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ORIGINAL RESEARCH

Treatment Patterns, Effectiveness, and Satisfaction Among Patients with Type 2 Diabetes Treated with Insulin in Saudi Arabia: Results of the RIMODIS Study

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ABSTRACT

Introduction: The alarming increase in type 2 diabetes mellitus (T2DM) in Saudi Arabia is aggravated by increasing obesity, sedentary lifestyle, and population aging. The RIMODIS study aimed at describing the practices in the therapeutic management of patients with T2DM treated with different insulin regimens.

Methods: This national, multicenter, non-interventional, cross-sectional disease registry on the real-life therapeutic management of insulin-treated patients with T2DM in Saudi Arabia enrolled 3010 patients. It primarily aimed at describing treatment patterns, complications, and glycemia levels. Patients completed the diabetes treatment satisfaction questionnaire (DTSQ). Data on different treatment patterns were analyzed using chi-square or Fisher's exact test. Outcomes were analyzed according to the different insulin regimen subgroups (basal versus premixed).

Results: Over 60% of patients were treated with premixed insulin and most patients were also prescribed oral antidiabetics (OADs). Patients on insulin alone seemed to achieve better glycated hemoglobin (HbA1c) control. Adding OADs to insulin slightly increased treatment satisfaction scores, with scores higher in patients on basal insulin compared to premixed insulin. Hypoglycemia was lower when adding OADs to insulin. Most patients showed high treatment adherence; however, two-thirds of study patients failed to achieve glycemic target levels.

Conclusion: Most patients are treated with a combination of insulin and OADs, associated with glycemic control and low incidence of hypoglycemia. However, we highlight suboptimal glycemic target achievement, underscoring the need to improve T2DM clinical management and promote healthier lifestyle among patients in Saudi Arabia.

Keywords: Antidiabetic therapy; Clinical management; Glycemic control; Saudi Arabia; Type 2 diabetes

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Key Summary Points
Why carry out this study?
Type 2 diabetes (T2DM) is alarmingly increasing in Saudi Arabia, a country witnessing an escalation in obesity, sedentary lifestyle, and population aging.
RIMODIS is a national, multicenter, non-interventional, cross-sectional disease registry aimed at investigating the real-life therapeutic strategies of managing insulin-treated patients with T2DM in Saudi Arabia, and their treatment satisfaction.
What was learned from the study?
Most patients with T2DM suffered from comorbidities such as obesity, hypertension, and dyslipidemia, and were under medication.
Although most patients showed high adherence to their diabetes treatment, a high percentage failed to achieve glycemic control, and attributed the failure mostly to poor diabetes education and to the lack of experience in self-managing insulin dosage.
Patients on basal insulin showed better treatment satisfaction compared to patients on premixed insulin, and adding oral medication to insulin treatment slightly improved patient satisfaction.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.14663103.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) causes substantial morbidity and mortality. Increasing obesity, sedentary lifestyle, and population aging are major contributors to the global increase of T2DM incidence. Moreover, diabetes-related complications consume a disproportionate share of healthcare resources. Strategies to reduce the disease burden in patients with T2DM include lifestyle measures (diet and exercise), as well as rigorous treatment of hypertension, dyslipidemia, and hyperglycemia [1]. Insulin therapy is often inevitable for patients with T2DM, because the disease is characterized by the progressive decline of β-cell function [2]; insulin production decreases with time and, therefore, patients need to start insulin therapy. International collaborations of different registries from various countries have aimed at better understanding the global pattern of managing diabetes and its complications [3, 4]. Recent guidelines for T2DM management stress the importance of an individualized approach to the treatment of patients with T2DM and the necessity to achieve and maintain target glucose level [5].

The prevalence of T2DM in the adult population in Saudi Arabia was 18.3% in 2020 [6]. However, data from the international registries are not conclusive and there is a dearth of information on diabetes management in Saudi Arabia. In 2009 in Saudi Arabia, a study showed that the majority of patients with T2DM did not attain recommended glycemic targets of glycated hemoglobin (HbA1c) < 7% (53 mmol/mol) and this indicates the presence of a gap between international guidelines/recommendations and actual practice [7].

This situation highlights the need to better assess the current practices in diabetes management in Saudi Arabia and to put in place some actions to improve the quality of care for these patients. The main objective of the RIMODIS registry (current p*R*actice *I*n the *M*anagement *O*f type 2 *D*iabetic patients treated with *I*nsulins in *S*audi Arabia) was to collect data in a standardized manner that would reflect current practices in the therapeutic

management of patients with T2DM treated with insulin. The study also aimed at studying the proportion of patients on different insulin regimens reaching glycemic targets, to describe the treatment impact on the glycemic control, patient compliance and treatment satisfaction, and to assess occurrence of hypoglycemia episodes.

