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**Original Research Article**

# Validation of the model medication adherence questionnaire to measure the adherence to oral medication among patients with type 2 diabetes mellitus in Sri Lanka

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## ABSTRACT

**Background:** The model medication adherence questionnaire (MMA) measures oral medication adherence among patients with type 2 diabetes (DM). The validity of the questionnaire needs to be objectively demonstrated.
**Methods:** A descriptive cross-sectional study was carried out among adult patients with type 2 DM who attended clinics in District General Hospital (DGH) Gampaha. A sample of 150 patients was recruited consecutively to establish the criterion and construct validity. The criterion was the composite index of pill count, recital dosage and regular clinic attendance. Sensitivity and specificity with 95% confidence-intervals (CI) were established. Construct validity: convergent and discriminative, was assessed. Results were analyzed by Spearmen correlation and Man-Whitney-U test with p values.
**Results:** The accuracy of the test was denoted by the area under the curve which is 0.87 (95% CI 0.81–0.93) with p<0.0001. The best cut-off point was 70. Patients who score >70 have good adherence to the medication while ≤70 have average adherence. This has a sensitivity of 92.9% (95% CI 85.5–96.9%), a specificity of 72.5% (95% CI 58–83.7%) with a misclassification rate of 14%. The positive likelihood ratio (LR) is 10.2. High positive LR (>10) represents that adherence is very likely in a person with a score >70. The negative likelihood ratio is 0.3 and is in the intermediate range. It suggests that a score <70 is suggestive but insufficient to rule out the non-adherence. The ideal cutoff to predict the optimum HbA1C of MMA is 67.
**Conclusions:** MMA is a valid questionnaire to measure medication adherence.

**Keywords:** Diabetes, Sensitivity, Specificity, Compliance, Likelihood ratio test

## INTRODUCTION

Adherence to diabetic oral medication is a complex human behaviour and difficult to measure.[1] Adherence is defined as the extent to which medication is taken as prescribed.[2] Nevertheless, measuring adherence in patients is vital in treatment and health service quality assurance.[3] Only a valid and reliable tool produces an accurate measure of adherence; when widely accepted, defined as the "criterion/gold standard".[4] There is no consensus among experts on the gold standard measure to use in research on medication adherence.[1,4-12]

Some authors claim medication event monitoring system (MEMS) is the most accurate measure available up to date and should be regarded as the gold standard even though some argue that it is a proxy measure of adherence.[13-15] MEMS records drug container opening timing by an electronic recorder in the lid which should be read using a computer.[13] However, wider use of MEMS is limited due

to high cost, electronic malfunction (5-20%), unable to use multiple drugs, and influence on patients' natural medication-taking behaviour.[10,16] Only a few validation studies on medication adherence have used MEMS as the criterion.[15,17] The majority have assessed construct validity in different forms and have demonstrated convergent validity among these forms.[18]

Oral medication treatment for DM is complex: multiple medications, complex dosing schedules, frequent adjustments and the need to be taken for a long time. Hence assessing adherence to DM medication is a challenge. Clinicians establish adherence by checking the glycemic control by FBS or HbA1C. Glycemic control depends on many other confounding factors other than adherence to medication.[16] Moreover, FBS reflects the glycemic control only on the previous day even though the clinician's interest is about the previous month's adherence status.[19] HbA1C measures glycemic control in the previous three months and it is not available in the government sector due to high cost: it's rarely measured in the clinical setting.[20,21] According to the evidence physician's estimate of the patient's level of adherence is a biased estimate.[16] The absence of a freely available valid and reliable method to measure adherence to DM medication in a clinical setting is a gap in the existing healthcare provision system.

