original article

Predictors of medication regimen complexity and its impact on hemoglobin a1c in type 2 diabetes patients: a retrospective analysis in ambulatory care in Makkah City

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BACKGROUND: Type 2 diabetes mellitus (T2DM) is a widespread chronic disease that poses a significant management challenge due to the complexity of the associated medication regimens, which can have a considerable impact on patient outcomes.

OBJECTIVES: Explore the complexity level of diabetes medications among patients with T2DM and to identify the predictors of medication regimen complexity (MRC) and its correlation with hemoglobin A1C (HbA1c) levels.

DESIGN: Retrospective, cross-sectional study

SETTING: An ambulatory care setting of a tertiary hospital in Makkah City, Saudi Arabia

PATIENTS AND METHODS: Patients with T2DM referred to the diabetic clinic were identified and assessed for eligibility. The data were collected from patient electronic medical records between October 2022 and September 2023. The MRC Index was used to evaluate the complexity of the patients' medication regimens.

MAIN OUTCOMES MEASURES: MRC index scores and HbA1c levels

SAMPLE SIZE: 353 records of patients with T2DM

RESULTS: The analysis revealed that 61.8% (n=218) of patients had high MRC, with the dosing frequency contributing significantly to their MRC (mean=3.9, SD=1.9). Having polypharmacy and longstanding T2DM were predictors of high MRC (odds ratios=4.9 and 2.6, respectively; $P \leq .01$). Additionally, there was an inverse association between the patients' diabetes-specific MRC index scores and their glycemic control (odds ratios=0.2, $P < .001$).

CONCLUSION: The study findings highlight the importance of considering MRC in managing T2DM. Simplifying medication regimens and optimizing medication management strategies can improve patient outcomes. Further research is needed to explore interventions to reduce MRC and enhance diabetes management in this population.

LIMITATIONS: Retrospective study design measuring the MRC at a diabetes-specific level.

CONFLICT OF INTEREST: None.

Diabetes mellitus is acknowledged as a significant health concern with increasing prevalence and long-term morbidity worldwide, including in Saudi Arabia. Previous reports from the International Diabetes Federation have predicted an approximately 16% increase in the prevalence of diabetes in Saudi Arabia between 2011 and 2030, with a high number of reported deaths associated with diabetes, especially type 2 diabetes mellitus (T2DM).[1-3] The federation has ranked Saudi Arabia as sixth among the top 10 countries globally with respect to the prevalence of diabetes,[3] which draws attention to the alarming increase in diabetes mellitus and its associated complications in Saudi Arabia.

The achievement of optimal and sustained glycemic control in diabetes is significantly reliant on the proper use of antidiabetic medications and lifestyle changes. The progressive nature of diabetes and the difficulties associated with its long-term management have resulted in the increased use of complex therapeutic regimens.[4] The American Diabetes Association (ADA) supports using combined antidiabetic regimens over the up-titration approach, particularly in patients who do not respond to antidiabetic monotherapy.[4] The available evidence has shown that lower doses of combination therapy are associated with greater efficacy than high-dose monotherapy.[5] Furthermore, some have argued that up-titration to the maximal dose of an agent may be less effective than adding a second agent and is associated with a higher rate of adverse effects.[5,6] For example, in the United Kingdom, only 25% of patients were able to maintain the target glycemic level of a hemoglobin A1C (HbA1c) <7.0% by following a simple monotherapy regimen after nine years of treatment, whereas combination therapy was used successfully in 75% of patients.[6] Similar findings were reported in a review that addressed the benefits and drawbacks of fixed-dose combination therapy in patients with chronic illnesses. The researchers pointed out that combining antidiabetic agents that had different mechanisms of action produced more benefits in achieving glycemic goals than up-titrating monotherapy.[5] However, several elements can make a therapeutic regimen complex, such as prescribing multiple drugs, the use of different dosage forms, complex dosing schedules, and the need for special administration information and proper medication use, all of which may impair pharmacotherapy adherence.[7] Although different medication regimens may be beneficial in achieving target glycemic control, using a complex antidiabetic medication regimen may not be associated with better outcomes.[7-9] The associations between medication regimen complexity (MRC) and health outcomes have been assessed in previous studies. However, only a few have evaluated this association at a diabetes-specific level with consideration of antidiabetic medications only.[9,10] These studies revealed that patients with T2DM on complex regimens experienced poor clinical outcomes, medication adherence, and quality of life.[9,10] However, no evidence is available regarding the impact of MRC on glycemic control in countries with an increasing prevalence of T2DM, like Saudi Arabia, so it is necessary to determine this association. In addition, the rapid development of new drugs and changes in epidemiological and demographic profiles warrant research on this topic. The findings may assist in improving the medication-related outcomes of patients who use complex regimens. Therefore, we aimed to explore the complexity level of diabetes medicine regimens among patients with T2DM in Makkah City and to identify the predictors of MRC and its correlation with HbA1c levels. The focus of the study was on T2DM due to its progressive nature, the increased number of diabetes medications available, and their pharmacological classes.