METHODS

Study Design

This was a national, multicenter, non-interventional, cross-sectional disease registry on the real-life therapeutic strategy of managing insulin-treated patients with T2DM in Saudi Arabia. Participating centers were randomly selected from a list of physicians in primary care centers governed by the Ministry of Health (MOH) in Saudi Arabia, routinely involved in diabetes management, including primary care physicians, endocrinologists, and internal medicine specialists. The registry was conducted in accordance with the Helsinki declaration of 1964 and its subsequent amendments, and was approved in accordance with the local regulations by the institutional review board (IRB) of the King Fahed Medical City for all participating centers governed by the MOH in Saudi Arabia (IRB registration number with KACT, KSA: H-01-R-012; IRB registration number with OHRP/NIH, USA: IRB00010471). All enrolled patients provided a signed written consent to participate in the study. Eligible patients were adult men or women with T2DM who had been initiated on insulin at least 6 months prior to the study with no change in type of treatment within the previous 3 months. T2DM is defined as a metabolic disorder characterized by hyperglycemia: blood sugar levels > 126 mg/dL and HbA1c > 5.9% [8]. Patients who were concomitantly participating in another trial or those with type 1 diabetes or receiving insulin treatment for reasons other than T2DM were excluded from the study. To avoid bias, patients who signed the study-specific informed consent and who met the eligibility criteria were included sequentially.

Data Collection

Data were collected for each patient on individual paper Case Report Forms (CRF) completed by the physician or delegated staff at the documentation visit. In addition, patients were asked to complete a questionnaire that reflects their satisfaction with their diabetes treatment.

Safety Considerations

No safety data were collected specifically during this study. However, adverse events with special interest in T2DM (hypoglycemia and weight gain), having occurred within the 6 months prior to study entry, were collected for each study patient. Hypoglycemia was defined by a glucose concentration $\leq$ 70 mg/dL (3.9 mmol/L) with associated symptoms [9].

Statistical Considerations

Sample Size

As the sample size determination is maximized using worst-case percentage (50%), and according to the formula $N = Z^2\ P(1 - P)/d^2$, at least 2401 patients with T2DM were required to estimate an observed percentage of 50% with an absolute precision of 2% and a 95% confidence interval (CI). Assuming that 20% of participating subjects would not be evaluable for the primary analysis because of missing values or unfulfilled eligibility criteria, approximately 3000 patients were planned to be enrolled in the study.

Study Populations

The enrolled population included all patients who signed the informed consent form. The analysis population included all patients from the enrolled population who satisfied all eligibility criteria.

Study Outcomes

Primary evaluation criteria included the description of patients' antidiabetic therapy, diabetes complications and cardiovascular risk factors, blood glucose monitoring, fasting

plasma glucose (FPG), and prandial plasma glucose (PPG). Secondary endpoints were the evaluation of HbA1c target achievement, patient satisfaction (according to diabetes treatment satisfaction questionnaire [DTSQ] score), and occurrence of hypoglycemia episodes. Laboratory test results (glucose and lipid profile) were also collected and analyzed.

General Considerations

Numeric variables were summarized as number of observed values, number of missing data; mean ± standard deviation (SD); minimum and maximum; median; 1st and 3rd quartiles (Q1 and Q3); two-sided 95% Wald CI of the mean for all endpoints. Categorical variables were summarized as number of observed data, number of missing data; counts and percentages; two-sided 95% CI using the Agresti–Coull method for all endpoints.

Chi-square or Fisher's exact test, depending on the expected counts, was used to test the difference between insulin treatment patterns according to HbA1c target achievement.

The *t* test or Wilcoxon/Mann–Whitney test (depending on data normality) was used to test the differences between treatment groups according to DTSQ score.

When applicable, all outcomes were analyzed according to the different insulin regimen subgroups. Missing data were not taken into consideration to calculate percentages and probabilities associated with tests.

RESULTS

Study Participants

Patient Disposition and Demographics

Patients were recruited over a 2-year period between 9 December 2016 and 17 December 2018 in 18 centers across Saudi Arabia. Out of the 3019 enrolled patients who signed the consent form, nine were excluded from the study for not having met eligibility criteria and a total of 3010 patients were included in the analysis population. The DTSQ was completed by 2960 (98.1%) patients. Patient gender, age, and lifestyle data are summarized in Table 1.