MMA is a 15-item interviewer-administered questionnaire on a five-point Likert scale to measure adherence to the oral medication of DM type 2 patients. MMA measures adherence to oral medication in 15 items on a five-point Likert scale. Fourteen items are directed at adherence behaviour during the previous month and one item on the previous day and the score ranges from 0-5. One item directed at the previous day's behaviour and score 0-3. The total score ranges from 03 to 73. MMA's 64.4% variance is explained by sick role behaviour, autonomy, forgetfulness and barriers to medication taking of which sick role behaviour and autonomy are novel concepts for adherence literature.[22] Therefore, it is essential to validate the MMA to demonstrate the credibility and trustworthiness to be used in everyday clinical settings. The objective of this study was to establish the validity of MMA by multiple methods objectively; convergence, discriminant and criterion validity.

## METHODS

A descriptive study was conducted to validate the newly developed MMA questionnaire in outpatient (medical/ OPD/family medicine) clinics in District General Hospital (DGH), Gampaha from September 2019 to November 2019. Diagnosed adult patients (≥18 years of age) with DM type 2 on medication for one year or more were recruited. Patient on Insulin was excluded since they have a unique adherence behaviour. Patients who had changed their medications during the last three months were also excluded since the time to adjust to the new schedule took time.

The research protocol was approved by the research ethics approval committees of the faculty of medicine, University of Kelaniya and the Medical Research Institute (P/87/2019), Sri Lanka. The study was conducted following the ethical standards laid down by the ethics review committee approvals and the Declaration of Helsinki. In addition, administrative approvals were received from the administrators of the DGH Gampaha and the clinical consultants who lead the clinics. Written consent was obtained from all patients after informing them about their rights, risks, and benefits, before their inclusion in the study.

The sample size to establish the criterion validity was calculated for cases needed to establish sensitivity and noncases needed for specificity. The result was multiplied by the 38.8%, prevalence of good adherence in Sri Lanka.[23] The "MMA questionnaire" was anticipated to perform better with a sensitivity of 86 % and specificity of 68%. Sample size calculation was done to detect the sensitivity of MMA as the diagnostic test.[24] Absolute precision was considered as 10% due to the resource-limited setting.[25] The minimum sample to be included according to the test sensitivity was 120 DM patients and the test specificity was 40 DM patients with 95% confidence. Hence, the maximum value of 120 was selected as the minimum sample size required to establish the expected sensitivity and specificity. Anticipated non-response rate was taken as 10% and loss to follow up 20% which was added to the final sample size of 156 patients. All the eligible consecutive patients were recruited for the study until the sample size was reached.

MMA measures adherence by quantification of the adherence behaviour during the previous month. Exploratory factor analysis has demonstrated that sick role behaviour, autonomy, forgetfulness and barriers to medication taking are the constructs of the MMA.[22] The present study assessed construct validity (convergent and discriminate validity) by comparing with the measures; many can be objectively demonstrated: pill counts percentage, recital dosage percentage, regular clinic attendance, recall screen, self-reported adherence, regular FBS measurement, short-term glycemic control, presence or absence of hyperglycemia/hypoglycemia and hospitalizations were used to test the convergent validity. Discriminative validity was checked among groups with optimum or raised HbA1C which reflects long-term glycemic control.

The pill count represents the proportion of prescribed pills, a patient consumed in a given time. The pill count percentage was calculated by dividing the number of tablets consumed (the difference between the number of tablets received and the number of tablets remaining) by the number of tablets that should have been taken by the day of the interview.

$$\text{Pill count percentage} = \left( \frac{\begin{pmatrix} number\ of\ tablets \\ received \\ from\ the\ clinic \end{pmatrix} - \begin{pmatrix} the\ number\ of \\ tablets \\ remained \end{pmatrix}}{\begin{pmatrix} Number\ of\ tablets\ that \\ should\ have \\ been\ taken\ per\ day \end{pmatrix} \times \begin{pmatrix} \text{number of days between} \\ \text{dispensing} \\ \text{and interview} \end{pmatrix}} \right) 100\%$$

Recital dosage represents the proportion of the prescribed dose, consumed by the patient yesterday. To calculate the consumed dose, pills were shown to the patient and the amount consumed yesterday was asked; when the patient is on more than one pill, the average was calculated. The prescribed dose was extracted from the prescription and the percentage was calculated as below.