PATIENTS AND METHODS

Study design

In this cross-sectional study, we performed a retrospective database analysis of the patient records from an ambulatory care setting of a tertiary hospital in Makkah City, namely, King Abdulaziz Hospital (KAAH). The hospital has a strategic location and is one of the largest medical complexes in the central region of Makkah, with a 300-bed capacity. KAAH provides important medical services to Makkah citizens as well as pilgrims and Umrah performers.

The hospital records of patients with T2DM attending KAAH as outpatients and non-hospitalized patients over one year (from October 2022 to September 2023) were analyzed. The patients' prescriptions were assessed to identify low, moderate, and high MRC cohorts. The medication analysis was conducted at a diabetes-specific level, which necessitated the inclusion of antidiabetic medications.

Patient identification and selection

To simplify the identification of patients with T2DM from the hospital records, a list of those referred to the diabetes counseling clinic over one year was obtained from the pharmacy supervisor in the hospital. This list included only the patients' hospital medical record numbers and dates of referral. The patients' data were

extracted from the hospital database and transferred to a Microsoft Excel sheet, where each patient was assigned a unique identification number for use in all the study documents and electronic databases. The identification of the eligible patients and data extraction were conducted from October to December 2023.

The included patients (outpatient, non-hospitalized) were adults (≥18 years) with T2DM referred by healthcare professionals to the diabetic clinic at KAAH and treated with at least one antidiabetic medication. The patients were required to have a definite diagnosis of T2DM identified from their records, progress notes written by their physicians, or a history of diabetes medication prescriptions. They also needed to have a recent prescription for diabetes medicines and an HbA1c reading within six months following their latest prescription. Eligible patients were included in the study regardless of their race or nationality. Those who did not meet the inclusion criteria or were not followed up in the hospital (e.g., who were referred to primary healthcare centers) were excluded. We also excluded hospitalized patients, as healthcare providers would have administered and managed their medications. In addition, some hospitalized patients may have had temporary changes in their regimens (e.g., discontinuing their oral antidiabetic medications with only insulin administered during their hospital stay).

Ethical approval

The Health Local Committee for Research Ethics in Makkah Region, Saudi Arabia, approved the study (H-02-K-076-1023-1019). All ethical guidelines and regulations were strictly followed to ensure patient confidentiality and data security throughout the study.

Data collection

After identifying all the eligible patients, four researchers reviewed the antidiabetic medication for each included patient and assigned scores according to the criteria of the medication regimen complexity index (MRC index).[11] The MRC index is a validated tool comprising 65 items, in which the dosage forms, dosing frequencies, and supplementary directions for each medication administered are evaluated.[11] It is used to determine the complexity of medication use at a patient level by including all medications regardless of the medical condition or be applied at a disease-specific level. The MRC index groups patients' medication complexity into one of the following categories: low MRC for a score ≤4, moderate MRC for a score >4 and ≤8, and high MRC for a score of >8, where a higher MRC index score indicates a more complex medication regimen.[9,10] The research team identified supplementary directions for medication administration (e.g., before/after food, crushing instructions) from the hospital records, medication package inserts, and other drug information references, such as Lexicomp and the British National Formulary. The principal investigator shared the scoring method and supplementary directions with the research team to ensure a high level of agreement when computing the complexity scores. After completing the scoring process, the principal investigator reviewed the scores of 10% of the total sample to identify any inconsistencies and errors. All the researchers were in complete agreement regarding the scores.