Table 1 Patient characteristics

	Analysis population (*N* = 3010)
Gender	*N* = 3009
Female, *n* (%)	1627 (54.1%)
Age	*N* = 3009
Mean in years ± SD [min; max]	58.0 ± 11.5 [18.0; 99.0]
Marital status, *n* (%)	*N* = 3009
Married	2507 (83.3%)
Widowed	348 (11.6%)
Single	92 (3.1%)
Other	62 (2.0%)
Smoking status, *n* (%)	*N* = 3009
Never smoked	2409 (80.1%)
Former smoker	327 (10.9%)
Current smoker	273 (9.1%)
Physical activity, *n* (%)	*N* = 3009
Unknown	72 (2.39%)
No	1288 (42.8%)
Yes	1649 (54.8%)
< 60 min per week	702 (42.6%)
60 min to 3 h per week	688 (41.7%)
> 3 h per week	259 (15.7%)

SD standard deviation

Medical History

Weight at baseline ranged from 32.0 to 159.0 kg (mean = 81.1 ± 16.1 kg) and the average height was 1.6 ± 0.1 m. Body mass index (BMI) was computed for 2990 patients who had available weight and height measurements and ranged from 15.6 to 57.4 kg/m^2 (mean = 31.7 ± 6.1 kg/m^2). Importantly, 2615 patients were overweight (881 [29.5%]) or obese (1734 [58.0%]). Systolic blood pressure ranged from 83 to 240 mmHg (mean = 134.7 ± 18.4 mmHg); diastolic blood pressure ranged from 50 to

120 mmHg (mean = 76.1 ± 10.0 mmHg). Most patients (513 [61.5%]) received platelet aggregation inhibitors. Lipid profile was also analyzed and reported as follows: high density lipoprotein (HDL) cholesterol was at 45.1 ± 18.4 mg/dL, low density lipoprotein (LDL) cholesterol at 111.6 ± 44.5 mg/dL, total cholesterol at 187.4 ± 46.5 mg/dL, and triglycerides at 162.0 ± 81.0 mg/dL.

Diabetes Characteristics

At the time of the study visit, patients had had diabetes for an average of 13.8 ± 7.1 years. Table 2 displays diabetes-related characteristics and glycemia profile such as mean values of HbA1c, FPG, and PPG, in addition to the proportion of patients in the different insulin regimens (basal or premixed) and treatment patterns (insulin alone or concomitantly with oral antidiabetics [OAD]). Diabetes complications are also listed in Table 2, with cardiovascular complications, peripheral neuropathy, retinopathy, sexual dysfunction, and nephropathy being the most commonly occurring ones.

Analysis of Primary Endpoints

Current Antidiabetic Therapy

Around half of the patients self-adjusted their insulin dose (51.4%) and over 70% of all patients used a disposable pen. Figure 1 displays the patient distribution across insulin regimens (with and without concomitant OAD) and describes their insulin daily doses and their treatment patterns. Over 60% of patients were treated with premixed insulin and most patients were prescribed OADs on top of their insulin treatment (Fig. 1i, ii). Interestingly, a single OAD was more frequently added to premixed insulin (73.9%), while basal insulin was mostly accompanied by two, three, or four OADs ($P < 0.001$). Biguanides were by far the most frequently reported OADs, whether alone (57.3%) or with other OADs; followed by dipeptidyl peptidase IV inhibitors (2.7%) and sulfonylureas (2.4%). Among all insulin regimens, there was no significant difference in the doses of insulin whether it was supplemented with OADs or not (Fig. 1iii). Of the 845 patients (28.8%) who had their HbA1c controlled (below 7% [53 mmol/mol]) at baseline, the proportion of patients treated with basal insulin was not significantly different from patients treated with premixed insulin ($P = 0.111$). However, proportions of patients with HbA1c target achievement were significantly different on the basis of treatment pattern ($P = 0.04$), with 32.4% of patients achieving controlled HbA1c on insulin alone and 28.0% of patients achieving controlled HbA1c on insulin with OAD (Fig. 1iv).

Comorbidities and CV Risk Factors

Comorbidities and concomitant medications are described for the study population in Fig. 2. Dyslipidemia (26.9% of patients) topped the list of the most frequently reported medical conditions (Fig. 2i). Almost all hypertensive patients (99.6%) were on antihypertensive therapy, mainly monotherapy (52.4%) or dual therapy (34.9%) (Fig. 2ii). Most of the patients with dyslipidemia (95.1%) were on lipid-lowering therapy, mainly statins (98.8%) (Fig. 2iii). Most of the antihypertensive agents were angiotensin-converting enzyme inhibitors, calcium channel blockers, diuretics, beta-blockers, and angiotensin II receptor blockers. Upon cardiovascular risks evaluation, around 40% of the patients were found to have both dyslipidemia and hypertension.

Conditions of interest in diabetes and that were screened on a regular basis were mostly blood pressure, screened in 2968 (98.6%) patients at a mean frequency of 9.3 ± 7.6 times per year, followed by blood lipid measurements, blood test for kidney function, foot examination, eye screening, urine test for kidney function, cardiac assessment, and neurological assessment.