$$\text{Recital dosage percentage} = \left( \frac{\begin{matrix} \text{Number of tablets taken} \\ \text{per day} \\ \text{as shown by the patient} \end{matrix}}{\begin{matrix} The\ \text{Prescribed number of tablets} \\ \text{per day} \\ \text{as per the prescription} \end{matrix}} \right) \times 100\%$$

Regular attendance at the clinic was defined as attendance within two weeks of the scheduled consultation during the last 12 months. Answers in the MMA were set to quantify last month's usual adherence behaviour. To establish the relationship between different ways of asking adherence and the MMA responses, two questions were used to test the correlation between the methods: recall screen- number of doses or pills missed (of DM medication) during the last three days- and self–reported adherence - responding yes to the question "do you take medication?" - as a general statement.

Regular FBS measurement was the presence of FBS recorded during the last six months. If FBS is recorded <6 times was considered as no regular blood sugar measurement. Short-term glycemic control was the average FBS at the recruitment and one month following recruitment. Long-term optimum glycemic control is HbA1C ≤7% according to the Sri Lankan guidelines.[26] HbA1C >7% was defined as having raised HbA1C.

The presence of symptoms of hypoglycemia/ hyperglycemia was defined as the presence of either one of the symptoms during the last two weeks- nocturia (frequency of passing urine at night >3 times), thirst (feeling thirst more than normal), excessive sweating (presence of episodic sweating with hunger), unfit (feeling tired or weakness), faintishness (feeling unbalanced). Previous hospitalizations were assessed as asking for admission to ETU/ward within the last three months.

A composite criterion was developed as the reference standard to establish criterion validity. Pill count percentage of>80% and recital dosage percentage of >80% and clinic attendance of ≥11 (80%) were used as the reference standard.[15] Based on the cumulative composite score, the sample was divided into two groups; good and average adherence. Cut off point is set at 80% as per the literature. Good adherence is represented by >80% of the composite score while ≤80% indicates average adherence.[27]

An interview-administered questionnaire was used to assess socio-demographic details. Informed written consent to participate was taken. A trained data collector who was blind to the hypothesis and the MMA questionnaire status elicited self-reported dosage, by showing the medications to the patients, counting dispensed pills and transferring data (details of the duration of disease, past FBS values, medication prescribed and other details) to the record sheets in a separate room situated closer to the dispensary. The other two data collectors did unannounced home visits to count the remaining pills. When counting pills if there was a discrepancy of >10, the whole procedure was repeated. Pill counts remaining after consumption was counted at the patients' home, visiting home unannounced two weeks from the initial encounter. Pill counts were recorded at the point of issuing the drugs at the dispensary and patients were asked to use the same pack even if they had access to surplus medicine at home. The number remaining in the pack was recorded in a separate record sheet which also recorded the details of whether the patient has used another separate pack during the last two weeks. HbA1C was done in a randomly selected subsample of 75 patients; all the patients who came on a particular day were selected. Among the selected all the patients who consented were recruited to the study. Data collectors were kept blind to the study hypothesis to minimize interviewer bias. Self-reported data were cross-checked with written documents as far as possible. All the questionnaires were checked for reliability and judgmental validity was used to elicit the information.

Convergent validity was established by comparing the total score of the questionnaire with pill count percentage, recital dosage percentage, regular clinic attendance, recall screen, self-report adherence, regular FBS measurement, short-term glycemic control, symptoms of hypo/hyperglycemia, and ETU/Hospital admissions. Discriminative validation (extreme groups) was established based on that patients who are non-adherent are likely to have raised HbA1C. Spearman r was calculated between the scores of the questionnaire and the continuous variables. Man Whitney U test was applied to test the distribution of MMA scores among two groups in categorical variables.

The ROC curve was used to establish the optimal cutoff point. Sensitivity, specificity (with CI), misclassification rate, and likelihood ratios were calculated. Selection of the cut-off point is a trade-off between the sensitivity and the specificity, misclassification rate and likelihood ratios.