Variables that could have affected the study outcomes, namely, age, comorbidities, the number of regular medications, polypharmacy (≥5 medications),[12] diabetes complications (microvascular and/or macrovascular, or any diabetes-related complication as documented in the patient records),[13] and duration of T2DM, were included in the patient data extraction sheet. Comorbidities were considered if the patient had at least two long-term conditions (e.g., diabetes and hypertension) regardless of the type of long-term condition.[14] Patients were considered newly diagnosed if they had been diagnosed with T2DM within the previous 12 months.[15-17] The date of their diagnosis with T2DM was identified using one of the following methods: (1) the progress notes written by the physicians, which indicated the diabetes medication history, (2) the date of the T2DM diagnostic code (i.e., when the code of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems was entered in the system), and (3) the history of antidiabetic medications.

The post-HbA1c reading (obtained from the laboratory section) was collected between 3 and 6 months after the index date (i.e., the last date diabetes medications were dispensed). The timeframes for measuring HbA1c were in line with the ADA guidelines used in Saudi Arabia.[4] As per the ADA guidelines, the HbA1c levels of patients with stable T2DM can be measured at 6-month intervals (twice a year), while newly diagnosed patients, patients with uncontrolled T2DM, and those who have had changes in their treatment plans require monitoring at least four times per year.[18] If a patient had more than one HbA1c reading following the last date medication was dispensed, we reported the first reading. The patients' HbA1c levels were categorized into two groups: controlled T2DM if HbA1c ≤7% and uncontrolled T2DM if HbA1c >7%. An HbA1c level ≤7% is a reasonable universal target

for most patients with diabetes if achieved safely.[4] Comparing this parameter between the patients with high MRC and other categories was essential to identify the impact of MRC in improving or worsening the patients' HbA1c levels.

Data analysis

The data analysis was performed using IBM SPSS, version 23. Frequency and percentage were used to present the categorical variables and mean and standard deviation (SD) for the numerical variables. The chi-squared test was used to ascertain the associations between the categorical variables. Multivariate logistic regression was performed to determine the predictors of MRC and its association with HbA1c levels and to identify any interactions between these factors. It was also used in the subgroup analysis to evaluate the HbA1c levels against the measurement timeframe (i.e., within 3 or 6 months). The logistic regression model was adjusted for the variables that showed a significant association with diabetes management, that is, age, gender, comorbidities, polypharmacy, having longstanding T2DM or being newly diagnosed, having a diabetes complication(s), and MRC level. The level of significance was set at .05 with a 95% confidence interval (CI).

RESULTS

A total of 478 records for patients with T2DM were identified from the hospital database. However, some patients did not meet the inclusion criteria, as they had been newly diagnosed and had no recent HbA1c readings (n=8). Others had been admitted to the hospital to stabilize their conditions and were then followed up at the primary healthcare centers. These patients therefore did not have recent HbA1c readings or a full history of antidiabetic medications (n=117). After excluding the patients with missing data, 353 records for patients with T2DM met the inclusion criteria. The characteristics of the included patients are provided in **Table 1**.

As shown in **Table 1**, most of the included records were for patients between 40 and 64 years of age (n=233, 66%), while the records of elderly patients (≥ 65 years) accounted for 23.8% (n=84) of the total sample. Most of the patients had comorbidities (n=321, 90.9%), were not newly diagnosed with T2DM (n=314, 89%), and did not have diabetes complications (n=205, 58.1%). With respect to medication-related characteristics, 70.8% (n=250) had polypharmacy, and 53.2% (n=188) were using both oral and injectable drugs. The HbA1c levels of the majority of the included patients had been measured within 3 months of their most recent hospital admission or follow-up visit (n=261, 73.9%). In contrast, the HbA1c levels of 26.1% (n=92) had been measured within 6 months of their most recent follow-up visit.