Blood Glucose and HbA1c Monitoring

Among patients in the analysis population, 2648 patients (88.0%) own a glucose meter, and 2373 out of those patients (89.6%) self-monitor their blood glucose levels, everyday (796 patients [33.5%]), occasionally from time to time (1261 patients [53.1%]), and very

Table 2 Diabetes characteristics

	Analysis population *N* = 3010
Duration of diabetes, years ± SD	13.8 ± 7.1
Insulin regimens	
Basal insulin	600 (20.3%)
Premixed insulin	1891 (63.9%)
Treatment pattern	
Insulin only	562 (18.7%)
Insulin and OADs	2448 (81.3%)
Glycemia profile	
HbA1c, % (mmol/mol)	9.0 ± 1.7 (75 mmol/mol)
FPG, mg/dL	174.9 ± 67.5
PPG, mg/dL	240.9 ± 75.8
Diabetes complications, *n* (%)	
Cardiovascular complications	369 (12.3%)
Myocardial revascularization (CABG or PCI)	96 (26.0%)
Myocardial infarction	76 (20.6%)
Stable angina leading to hospitalization	71 (19.2%)
Peripheral vascular diseases	61 (16.5%)
Stroke	43 (11.6%)
Nephropathy	114 (3.8%)
Microalbuminuria	54 (47.4%)
Macroalbuminuria	40 (35.1%)
Renal failure	29 (25.4%)
Other relevant complications	983 (32.7%)
Peripheral neuropathy	535 (54.4%)
Retinopathy	446 (45.4%)
Sexual dysfunction	290 (29.5%)

CABG coronary artery bypass graft, *FPG* fasting plasma glucose, *HbA1c* glycated hemoglobin, *PCI* percutaneous coronary intervention, *PPG* prandial plasma glucose, *SD* standard deviation

occasionally or practically never (224 patients [9.4%]). Specifically, though most patients had had their FPG measured (2668 patients [88.6%]), FPG is mostly assessed irregularly (1922 patients [73.9%]); a smaller proportion of patients evaluate their FPG every morning (377 patients [14.5%]) or weekly (272 patients [10.5%]). Similarly to FPG, PPG assessment is mostly performed irregularly (1391 [78.2%]), and most commonly 2 h after breakfast (1218