The tool should be sensitive enough to detect patients with adherence thus enabling appropriate interventions while it should be specific enough to identify only patients with adherence.

## RESULTS

Eligible 155 patients were invited to participate. Four patients from the medical clinic and one patient from the OPD clinic refused to participate. Therefore, the none response rate was 3.3%. The final study sample was 150 participants. The mean age of the participants was 60.6 years (SD=9.3). The majority of the study participants were females (n=92, 61.3%), married (n=104, 69.3%) and Sinhala 98% (n=147) (Table 1).

**Table 1: Social demographic data of the study population.**

| Characteristics | Number (n=150) | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| ≤60 | 73 | 48.7 |
| >60 | 77 | 51.3 |
| **Sex** | | |
| Male | 58 | 38.6 |
| Female | 92 | 61.3 |
| **Marital status** | | |
| Married | 104 | 69.3 |
| Single | 46 | 30.6 |
| **Race** | | |
| Sinhala | 147 | 98.0 |
| Tamil | 3 | 2.0 |
| **Religion** | | |
| Buddhist | 131 | 87.3 |
| Catholic | 19 | 12.7 |
| **Education** | | |
| <OL | 65 | 43.4 |
| ≥OL | 85 | 56.6 |
| **Current employment** | | |
| Employed | 64 | 42.7 |
| Not employed | 86 | 57.3 |

### *Convergent validity*

The construct of the MMA consisted of the following variables; pill count, recital dosage, regular clinic attendance, recall screen, self-report adherence, symptoms of hypo/hyperglycemia, and ETU/Hospital admissions. Table 2 demonstrates the results of the Man Whitney U test results for categorical variables; regular clinic attendance, recall screen, self-reported adherence, regular FBS, short-term glycemic control, symptoms of hypo/hyperglycemia, and ETU/Hospital admissions.

### *Pill count percentage*

The majority of the patients used two drugs (n=86, 57%), any combination of metformin, tolbutamide, or glibenclamide. The rest of the patients were taking a single drug (n=64, 42.67%). The average pill count was calculated when using two medications. The range of pill count percentage was 32.14%-123%. Two patients were using a regular medication dose more than prescribed. The median of the pill count was 92 (IQR 72.3-100). The Spearmen correlation coefficient between the total score of the MMA questionnaire and the percentage of the consumed pill count is 0.39 (p=0.01).

### *Recital dosage percentage*

The recital dosage percentage ranges from 33.3-133%. Two patients reported taking more than the prescribed dose. The median score was 100 (IQR 66.6–100). The Spearmen correlation coefficient between the total score of MMA and recital dosage percentage was 0.54 (p=0.001).

### *Regular clinic attendance during the previous year*

A statistically significant difference exists between the distribution of MMA scores between the regular clinic attendance group and the non-regular clinic attendance group. U value, medians and statistical significance are depicted in Table 2.

### *Recall screen*

The recall screen included the number of doses or pills missed during the last three days. The number of doses missed ranges from zero to 15. The median of the doses missed was zero (IQR zero to two). The majority of the patients, 57.6% (n=86), didn't miss a single dose during the last three days. Spearmen r correlation coefficient between the total score of the MMA and the number of doses missed was -0.52 (p<0.001). When the total score (thus adherence) increases, the number of doses missed stated by the patient decreases. The range of the number of pills missed during the last three days was zero to 45. The median was zero (IQR zero to four). The majority of patients, 58.7% (n=88) didn't miss a single pill during the last three days. Spearmen r correlation coefficient between the total score of the MMA and the number of doses missed was -0.48 (p<0.001). When the adherence (MMA total score) increases, the number of pills missed stated by the patient decreases.

### *Regular FBS measurement*

The response rate was 99.3% with one missing value which was excluded from the analysis. The distribution of the MMA score was not statistically significantly different among the two groups who measured FBS regularly or not (Table 2).