As **Table 2** shows, most of the patients required 2–3 antidiabetic medications daily (n=201, 56.9%). The diabetes-specific MRC index scores ranged from 2 to 25 (mean=10.3, SD=4.5): 11.6% (n=41) of the patients had low levels of MRC, 26.6% (n=94) moderate levels, and 61.8% (n=218) high levels. Dosing frequency scores contributed most to the MRC index score (mean=3.9, SD=1.9) compared to the medication additional directions scores (mean=3.4, SD=2.5), dosage form scores (mean=2.9, SD=1.4), and antidiabetic medication count (mean=2.5, SD=1.1). Most of the reviewed HbA1c levels indicated that the patients had uncontrolled T2DM (n=224, 63.5%).

Predictors of MRC levels

Table 3 displays the factors associated with the patients' MRC levels. We found that those with a high MRC level had a significantly higher mean age than those with low to moderate MRC levels (57.7 vs. 52.9 years; P=.001). The patients with comorbidities and polypharmacy had considerably higher MRC levels than those with low to moderate MRC levels (63.9% vs. 36.1% and 73.6% vs. 26.4%, respectively; P≤.01). Those who had longstanding T2DM also had significantly higher MRC level than the other patients (65% vs. 35%, respectively; P<.001). In addition, the patients with complications from T2DM had considerably higher MRC levels than their cohort (73% vs. 27%, respectively; P<.001).

However, the adjusted regression analysis (**Table 4**) showed that only polypharmacy and diabetes status preserved their significant effects on MRC. Polypharmacy was significantly predictive of having a high MRC level (odds ratio=4.9, 95% CI=2.79-8.67); it increased the risk of having high MRC by an extraordinary 392%. Furthermore, having a chronic case of diabetes increased the possibility of having high MRC by 158% (odds ratio=2.6, 95% CI=1.19-5.60). The other factors did not significantly predict an increased risk of having high MRC in the patients with T2DM.

Impact of MRC on HbA1c status

Table 5 presents the results of the adjusted multivariate analysis for the association between MRC index scores and HbA1c status. We found that having a high MRC index score (> 8) was significantly predictive of having a lower chance of controlled T2DM (odds ratio=0.2, 95% CI=0.12-0.52), as it decreased the potential for having controlled T2DM by 75%. Being newly diagnosed with

Table 1. Demographic and clinical characteristics of the study cohort (n=353).

Demographic characteristics	N (%)
Age (years)	55.9 (12.6)[a]
<40	36 (10.2)
40-64	233 (66)
65-79	78 (22.1)
≥80	6 (1.7)
Gender	
Male	152 (43.1)
Female	201 (56.9)
Clinical characteristics	
Presence of comorbidities	
No	32 (9.1)
Yes	321 (90.9)
Diabetes duration	
Newly diagnosed	39 (11)
Chronic case	314 (89)
Presence of diabetes complications	
No	205 (58.1)
Yes	148 (41.9)
Type of diabetes complications	
Cardiovascular diseases	50 (14.2)
Nephropathy	45 (12.7)
Neuropathy	32 (9.1)
Stroke	18 (5.1)
Retinopathy	17 (4.8)
Diabetic ketoacidosis	5 (1.4)
Foot problems	4 (1.1)
Peripheral vascular diseases	3 (0.8)
Others (e.g., dual sensory loss, hearing impairment, dermopathy)	14 (4)
Medication-related characteristics	
Presence of polypharmacy	
No	103 (29.2)
Yes	250 (70.8)
Types of diabetes medication	
Oral drugs	116 (32.9)
Injectable drugs	49 (13.9)
Both	188 (53.2)
Timeframe of measuring HbA1c	
Within 3 months	261 (73.9)
Within 6 months	92 (26.1)

Data are number (percentage). [a]Mean (SD). Some patients had more than one diabetes complication.

diabetes also significantly predicted having controlled T2DM (odds ratio=2.3, 95% CI=1.11-4.97); increasing the chance of having a controlled T2DM by 134%.

Subgroup analysis

A subgroup analysis was conducted to identify any differences in the findings when considering the time-frames for measuring HbA1c levels. **Supplementary Table 1** shows the results of the multivariate analyses when measuring HbA1c within 3 or 6 months. We found that a high MRC index score significantly predicted a lower potential for controlled T2DM when HbA1c levels were measured within both 3 and 6 months (odds ratios=0.3 and 0.1, respectively; $P \leq .02$). However, the chance of having controlled T2DM decreased by 73% at 3 months compared to 94% at 6 months.