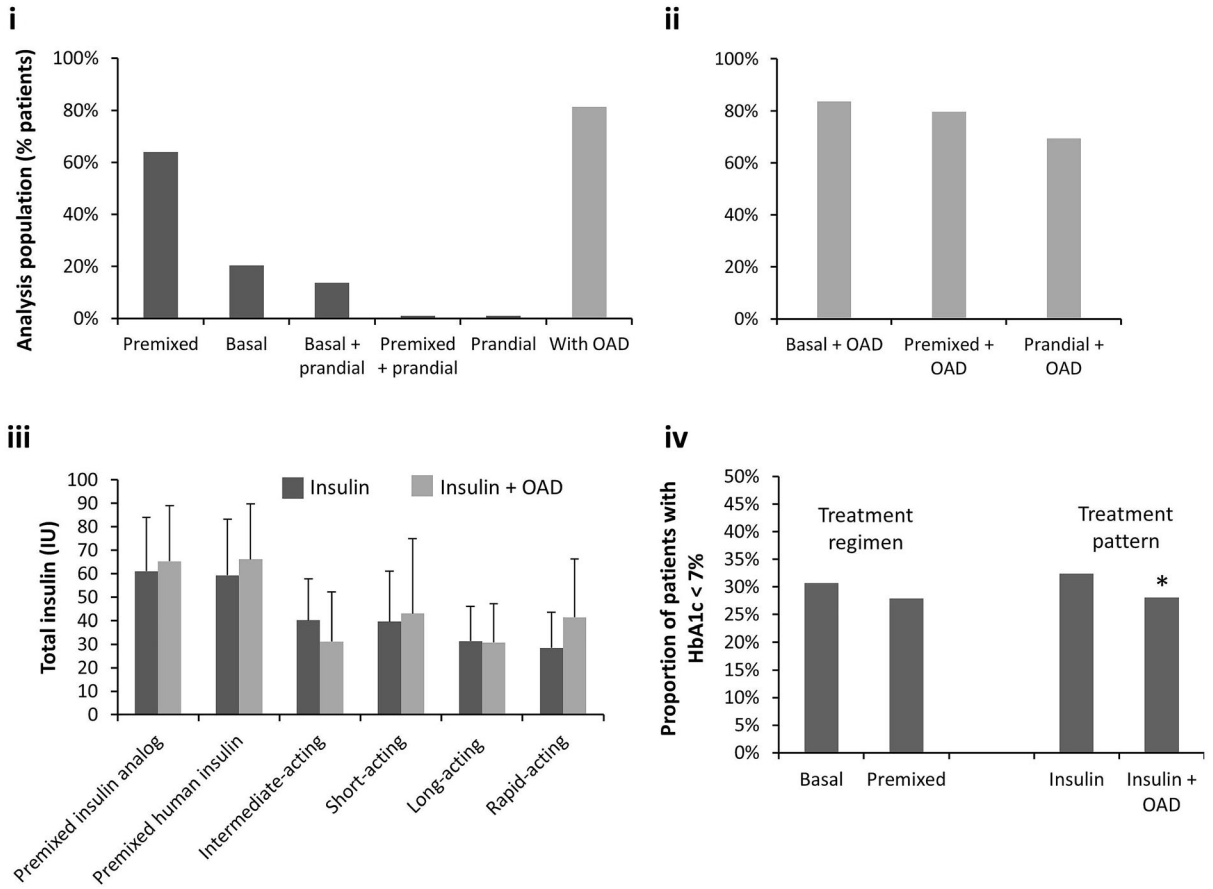

Fig. 1 Patient distribution across diabetes treatment modalities. **i** Proportion of patients in the analysis population on different insulin regimens, and on insulin with OAD. **ii** Proportion of patients in the analysis population on OAD, as an add-on treatment to insulin. **iii** Total insulin dose per day, whether insulin alone or concomitantly with OADs. **iv** Proportion of patients who had controlled HbA1c at baseline

patients [70.1%]), followed by 2 h after lunch (418 patients [24.1%]) or dinner (150 patients [8.6%]). As for HbA1c levels, 252 patients (8.4%) reported having never been tested for HbA1c levels; of those who have (2664 patients [88.5%]), testing occurred on average 1.7 ± 1.0 times, and up to 30 times for some patients.

Patterns of blood glucose monitoring (FPG, PPG, and HbA1c assessment) or follow-up blood works were comparable with respect to treatment with insulin alone or in association with OAD.

Patient Satisfaction

Out of 3010 patients, 2986 patients (99.2%) had completed the DTSQ.

Patients' scores on the DTSQs for the evaluation of the treatment satisfaction ranged from 0 to 36 with a mean of 27.0 ± 6.0 and a median of 28.0. Though patients on insulin and OAD therapy showed only a slightly higher treatment satisfaction score compared to patients on insulin treatment alone, this difference was statistically significant ($P < 0.05$). Treatment satisfaction was also evaluated in terms of insulin regimen (basal or premixed). DTSQ scores were higher in patients on basal insulin, reflecting greater satisfaction with their diabetes

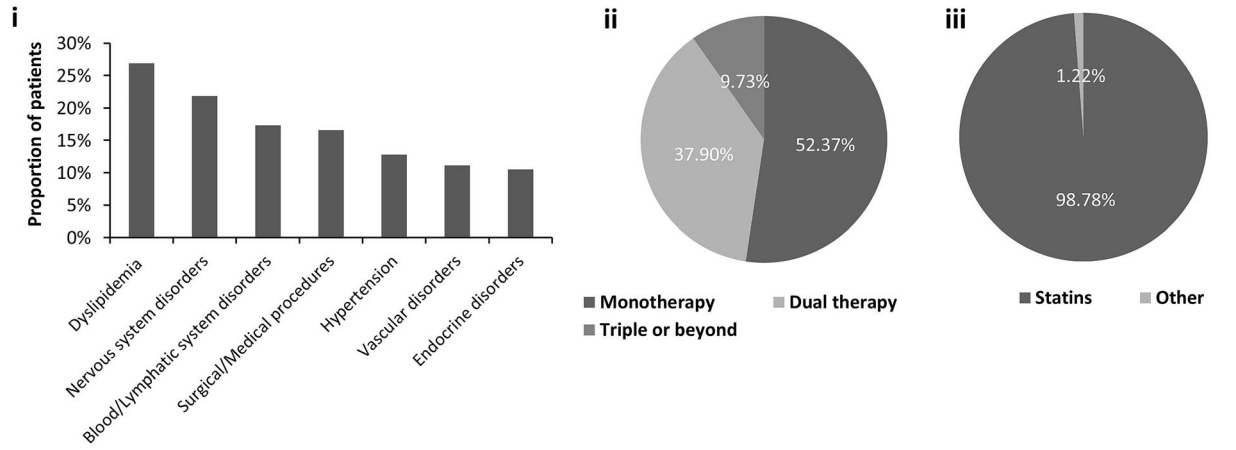

Fig. 2 Comorbidities and major concomitant medications at baseline. **i** Proportion of patients reporting the most common diabetes comorbidities. **ii** Distribution of antihypertensive therapy regimens among treated hypertensive patients. **iii** Proportion of patients treated with lipid-lowering agents, mostly statins

treatment ($P = 0.001$) compared to patients on premixed insulin.