### *Short-term glycemic control - FBS at the recruitment*

The response rate was 76% with missing data in 36 patients who were excluded from the analysis. FBS at the recruitment ranges from 49.2–334 mg/dl with a mean of 134.8 mg/dl (SD 44.37 mg/dl). Spearman correlation coefficient between the adherence score and the recruitment FBS is -0.02 (p=0.98) which is not statistically significant.

***Self-reported adherence***

A statistically significant difference exists between the distribution of MMA scores between the self-reported adherence group and the self-reported non-adherence group (Table 2).

***Presence of symptoms of hypo/hyperglycemia***

The observed difference in the distribution of scores between the groups of presence and absence of symptoms of hypo/hyperglycemia are statistically significant (Table 2).

***Hospital /ETU admissions***

The observed difference in the distribution of score between two groups of Hospital /ETU Admissions and not admissions are statistically not significant (Table 2).

***Discriminative validation (known groups)***

Measures with concepts unrelated to MMA were proven to be unrelated; Not having long-term glycemic control has to be unrelated to MMA. Even though only 30% of glycemic control is explained by adherence, it is unlikely that patients with higher adherence would have long-term glycemic control since the other self-management behaviours are also associated with the medication adherence behaviour.

***Long-term adequate glycemic control***

Adherent patients are likely to have lower HbA1C. A statistically significant difference in the distribution of the total score was observed across two groups of higher HbA1C and lower HbA1C. U value, medians and statistical significance are depicted in Table 2.

***Criterion validity***

Figure 1 shows the ROC curve between the dichotomized composite score and the total score. The area under the curve is 0.87 (95% CI 0.81 – 0.93) with p<0.0001 which denotes the accuracy of the test. It denotes that if we take two patients, one with adherence and the other one is nonadherence, the probability is 0.87 that a patient with adherence has a positive result than the non-adherence patient. In the population the probability range lies between 0.81–0.93 with 95% confidence and the observed result is statistically significant.

Seventy was selected as the best cut-off point for the questionnaire. Patients who score >70 have good adherence to the medication while ≤70 have average adherence. This has a sensitivity of 92.9% (95% CI 85.5–96.9%), a specificity of 72.5% (95% CI 58–83.7%) with a misclassification rate of 14%. The positive likelihood ratio (LR) is 10.2. High positive LR (>10) represents that adherence is very likely in a person with a score >70. The negative likelihood ratio is 0.3 and is in the intermediate range. It suggests that a score <70 is suggestive but insufficient to rule out the non-adherence (Table 3).

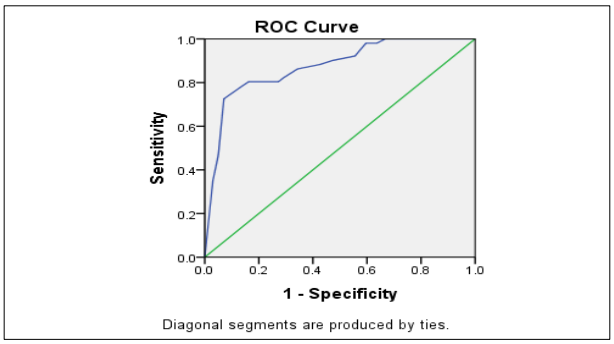


**Figure 1: ROC curve of high adherence to medication among adult DM patients in the validation sample.**

***The best cutoff point of MMA to detect good glycemic (HbA1C<7%) control***

The ROC curve was plotted between the good/bad glycemic control (HbA1C) and the total score of MMA to find the best cut-off to detect good glycemic control. Figure 2 ROC depicts the curve between HbA1C and the total score of MMA.

