in 59 (53.94%) diabetic patients, followed by cataracts in 41 (37.47%) and IHD in 33 (30%) patients.

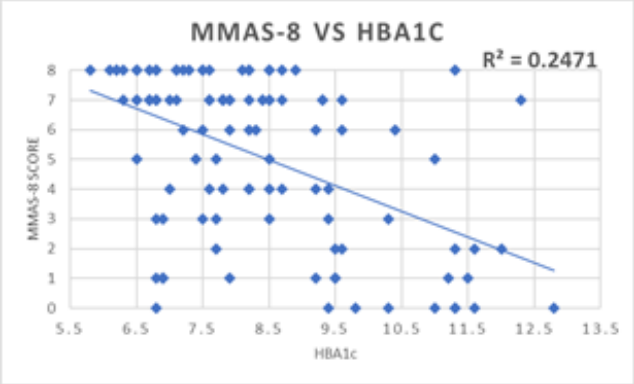


**Figure-1** Graph showing Comparison of MMAS-8 VS HBA1C

Of all 110 individuals, only 29 (26.36%) individuals had good glycemic control i.e., HbA1c <7% with an average glycosylated haemoglobin percentage measuring 8.29% ± 1.59%. As per the MMAS-8 score, 25 (22.73%) patients reported good adherence, 31

(28.18%) patients reported fair adherence while the rest 54 (49.09%) were found to have bad adherence. The average MMAS-8 score was 5.17.

An odds ratio of 3.85 (95% confidence interval 1.53-9.68) was seen between bad adherence and risk of bad diabetic control. Correlation calculation revealed a negative correlation measuring -0.50 between HbA1c and MMAS score (Figure 1). The correlation was also calculated between HbA1c and the rest of the variables (details in Table II). Notable associations (more than 0.2 or less than -0.2) included duration of diabetes, BMI, sleep quality, treatment with both oral hypoglycemic agents and insulin, with individuals having a history of cerebrovascular accidents and those having 3 or more comorbid conditions in addition to diabetes. A negative correlation measuring -0.28 was seen in individuals on oral hypoglycemics.

A negative correlation was noticed measuring -0.27 and -0.213 when comparing MMAS-8 scores and individuals on both insulin and oral hypoglycemic agents and when comparing MMAS-8 scores with individuals with 3 or more co-morbid conditions signifying a weak negative correlation between polypharmacy and compliance. Univariate regression analysis of each individual measured variable is given in Table-2.

**Table-2** Correlation Of Hba1c And MMAS-8 With Various Variables

| Association | Coefficient of correlation (R) | R squared | Beta (lower 95%, upper 95%) | P-value |
|---|---|---|---|---|
| HbA1c with Age | 0.143 | 0.020 | 0.018 (-0.003, 0.040) | 0.094 |
| HbA1c with Gender | -0.110 | 0.012 | -0.588 (-1.049, -0.127) | 0.013 |
| HbA1c with Education | -0.105 | 0.011 | -0.126 (-0.397, 0.145) | 0.359 |
| HbA1c with MMAS-8 Score | -0.497 | 0.247 | -0.228 (-0.314, -0.141) | <0.001 |
| HbA1c with Pittsburgh Sleep Quality Index | -0.339 | 0.114 | -0.504 (-1.008, 0) | 0.050 |
| HbA1c with Duration of Diabetes | 0.253 | 0.064 | 0.009 (-0.068, 0.087) | 0.808 |
| HbA1c with BMI | 0.336 | 0.112 | 0.420 (0.174, 0.667) | 0.001 |
| HbA1c with OAH Treatment Only | -0.281 | 0.079 | 0.058 (-0.642, 0.758) | 0.870 |
| HbA1c with Insulin treatment only | 0.032 | 0.001 | 0 | NA |
| HbA1c with both oral and Insulin treatment | 0.267 | 0.071 | 0 | NA |
| HbA1c with CKD | 0.143 | 0.020 | -0.075 (-0.677, 0.528) | 0.807 |
| HbA1c with Hypertension | 0.065 | 0.004 | -0.173 (-0.641, 0.295) | 0.464 |
| HbA1c with IHD | 0.023 | 0.001 | -0.400 (-0.970, 0.170) | 0.167 |
| HbA1c with Cataract | -0.043 | 0.002 | -0.240 (-0.467, -0.013) | 0.038 |
| HbA1c with CVA | 0.228 | 0.051 | -0.048 (0.684, 0.588) | 0.882 |
| HbA1c with ≥3 Comorbid | 0.358 | 0.128 | 1.408 (0.536, 2.280) | 0.001 |
| MMAS-8 with both oral and Insulin treatment | -0.273 | 0.075 | | |
| MMAS-8 with ≥3 Comorbid | -0.213 | 0.045 | | |

## 5. Discussion

Diabetes Mellitus is an endocrine disorder due to insulin deficiency or resistance. Its prevalence in lower to middle-income countries is rapidly on the rise with an estimated prevalence in Pakistan noted at an alarming 26.7%[15]. Due to rising prevalence, costs associated with diabetes management are also on a rampant rise. It is estimated that the overall cost of management of diabetes is about 1.67% of Pakistan's total gross domestic product or $24.42 Billion[16]. Complications of uncontrolled diabetes are one of the core factors driving its cost upwards at this alarming rate.