DISCUSSION

This retrospective study is the first conducted in Saudi Arabia to explore the prescribing pattern of T2DM medications in relation to regimen complexity. Most of the patients in the sample had high MRC with regard to their diabetes medications. We also explored different predictors of MRC levels and identified their inverse association with HbA1c levels. The diabetes-specific MRC index (>8) and mean scores identified among the Saudi population in this study were higher compared to those for the populations of other international studies. The prevalence of patients with high diabetes-specific MRC levels reported in the literature ranges from 22% to 43% compared to 61.8% in this study,[7,10,19] and the means scores are between 6.6 and 7.9 compared to 10.3 in this study.[8,19-21] These findings suggest that diabetes treatment protocols and regimens are more intricate and demanding in Saudi Arabia, which is having an impact on patient adherence to treatment plans and

Table 2. Treatment characteristics of the study cohort and glycemic control level.

Variable	N (%)	Mean (SD)
Medication burden		
Total number of medications per day		
1-2	26 (7.4)	
3-4	78 (22.1)	5.8 (2.4)
5-6	125 (35.4)	
≥7	124 (35.1)	
Number of antidiabetic medications per day		
1	76 (21.5)	
2	101 (28.6)	
3	100 (28.3)	2.5 (1.1)
4	62 (17.6)	
5	14 (4)	
Medication regimen complexity level		
Low MRC level (score of ≤4)	41 (11.6)	
Moderate MRC level (score >4 to ≤8)	94 (26.6)	
High MRC level (score of >8)	218 (61.8)	
Medication regimen complexity index scores		
Total diabetes-specific MRC index		10.3 (4.5)
Dosage form score		2.9 (1.4)
Dosing frequency score		3.9 (1.9)
Additional directions score		3.4 (2.5)
Glycemic level (%)		
Controlled T2DM (HbA1c ≤7.0%)	129 (36.5)	7.9 (1.8)
Not controlled T2DM (HbA1c >7.0%)	224 (63.5)	

MRC:medication regimen complexity; T2DM: type 2 diabetes mellitus; HbA1c: hemoglobin A1c.

leading to poor clinical outcomes. However, it may also indicate greater progression in patients' diabetes status, which would require more comprehensive treatment strategies to be applied.

When adjusting for the patient variables, only polypharmacy and diabetes status were found to be significantly predictive of a high level of MRC in the patients with T2DM. This finding is both alarming and crucial, as it also correlates strongly with poor glycemic control, which is a key concern in diabetes management. Previous studies have reported similar findings,[20,22] and the researchers in one study demonstrated that reducing polypharmacy through an intervention to optimize medication use significantly improved glycemic control.[22] This intervention focused on ensuring that patients received the necessary medications for their comorbidities while also eliminating unnecessary medications, which led to a simplified medication regimen and improved outcomes. Nevertheless, the inclusion criteria were non-compliant patients with uncontrolled diabetes.[22] The researchers in another study similarly established that the patients with T2DM were at risk of medication interactions due to the use of multiple medications.[20] However, it must be noted that the prevalence of polypharmacy among patients with T2DM is due to concurrent chronic conditions and the progressive nature of the disease, so multiple medications are necessary to manage the conditions effectively. Addressing polypharmacy therefore requires interdisciplinary collaboration, technology-driven solutions, and patient-centric interventions to optimize medication management and improve patient outcomes.[23-25]

In the current study, we found that the individuals newly diagnosed with T2DM were significantly more likely to have controlled blood glucose levels than those with a chronic case T2DM. This aligns with the results of the study by Ayele et al, who found a similar association among the Ethiopian population in that individuals who had been living with T2DM for over 10 years were twice as likely to experience poor glycemic control compared to those who had been diagnosed with T2DM for less than 10 years.[7] These findings can be attributed to the progressive nature of diabetes over time and the challenges associated with its management, with the maintenance of glycemic control consequently necessitating the use of multiple medications. Moreover, individuals with a longer duration of T2DM may develop diabetes-related complications, such as cardiovascular disease and neuropathy, which may further complicate the management of their diabetes and contribute to the complexity of their medication

Table 3. Factors associated with medication regimen complexity (MRC) level.