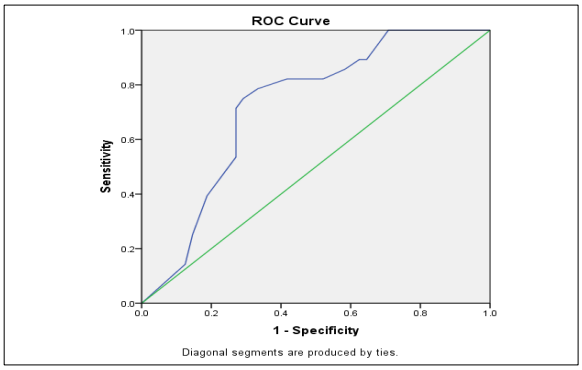


**Figure 2: ROC curve between HbA1C and the total score of MMA.**

***Subgroup analysis of the patients with HbA1C***

Basic demographic data of the subgroup with HbA1C is demonstrated in Table 4. The ROC curve is plotted to detect the best cut-off of the total score to find adequate glycaemic control (HbA1C≤7%) and inadequate control (HbA1C>7%). Accordingly, the total score of 67 will be the best cut-off to detect good glycaemic control among DM patients. It has 75% of sensitivity and 70% of specificity with a misclassification rate of 27%. The positive likelihood ratio is 2.6 and the negative LR is 0.4. Intermediate Positive LR (1-4) represents that good glycaemic control is suggestive in a person with a score >67. The negative LR is 0.4 and is in the intermediate range. It suggests that the score <67 is suggestive but insufficient to rule out good glycaemic control (Table 5).

**Table 2: Distribution of the MMA score by independent categorical variables.**

| Variable | Yes | No | U value | Statistical significance (p) |
|---|---|---|---|---|
| **Regular clinic attendance** | | | | |
| Number of patients | 83 | 67 | 4625 | <0.0001 |
| Median of the MMA score | 63 | 71 | | |
| IQR | 50-73 | 61-73 | | |
| **Self-reported adherence** | | | | |
| Number of patients | 130 | 20 | | |
| Median of the MMA score | 68 | 62.5 | 811.5 | 0.007 |
| IQR | 63 -71 | 57 – 65.5 | | |
| **Regular FBS measurement** | | | | |
| Number of patients | 103 | 46 | | |
| Median of the MMA score | 67 | 67 | 2299 | 0.77 |
| IQR | 61 -71 | 53 – 70 | | |
| **Symptoms of hypo/hyperglycemia** | | | | |
| Number of patients | 105 | 45 | | |
| Median of the MMA score | 66 | 70 | 3012 | 0.008 |
| IQR | 66 -70 | 63.5 - 73 | | |
| **Hospital /ETU admissions** | | | | |
| Number of patients | 27 | 123 | | |
| Median of the MMA score | 64 | 66 | 2060 | 0.05 |
| IQR | 59 - 70 | 62-71 | | |
| **Long term glycemic control** | | | | |
| Number of patients | 28 | 48 | | |
| Median of the MMA score | 70 | 65 | 372 | 0.001 |
| IQR | 67.5–71.75 | 58-70 | | |

**Table 3: Distribution of criterion by different cut-off values of MMA, sensitivity, specificity and likelihood ratios.**

| Score | Reference standard | | | | Sensitivity | Specificity | Misclassific-ation rate | Likelihood ratio | |
|---|---|---|---|---|---|---|---|---|---|
| | Yes | | No | | | | | Positive | Negative |
| | N=51 | n (%) | N=99 | n (%) | | | | | |
| **65** | 45 | 88.2 | 42 | 42.4 | 88.2 | 57.6 | 32.2 | 2.08 | 0.20 |
| **66** | 44 | 86.3 | 34 | 34.3 | 86.3 | 65.7 | 27.3 | 2.52 | 0.21 |
| **67** | 42 | 82.4 | 29 | 29.3 | 82.4 | 70.7 | 25.3 | 2.81 | 0.25 |
| **68** | 41 | 80.4 | 27 | 27.3 | 80.4 | 72.1 | 24.6 | 2.95 | 0.27 |
| **69** | 41 | 80.4 | 16 | 16.2 | 80.4 | 83.8 | 17.3 | 4.96 | 0.23 |
| **70** | 37 | 72.5 | 7 | 7.1 | 72.5 | 92.9 | 14 | 10.21 | 0.30 |
| **71** | 24 | 47.1 | 5 | 5.1 | 47.1 | 94.9 | 21.3 | 9.24 | 0.56 |
| **72** | 18 | 35.3 | 3 | 3 | 35.3 | 97 | 24 | 11.77 | 0.67 |