Patients also reported their perception of the frequency of hyperglycemia and hypoglycemia events in two items of the DTSQ. On a scale where a score of 6 indicates "most of the time" and a score of 0 indicates "none of the time", perceived frequency of hyperglycemia and of hypoglycemia scored an average of 3.0 ± 1.7 and 1.7 ± 1.6, respectively. Figure 3 shows perceived hyperglycemia and hypoglycemia according to treatment regimen and treatment pattern. The difference between treatment pattern subgroups (insulin alone or insulin with OAD) did not show statistical significance as far as hyperglycemia frequency score is concerned ($P = 0.939$), while perceived frequency of hypoglycemia scored significantly higher in patients on insulin alone (1.9 ± 1.7) than in patients on insulin and OAD (1.7 ± 1.6) ($P < 0.001$). Upon comparing insulin regimen subgroups, perceived hyperglycemia seemed more frequent in patients on basal insulin (3.1 ± 1.8) than in those on premixed insulin (2.9 ± 1.7), reaching statistical significance ($P = 0.012$). Perceived hypoglycemia frequency, however, did not differ significantly.

Failure to Achieve Glycemic Control

In total, 845 (28.8%) patients of the analysis population had controlled HbA1c levels. Among those who failed to achieve glycemic control (2085 [71.2%]), 698 were on basal insulin and 1387 were on premixed insulin. Reasons behind not achieving glycemic control for patients on basal and premixed insulin, reported by over 20% of patients included poor diabetes education, lack of experience in self-management of insulin dosing, lack of support, lack of titration of insulin, fear of hypoglycemia, and weight gain. Additionally, 700 (23.3%) patients reported having occasionally forgotten to take their medication. Only 213 (7.1%) patients would stop their medication when they are feeling better; more so among patients exclusively on insulin (9.1%) than among patients on insulin and OAD (6.6%, $P = 0.038$).

Safety Considerations

Hypoglycemia Events

The occurrence of hypoglycemia events was analyzed and is summarized in Table 3. In total, 680 patients (22.6%) reported at least one hypoglycemia event having occurred in the 6 months prior to the study, with an average of

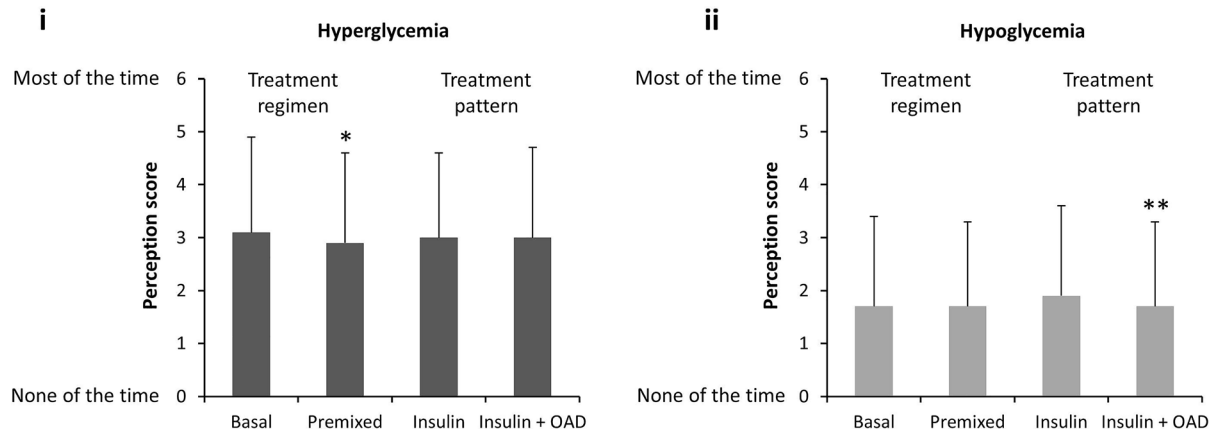

Fig. 3 Perception of hyperglycemia and hypoglycemia. Patients were asked to report their perceived frequency of hyperglycemia and hypoglycemia in the DTSQ, on a scale of 0 (none of the time) to 6 (all of the time). **i** Perception score of hyperglycemia, as perceived by study patients according to treatment regimen and treatment pattern. **ii** Perception score of hypoglycemia, as perceived by study patients according to treatment regimen and treatment pattern. $^{*}P < 0.05$ and $^{**}P < 0.001$

1.2 ± 1.2 events of hypoglycemia reported per patient per week. On average, a patient on basal insulin reported more hypoglycemia episodes (1.3 ± 1.0) per week than a patient on premixed insulin (1.2 ± 1.2; $P = 0.047$). The occurrence of these events was not significantly different among patients on insulin alone and those on insulin with OADs. Importantly, most hypoglycemia events were non-severe (665 [97.8%]). Reasons for hypoglycemia were attributed to insulin mismanagement in 32 patients.

Symptomatic events of hypoglycemia required emergency room visits for 35 patients, resulting in at least one hospital admission for 10 patients (28.6%), with an average length of stay of 2.5 ± 2.0 days. Patients who suffered hypoglycemia events took an average of 1.4 ± 2.2 sick leave days (ranging from 0 to 12 days) and hypoglycemia had no effect on productivity for around 90% of the patients. Of note, the number of sick leave days was significantly larger for patients on basal insulin (2.2 ± 3.0 days) than for patients on premixed insulin (0.8 ± 1.0 day) ($P < 0.05$).