Factor	Low to moderate MRC level (0-8)	High MRC level (>8)	*P* value
Age (mean, SD)	52.9 (14.7)	57.7 (10.8)	**.001**
Gender n (%)			
Male	53 (34.9)	99 (65.1)	.25
Female	82 (40.8)	119 (59.2)	
Presence of comorbidities n (%)			
No	19 (59.4)	13 (40.6)	**.01**
Yes	116 (36.1)	205 (63.9)	
Polypharmacy n (%)			
No	69 (67)	34 (33)	**<.001**
Yes	66 (26.4)	184 (73.6)	
Diabetes status n (%)			
Newly diagnosed	25 (64.1)	14 (35.9)	**<.001**
Chronic case	110 (35)	204 (65)	
Diabetes complication n (%)			
No	95 (46.3)	110 (53.7)	**<.001**
Yes	40 (27)	108 (73)	

Table 4. Multivariate logistic regression of factors predicting high medication regimen complexity (MRC).

Factor	*P* value	Odds ratio	Confidence interval
Age	.68	0.9	0.97-1.02
Gender (female vs. male)	.07	0.6	0.38-1.03
Presence of comorbidities (yes vs. no)	.81	0.9	0.37-2.17
Polypharmacy (yes vs. no)	**<.001**	4.9	2.79-8.67
Diabetes status (chronic vs. newly diagnosed case)	**.01**	2.6	1.19-5.60
Diabetes complication (yes vs. no)	.09	1.5	0.93-2.55

regimens.[13] Such complexity can make it challenging for some patients to consistently adhere to their treatment plans, which can in turn lead to uncontrolled glycemic levels and the need for additional support and care.[7,9] With regard to the impact on HbA1c levels, we identified an inverse association between high diabetes-specific MRC index scores and poor glycemic control among the patients, which aligns with the findings of international studies.[7-10,19] However, the proportion of patients with controlled glycemic levels in the current study was 36.5% lower than those found in the literature,[7,21] and the mean HbA1c levels were also higher than those previously reported.[9,26] This suggests that healthcare providers and policymakers in Saudi Arabia should implement policies and interventions that prioritize the proactive and regular review of patients at high risk of MRC.

Recommendations for practice

Researchers have identified different approaches to improve treatment progress and reduce MRC.[8-10,19,27-32] These are categorized into three themes: the prescribing pattern, the healthcare system, and a patient-centered approach. Prescribing pattern improvement strategies could include simplifying medication regimens by de-prescribing unnecessary, redundant, or less effective medications, simplifying or reducing dosage frequency

Table 5. Multivariate logistic regression of factors predicting the HbA1C control level.

Factor	*P* value	Odds ratio	Confidence interval
Age	.55	0.9	0.97-1.01
Gender (male vs. female)	.48	1.2	0.74-1.91
Presence of comorbidities (no vs. yes)	.06	0.4	0.16-1.04
Polypharmacy (no vs. yes)	.43	1.3	0.70-2.28
Diabetes status (newly diagnosed vs. chronic case)	**.02**	2.3	1.11-4.97
Diabetes mellitus complication (no vs. yes)	.22	1.4	0.83-2.23
MRC range			
Low level (scores of 0 to 4) (referent)			
Moderate level (scores of 5 to 8)	.17	0.6	0.27-1.26
High level (scores >8)	**<.001**	0.2	0.12-0.52

(e.g., tapering from multiple subcutaneous insulin injections to once-daily basal insulin), prescribing fixed-dose combination medications, or maximizing medication doses before adding medications.[8-10,19,27-29] Using multipurpose medications that treat different underlying conditions and combining indications in a single medication are also strategies to reduce the medication burden and MRC in patients with T2DM.[8] However, physicians and prescribers should weigh the potential benefits and harm to patients before considering any medication changes, especially when a patient has a medication with complex directions for use and an increased risk of side effects.[30] In addition, evidence-based research must be reviewed before switching patients from one therapeutic regimen to another to identify the therapeutic effectiveness in the targeted patients.[28] For healthcare system improvement strategies, technology software or MRC tools embedded within the hospitals' medical record system can aid clinical decision-making by highlighting high-risk patients and evaluating and addressing the complexities inherent in medication prescriptions.[8] Medication therapy management tools can also help tailor and prioritize approaches to personalized care plans and ensure the completeness and accuracy of medication regimens.[31] Patient-centered improvement strategies to reduce the impact of MRC include the use of medical reminder devices, coordinating medication administration with regular daily activities, and improving patients' understanding of their prescribed medications and need for self-care.[8,9,31] Providing psychological and behavioral support is also recommended for patients with T2DM, as it can reduce diabetes-specific emotional distress and lead to better outcomes (e.g., increased adherence and glycemic control).[9,32]