**Table 4: Basic social demographic data of the subgroup with HbA1C.**

| Characteristic | Number | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| ≤60 | 30 | 39.5 |
| >60 | 46 | 60.5 |
| **Sex** | | |
| Male | 27 | 35.5 |
| Female | 49 | 64.5 |
| **Marital status** | | |
| Married | 55 | 72.4 |
| Single | 21 | 27.6 |
| **Race** | | |

Continued.

| Characteristic | Number | Percentage (%) |
|---|---|---|
| Sinhala | 75 | 98.7 |
| Tamil | 1 | 1.3 |
| **Religion** | | |
| Buddhist | 67 | 88.2 |
| Catholic | 9 | 11.8 |
| **Education** | | |
| <OL | 32 | 41 |
| ≥OL | 34 | 59 |
| **Current employment** | | |
| Employed | 32 | 42.1 |
| Not employed | 44 | 57.9 |
| **Total number** | 76 | |

**Table 5: Distribution of HbA1C by different cut-off values of MMA, sensitivity, specificity and likelihood ratios.**

| Score | Reference standard (HBA1C) | | | | Sensitivity | Specificity | Misclassification rate | Likelihood ratio | |
|---|---|---|---|---|---|---|---|---|---|
| | Good | | Inadequate | | | | | Positive | Negative |
| | N=28 | n (%) | N=48 | n (%) | | | | | |
| **64** | 23 | 82.1 | 25 | 52.1 | 82.1 | 47.9 | 39.4 | 1.6 | 0.4 |
| **65** | 23 | 82.1 | 20 | 41.7 | 82.1 | 58.3 | 32.9 | 2.0 | 0.3 |
| **66** | 22 | 78.6 | 16 | 33.3 | 78.6 | 66.7 | 28.9 | 2.4 | 0.3 |
| **67** | 21 | 75 | 14 | 29.2 | 75 | 70.8 | 27.6 | 2.6 | 0.4 |
| **68** | 20 | 71.4 | 13 | 27.1 | 71.4 | 72.9 | 31.6 | 2.6 | 0.4 |
| **69** | 15 | 53.6 | 13 | 27.1 | 53.6 | 73.29 | 34.2 | 2.0 | 0.6 |
| **70** | 11 | 39.3 | 9 | 18.8 | 39.3 | 81.3 | 34.2 | 2.1 | 0.7 |
| **71** | 7 | 25 | 7 | 14.6 | 25 | 85.4 | 36.8 | 1.7 | 0.9 |

## DISCUSSION

MMA is a very useful questionnaire to detect adherence among DM patients on oral medication in clinical settings (LR>10). The criterion validity of MMA was established with good AUC, sensitivity (72.5%) and specificity (92.9%). As anticipated, the optimal cut-off point of MMA to differentiate adherence (70) was different from long-term glycemic control (67). Construct validity was established by moderate correlation with the other subjective and objective measures of adherence and different distribution of MMA scores among optimum or raised HbA1c groups.

Medication adherence is a multidimensional construct: a single measure will not reflect the true adherence status. In the absence of a single measure, a multi-measure approach is recommended to increase the accuracy of detecting adherence.[28] A composite criterion measure using more objective variables was developed with pill counts, recital dosage percentage, and regular clinic attendance with the consensus of the supervisor. This was a similar method used in detecting adherence to HIV medication.[18] a combined measure of pill counts, MEMS data and clinician's judgment had the strongest predictive power than each measure separately to detect adherence.[18] HbA1C is used as the criterion in the majority of validation studies of adherence scales. Nevertheless, it reflects the composite effect of lifestyle modification and various comorbid factors like renal disease, anaemia, myelodysplastic diseases, and Haemoglobinopathies as well. Eg- brief medication questionnaire BMQ, Morisky medication adherence scale (MMAS).[5,29-31] Only 24% of the risk for poor glycaemic control is attributable to inadequate medication adherence in the subgroup of patients with longer-duration illness.[32] Besides, using HbA1C for a larger sample is restrained by the high cost.