This study has assessed possible causes of uncontrolled diabetes in terms of HbA1c levels. Among assessed

factors, adherence with medications in terms of MMAS-8 score was found to be most (negatively) correlated with HbA1c levels. Among tested variables, the MMAS-8 score had the best-calculated correlation with HbA1c at the coefficient of correlation measuring at -0.497 and Beta -0.228 (95% confidence interval -0.314 to -0.141, p=<0.001). This Beta value signifies that a one-point MMAS-8 score difference leads to a 0.228% difference in HbA1c. It seems like a small amount but across the entire range of MMAS-8 score of 0-8, this signifies an HbA1c 1.824% modified my adherence alone, which can be quite meaningful clinically. Tominaga et al 2018 published a similar study based on the Japanese population. The calculated correlation between HbA1c and MMAS-8 was measured at beta -0.13 (95% CI –0.15 to –0.02, p = 0.012) comparable to HbA1c 1.12% across a range of MMAS-8[17]. Wong et al 2014 studied the association between the MMAS-8 score and glycaemic control among Chinese diabetes patients. He found a negative correlation between HbA1c and MMAS-8 score as well with a beta -0.109 (95% confidence interval -0.177 to -0.041, p=0.002)[18]. This signifies 0.872% HbA1c affected by MMAS-8 score across its range. This study was cross-sectional in nature and a direct causal relationship amongst study variables especially HbA1c and MMAS-8 scores cannot be ascertained however few interventional studies have demonstrated a causal link between adherence and HbA1c score, however few interventional studies such as Wolever et al demonstrated an improved HbA1c after coaching to increase HbA1c. A mean rise of 0.5% (p=<0.001) was seen in patients after improved adherence[19]. Similar improvements in HbA1c have been shown in other clinical trials which do not use MMAS-8 as a measure of adherence such as Arora et al, 2014, Bogner et al, 2012 and Nesari et al 2010[20–22]. Various methods have been tested to improve adherence and thus MMAS-8 score. regular phone calls by the nursing team were assessed by Nesari et al in 2010 resulting in an average improvement in HbA1c by 1.84% as compared to 1% in the control group (p<0.001)[22]. Tailored text messages were used by Silverio, 2022 as a reminder to ensure adherence and it resulted in an average improvement of 0.64% in the study population before and after intervention (p=0.002). Pharmacist counselling sessions were studied as a tool to improve MMAS-8 and reduce HbA1c by Alkhoshaiban et al, however, it moved only 11.8% of individuals from the low adherence group (MMAS-8 score <6) to moderate adherence (MMAS-8 score = 6-7) and none to High Adherence (MMAS-8 = 8)[23]. Improvement in HbA1c was modest but significant measuring at 0.32% (p=0.001). Other significant associations seen in our study were between HbA1c and sleep quality as ascertained by the PQSI scale (R=-0.339), HbA1c and BMI (R=0.336) and between HbA1c and patients with 3 or more co-morbid conditions (R=0.358). Tominaga et al also discovered an association between the number of medications used by patients and HbA1c with beta measured at 0.26 (95% CI 0.15 to 0.34, p=<0.001) and BMI with HbA1c measuring at 0.09% per point rise in BMI (95% CI 0.08 to 0.28, p<0.001)[17]. Wong et al also studied the association between multiple variables with diabetic control in the Chinese population and found a significant correlation between HbA1c and age, BMI and MMAS-8 score[18]. Medication adherence is also linked with healthy behaviour in patients as evidenced by Mirahmadizadeh et al in 2020 which linked good adherence to medications with low BMI and less smoking[24]. Similarly, Jannoo et al, in the Malaysian population revealed a significant link between good MMAS-8 and dietary habits and low MMAS-8 with low self-testing25. This study also indicated that raised BMI and HbA1c were linked with lower MMAS-8 scores. This study further builds evidence regarding the relationship between medication adherence in diabetes. Limitations of this study included firstly self-reporting basis of adherence on MMAS-8 score which might be biased and thus have lower validity. Secondly, this study was cross-sectional in nature and thus a causal link was not demonstrated. Lastly, our study contained a smaller sample from a single region of Pakistan. Future multicentric longitudinal studies are needed to provide better evidence in the Pakistani population to ascertain a causal link.

## 5. Conclusion

In conclusion, there is a correlation between medication adherence as measured by MMAS -8 score with control of diabetes as measured by HbA1c score in the range of 1.824% across the range of MMAS-8 score from 0-8. Sleep quality, BMI and multiple comorbid conditions were also linked with raised HbA1c.

**CONFLICTS OF INTEREST-** None

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**Potential competing interests:** None to report

**Contributions:**

F.A.S, M.H, W.A, S.R, N.A - Conception of study
B.S - Experimentation/Study conduction
F.A.S, M.H, W.A, S.R, N.A - Analysis/Interpretation/Discussion
F.A.S, B.S, M.H, W.A, N.A - Manuscript Writing
F.A.S, B.S, M.H, W.A, S.R, N.A - Critical Review
B.S, S.R- Facilitation and Material analysis

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