This study included patients with diverse demographic characteristics and measured key diabetes management variables. Consequently, the findings can be generalized to the Saudi population in other regions of Saudi Arabia that share the same healthcare system and cultural context. Nevertheless, the study had some notable limitations. First, it was a retrospective study based on existing medical records, which may have had limitations in terms of data completeness. Due to the retrospective design, it was not feasible to assess medication compliance and other related factors, such as patient attendance at education courses to improve their medication adherence.[7] Furthermore, our study only addressed the medications for T2DM and did not cover any other medications or supplements used by patients. Therefore, the findings may not have captured the full extent of MRC. However, research has shown that diabetes-specific MRC index scores and the number of diabetes medications used are more associated with HbA1c levels than overall or patient-level MRC index scores that include all the medications used by patients.[7,8,10,19] In addition, the limitation of capturing only some over-the-counter medications, vitamins, and supplements existed previously in the literature. Researchers indicated that while it was challenging to incorporate when determining patient-level MRC index scores, it could have led to underestimating the results.[8]

In conclusion, we identified high diabetes-specific MRC among Saudi patients with T2DM and explored different factors impacting MRC levels. Our findings highlight the need to manage medication complexity to optimize glycemic control, especially in patients at high risk of having complex regimens and poor out-

comes (i.e., those with polypharmacy and chronic cases of T2DM). Accordingly, it may be prudent to consider regimen simplification or other strategies to reduce MRC in patients with T2DM. Further research is needed to validate the current findings in diverse populations and to identify the impact of MRC on different outcomes (e.g., quality of life and compliance) among the Saudi population.

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SUPPLEMENTS

Supplementary Table 1. Association of MRC range with HbA1c status (at 3 and 6 months).

Factor	HbA1c status at 3 months			HbA1c status at 6 months		
	Not controlled	Controlled	*P* value	Not controlled	Controlled	*P* value
MRC range (n, %)						
Low level	15 (45.5)	18 (54.5)		1 (12.5)	7 (87.5)	
Moderate level	40 (58)	29 (42)	**.001**	7 (28)	18 (72)	**.001**
High level	120 (75.5)	39 (24.5)		41 (69.5)	18 (30.5)	

Supplementary Table 2. Multivariate logistic regression of factors predicting the HbA1C control level within 3 months.

Factor	*P* value	Odds ratio	Confidence interval
Age	.69	1.0	0.97-1.02
Gender (male vs. female)	.37	1.3	0.74-2.28
Presence of comorbidities (no vs. yes)	.06	0.3	0.10-1.06
Polypharmacy (no vs. yes)	.96	1.0	0.50-2.07
Diabetes status (newly diagnosed vs. chronic case)	**.01**	3.0	1.25-7.43
Diabetes complication (no vs. yes)	.07	1.7	0.96-3.13
MRC range			
Reference			
Moderate level	.15	0.5	0.22-1.27
High level	**.002**	0.3	0.12-0.63

Supplementary Table 3. Multivariate logistic regression of factors predicting the HbA1C control level within 6 months.

Factor	*P* value	Odds ratio	Confidence interval
Age	.70	0.9	0.94-1.04
Gender (male vs. female)	.65	0.8	0.28-2.24
Presence of comorbidities (no vs. yes)	.25	0.4	0.07-1.98
Polypharmacy (no vs. yes)	.13	2.6	0.75-9.06
Diabetes mellitus status (newly diagnosed vs. chronic case)	.59	1.5	0.32-7.37
Diabetes mellitus complication (no vs. yes)	.32	0.6	0.20-1.69
MRC range			
Reference			
Moderate level	.29	0.3	0.03-3.00
High level	**.02**	0.1	0.01-0.61