The majority of adherence scales are established cut-off points by subjective judgment: it is liable to errors. Eg- BMQ, MMAS.[5,29-31] Our study used an objective method - ROC curve- to establish cut-off points and demonstrated the optimal sensitivity and specificity for MMA to detect adherence. The sensitivity of MMA in detecting medication adherence was 72.5% and the specificity was 92.9%. It is higher than other scales; MMAS has a sensitivity range from 74.1% (Korean) to 77.6% (Malaysian) and a specificity of 38.3% (Korean) to 45.3% (Malaysian) in detecting adherence. Sinhala version of the BMQ has a sensitivity of 78.3% and a specificity of 55.2%. Thus most of the scales performed lower when identifying true negatives than the MMA.

Comparable to other adherence validation studies, a subgroup analysis was done to demonstrate the sensitivity and specificity of MMA against HbA1C. In addition, likelihood ratios were calculated. The total score of 67 was the best cut-off to detect adequate long-term glycemic control among DM patients. Even though it has 75% of sensitivity and 70% specificity with a misclassification rate

of 27%, positive LR is only 2.6 which indicates limited significance in the "rule in" high adherence to DM medication in clinical practice. However, HbA1C was done only in a sub-sample of 76.

Predictive values of a test are a useful indicator in increasing or lowering the pre or post-test probability of disease.[33] Nevertheless, it differs according to clinic and population since it depends on the prevalence of the disease. The likelihood ratio (LR) is a composite index of sensitivity and the specificity of the test: hence, does not depend on disease prevalence. Likelihood ratios are more important when taking judgments in clinical practice. It indicates how much a given test will raise or lower the pretest probability of disease.[34] The present study demonstrated that at the cut-off 70 of MMA, the positive likelihood ratio is 10.2 which indicates high clinical significance in ruling in high adherence. There is a lack of evidence about a similar approach in establishing cut-off points, sensitivity and specificity in questionnaires measuring adherence to DM medication in literature. The majority used arbitrary cut-off points based on subjective judgment.[35-37]

A significant correlation was found between objective measures of adherence such as pill count percentages, recital dosage percentage, long term glycemic control and subjective measures such as self-reported adherence, recall screen and MMA score denoting the accuracy of the construct of the scale. In other studies, the majority has used other questionnaires to validate the scale which is a more subjective method. Example- the construct validity of MMAS was assessed with four items MGL medication adherence questionnaire, and ASK 12 with MMAS.[38,39] Some authors have used the subscales of the same questionnaire to demonstrate convergent validity. Example – belief about medication questionnaire.[40] Discriminative validations of MMA by known groups was conducted to demonstrate that the distribution of the total MMA score was different among patients with good/ bad long-term glycemic control. A similar method was used in validating MMAS in Taiwan and Korea.[41,42] They performed the $\chi^2$ test to discriminate the adherence status of the scale and the long-term glucose controllers.

DGH Gampaha is situated in the suburban area draining a population from both urban and rural areas and representative of the majority of the country. However, MMA was validated among patients with diabetes who attended clinics and generalization of the study findings beyond clinic population should be done with caution. Moreover, HbA1C was done only in a subsample during validation due to financial constraints. However, the sample has >50% power of detecting criterion validity with 2:1 selection ratio, with a 0.5% criterion reliability.[43]

## CONCLUSION

The MMA can correctly identify 72.5% of patients with adherence and 92.9 % of patients with non-adherence. It has a high clinical significance in diagnosing how likely a patient has high adherence to oral DM medication. The difference in the cut-off points of MMA in deciding HbA1C and the criterion supports the importance of other self-management behaviours like physical activity and a healthy diet in achieving glycemic control in addition to medication.

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