Further analysis showed that a significantly higher proportion of patients on insulin alone (12.8%) reported at least one emergency room visit due to hypoglycemia, compared to patients following insulin and OAD treatment pattern (4.5%, $P < 0.001$).

Summary of Safety Data

No specific safety data were collected for this study. However, reported ADRs were summarized. In total, 22 events of hypoglycemia were reported as ADRs for a total of 22 patients; seven of these events were severe. Most actions taken to address hypoglycemia were oral ingestion of a source of glucose; 19 patients were reported to have recovered. Five cases were reported as hypoglycemia symptoms, namely sweating, tremors, dizziness, dyspnea, palpitation, and unconsciousness; these were probably consequent to hypoglycemia.

DISCUSSION

At the time of this report, the prevalence of T2DM in Saudi Arabia was estimated to be 18.3% by the diabetes country profile established by the IDF Atlas [6]. The amount of healthcare expenditure dedicated to diabetes in Saudi Arabia corresponded to an average of 24% of the total health dollars spent [6]. These numbers are alarming in a country with prevalent overweight, obesity, and a highly sedentary lifestyle [10], and where information on the real-life therapeutic management of diabetes is limited. The RIMODIS study examined the current management of patients with T2DM on

Table 3 Summary of safety considerations

	Insulin regimen		Treatment pattern	
	Basal	**Premixed**	**Insulin alone**	**Insulin + OAD**
Hypoglycemia				
At least one episode reported	206 (20.46%)	454 (23.61%)	150 (26.69%)	530 (21.65%)*
Severe episodes	8 (3.88%)	22 (4.85%)	10 (6.67%)	22 (4.15%)
Total number of episodes per patient	1.28 ± 1.05	1.20 ± 1.21*	1.31 ± 1.08	1.20 ± 1.17
Symptomatic episodes				
Mild	1.15 ± 0.99	1.09 ± 1.15*	1.14 ± 1.03	1.09 ± 1.11
Moderate	1.41 ± 0.90	1.12 ± 0.44	1.27 ± 0.67	1.20 ± 0.64
Severe	1.13 ± 0.35	1.10 ± 0.50	1.00 ± 0.00	1.15 ± 0.53
Due to insulin mismanagement				***N* = 32**
Inappropriate dose				14 (48.28%)
Meal size overestimation				13 (44.83%)
Poor treatment understanding				12 (41.38%)
Inappropriate injection timing				10 (34.48%)
Excessive correction dose				10 (34.48%)

OAD oral antidiabetic drugs
*$P < 0.05$

insulin therapy across Saudi Arabia, and its success in achieving glycemic control. In addition, the study evaluated the impact of diabetes treatment on patient satisfaction and compliance and the occurrence of hypoglycemia.

Though T2DM is reported to be slightly more prevalent among Saudi Arabia men [10], more women were recruited among the RIMODIS study population. The majority of the population never smoked and a little over half of the study population reported some level of physical exercise. Adults with T2DM should engage in at least 150 min of physical activity weekly, spread over at least 3 days [11]. Alarmingly though, most patients enrolled in the study were overweight or obese, matching recent estimates from the WHO [10]. Around 40% of patients with diabetes were also found to suffer from dyslipidemia and hypertension, conditions frequently encountered together [12, 13]. Over 50% of patients with hypertension were treated with calcium channel blockers or angiotensin-converting enzyme inhibitors, both safe, effective, and with a renoprotective role in this category of patients [14]. Statins were prescribed to virtually all patients with T2DM and dyslipidemia, a widely accepted CV risk factor; this is a practice the literature mostly approves [15–17], despite some question-raising findings [18, 19]. According to the American Diabetes Association, low-risk lipid values are as follows: LDL cholesterol < 100 mg/dL, HDL cholesterol > 50 mg/dL, and triglycerides < 150 mg/dL [20]. Averages reported in this study were greater than acceptable limits for LDL-cholesterol and triglycerides and lower than those for the HDL-cholesterol. Overall, patients with diabetes and dyslipidemia should have their blood lipid levels screened yearly, as per the recommendations [20]. Diabetes

complications were screened for at least once per year, which is in total compliance with the American Diabetes Association recommendations [20], reflecting proper diabetes management in Saudi Arabia.

In this study, a large proportion of patients were on premixed insulin. The several treatment modalities for T2DM reflect the challenge of managing this disease and motivated the establishment of treatment algorithms to guide medical decisions [21]. In fact, patients newly started on insulin are usually started on basal insulin (with OAD, mainly metformin); then, in the lack of glycemic control, their treatment is escalated to either basal plus or to the premixed regimen administered twice daily [21, 22]. Further treatment augmentation options are available, but in the present cross-sectional study, patients were not followed beyond the study visit.

The elevated overweight/obesity rates in the study population (and in Saudi Arabia as a whole) justify the prevalent use of combined basal insulin and OAD treatment in the management of T2DM, a combination believed to control glycemia without causing additional weight gain [21]. In addition, challenges in insulin titration and the risk of hypoglycemia [21] could also explain the limited use of basal insulin alone and the widespread use of OADs in diabetes management. The combination of insulin with sulfonylurea was only prescribed to a very limited number of patients. This could be explained by the known high risk of hypoglycemia of this treatment association [23, 24]. However, our study did not report any higher risk of hypoglycemia for this treatment group, probably highlighting the knowledge of physicians and the close monitoring of patients when this treatment is prescribed.

A high percentage of patients in the RIMODIS study had not reached their glycemic target of HbA1c < 7% (53 mmol/mol). Irrespective of insulin regimen (basal or prandial) and treatment pattern (insulin alone or in association with OAD), poor diabetes education and lack of experience in self-managing insulin dosage topped the list of reasons behind failing to reach glycemic targets. Interestingly, a recent study in Saudi Arabia reported on the beneficial effect of psychoeducational intervention programs, which resulted in the significant reduction of HbA1c mean value from 9.8% (84 mmol/mol) to 7.7% (61 mmol/mol) [25].

Hypoglycemia in the 6 months prior to study entry was higher than recently reviewed [21]. Close to one-third of emergency room visits due to hypoglycemia required additional care in the hospital, in accordance with a 2014 study in the USA [26]. Hypoglycemia might result from mismatched insulin and carbohydrate intake or exercise [21]. In this study, inappropriate insulin dosage and reduced food intake were the most commonly reported reasons for insulin-induced hypoglycemia, matching also the 2014 study [26]. Long-acting insulin analogues are associated with fewer nocturnal hypoglycemia events [27]; in this study, more hypoglycemia cases were reported by patients on basal insulin alone, compared to those having long-acting insulin therapy augmented with prandial (fast-acting) insulin.

Treatment satisfaction was also evaluated in this study, given its strong association with adherence to treatment and with overall quality of life of patients with chronic diseases such as T2DM. Major reasons for discontinuation of a prior insulin therapy were the lack of education and experience in self-managing insulin dosage, fear or occurrence of hypoglycemia, lack of support, and impact on social life, thus underscoring the tight relationship between patient compliance and treatment satisfaction. The DTSQ tool assesses treatment satisfaction and perceived frequency of hyperglycemia and hypoglycemia and has proved valuable for understanding and measuring patients' treatment satisfaction in assessments of new treatments and strategies [28]. Patients on combined insulin and OAD treatment seemed more satisfied with their diabetes treatment than patients on insulin alone, which might be explained by the high prevalence of lipohypertrophy in insulin-treated patients with diabetes caused by improper injection techniques and that is estimated at 38% [29, 30]. DTSQ scores were higher in patients on basal insulin, reflecting greater satisfaction with diabetes treatment compared to patients on premixed insulin. This finding matches reports by a study where patients

showed greater satisfaction when switching from premixed insulin to basal insulin [31]. According to DTSQ scores, patients perceived a higher frequency of hypoglycemia, compared to the number of hypoglycemia events actually documented. This might be due to hypoglycemia fear, but also to a misconception of hypoglycemia and limited testing.

Given the large sample size, with patients spanning age groups and disease duration spectra, findings of the RIMODIS study could be extrapolated to the general population of Saudi Arabia. In particular, overweight and obesity that were underscored in this study affect a large portion of the Saudi population, and in the absence of preventive measures and improved lifestyle habits, these conditions could result in prediabetes and diabetes. In addition, the study was conducted in many centers, across the country, and findings can therefore be applied to the overall Saudi population with T2DM.

Limitations of this Study

The RIMODIS study had some limitations due to its nature. First, dietary habits of study patients were not evaluated, though dietary hygiene plays a major role in diabetes management and response to treatment. Finally, the cross-sectional design of the RIMODIS study means that patients were not followed over time, and the outcome of their described diabetes treatment strategy could not be identified.

CONCLUSIONS

This cross-sectional analysis showed that over 60% of patients with T2DM in Saudi Arabia were treated with a premixed insulin regimen and only about one-third received combined basal insulin/OAD regimen. However, overall glycemic control was only achieved in 28.84% of the study patients with average HbA1c values around 9% (75 mmol/mol) associated with a low hypoglycemia risk reported.

Patients on basal insulin showed better treatment satisfaction compared to patients on premixed insulin, despite reporting more hypoglycemia events in the 6 months prior to the study. Patients on insulin treatment supplemented with OADs were slightly more satisfied with their treatment compared to patients on insulin alone, although the number of hypoglycemia events reported by these two subgroups was comparable.

The results further revealed an alarmingly high prevalence of overweight/obesity associated with CV risk factors among Saudi patients with diabetes, underscoring the need for the development of educational programs to promote lifestyle modifications and improve diabetes management in general.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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