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Diabetes Management, Quality of Life and Treatment Satisfaction in Adult Population in Jordan and Lebanon, Observations from the SIMPLIFY Study

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Abstract

Introduction: Type 2 Diabetes Mellitus (T2DM) has witnessed a rise in its prevalence worldwide and in the Middle East region. The overall burden associated with the disease is well characterized, but little is known about patient satisfaction in the region. The purpose of the study is to evaluate the quality of life (QoL) and treatment satisfaction of patients T2DM. Methods: The SIMPLIFY study was an observational, cross-sectional, multicenter, regional study that used patient-reported outcomes of T2DM patients in Jordan and Lebanon. Results: Patients were more satisfied when they were treated exclusively with oral medications, mainly metformin alone or combined with either sulfonylurea or dipeptidyl peptidase-4 inhibitor. Targets for glycated hemoglobin (HbA1c) values were better reached in patients treated with oral medications. Occurrence of comorbidities did not seem to be affected by oral or injectable medications or to affect patients' satisfaction. Data highlighted a suboptimal screening for albuminuria and showed that most patients were overweight or obese and around 30% suffered from hypoglycemia episodes. Conclusion: Data shed the light on the management of T2DM in Jordan and Lebanon and suggested the need for a more comprehensive approach to

T2DM management and selection of medications that would support weight control and a lower hypoglycemia incidence.

Keywords

Diabetes, Glycated Hemoglobin, Clinical Management, Patient Satisfaction, Quality of Life

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is a major cause of disability and has reached epidemic proportions worldwide [1]. Global data show an endemic rise in the prevalence of diabetes, mainly due to T2DM, with an estimated increase between 2017 and 2045 of 48% worldwide and of 112% in the Middle East and North Africa region [2]. In particular, an increase in the prevalence of diabetes in the Levant region was observed in the last two decades with a prevalence reaching around 12% in Jordan and 8% in Lebanon [2] [3], and a major increase is yet predicted by the World Health Organization (WHO) for the year 2030 in both countries [4].

Current diabetes care employs more patient-active strategies with individualized treatment goals and plans [5]. This is of prime importance since the ability of a patient to carry out their management plan is as vital as the plan itself [5], and engaging patients in healthcare decisions may enhance adherence to therapy [6] and Quality of Life (QoL) [5]. The complex nature of the disease has led to the development of many medications with different and multiple mechanisms of action [6] [7]. Furthermore, medications for the prevention or treatment of hypertension, dyslipidemia, cardiovascular diseases, and other comorbidities are essential for a complete management plan [5]. However, with the use of more complex medication regimen, the risk of adverse events, drug interactions, increased cost and lower compliance will rise [6].

For a tight glycemic control and prevention of complications, diabetes patients should strictly adhere to diabetes self-management program, ranging from compliance to their medications and self-monitoring of blood glucose (SMBG), to routine laboratory tests and annual eye, foot, and dental examination [5]. In addition, reports show that around 18% of T2DM patients present with depression [8] and lower health-related QoL compared with healthy subjects [9] [10].

While the overall burden associated with diabetes is relatively well characterized, there is little information available about the level of patient satisfaction in daily clinical practice in the Middle East region. The assessment of treatment satisfaction, beyond constituting a research tool to compare treatments, constitutes a solid assessment of the quality of diabetes care in clinical settings. Improving patients' satisfaction reflects positively on their self-efficacy and adherence to treatment, and it might also reduce the risk of dropout from treatment. Therefore, improving treatment satisfaction in diabetic patients plays an important

role in promoting the achievement of glycemic stability on the long term and eventually reducing the risk of developing diabetic complications [11].

The SIMPLIFY study was designed to observe, for the first time, the management of T2DM and to evaluate the QoL and treatment satisfaction of patients with T2DM in Jordan and Lebanon. The study also aimed at evaluating the percentage of patients reaching their clinical target for glycated hemoglobin (HbA1c). Patient satisfaction was compared between patient subgroups according to target achievement and comorbidities.

These data elucidated the management of T2DM in Jordan and Lebanon, with focus on daily routine treatment data to provide better understanding of diabetes, treatment patterns, clinical outcomes, comorbidities and risk factors.

2. Subject Eligibility and Study Design

The SIMPLIFY study was an observational, cross-sectional, multicenter, regional study to evaluate the QoL and treatment satisfaction of adult patients diagnosed with T2DM. Participating investigators were selected among public and private physicians. Institutional Review Board approval was obtained from all participating centers in Jordan and Lebanon. Eligible subjects were consecutively enrolled between May 7, 2016 and July 21, 2017, from local Jordanian and Lebanese adult patients with T2DM diagnosed at least 12 months (±three months) prior to inclusion in the study, treated with oral and/or injectable medications at the time of the study, with no change in the treatment or the dose in the previous six months and having an HbA1c test performed within one month (±10 days) of the visit and another within one year (±three months). During the single study visit, patients signed the informed consent form (ICF) and were checked for eligibility. Patients with type I diabetes, a recent history of diabetic ketoacidosis, secondary diabetes, psychotic disorder, haemoglobinopathy, as well as pregnant patients or patients participating in another clinical trial were excluded from the study.

3. Materials and Methods

3.1. Data Collection

Collected patient data included primary data originating from patient-reported outcomes (PRO) comprising the Audit of Diabetes-Dependent Quality of Life (ADDQoL), the Diabetes Treatment Satisfaction Questionnaire (DTSQ), and the Hypoglycemia Fear Survey-II (HFS-II) worry subscale, and relevant medical data collected on individual case report forms, including comorbidities and vital signs, disease-related variables at inclusion, current diabetes pharmacotherapy, significant non-drug therapies for diabetes, concomitant medication, laboratory values obtained prior to study visit, and the treating physician's specialty.

3.2. Study Definitions

According to the WHO, Body Mass Index (BMI) is used to classify a subject un-

der one of the following categories: BMI < 18.5 kg/m^2 indicates underweight, 18.5 ≤ BMI < 25 kg/m^2 is normal range, 25 ≤ BMI < 30 kg/m^2 indicates overweight and BMI ≥ 30 kg/m^2 indicates obesity.

The ADDQoL questionnaire evaluates patients QoL and is composed of two items, the first relating to the patient's general QoL and the second relating to the effect of diabetes on patients' QoL, followed by a series of 19 questions. The DTSQ questionnaire measures treatment satisfaction and its score values can range from 0 to 36, where 0 indicates complete dissatisfaction with the treatment and 36 full satisfaction. The HFS-II worry subscale questionnaire measures the worrying and fear of diabetes patients from hypoglycemia events.

3.3. Statistical Consideration

The sample size was calculated according to the standard deviation expected for the DTSQs, which is the questionnaire having shown the highest variability [1]. Under the hypothesis of normality, the formula used to estimate the required sample size for one primary outcome measure is: N = (2 × 1.96 × SD/width of 95% CI) 2. According to this formula, a sample size of 314 patients per country is required to estimate the mean score obtained for DTSQs (SD = 6.1) with a required precision set to 1.35 using a two-sided 95% CI. Assuming that approximately 30% of enrolled patients would not be evaluable for the primary outcome measures, 410 patients per country were planned to be enrolled in this study. Analysis was done on the reference population of both countries, defined as all patients included in the study who signed the ICF and who fulfilled eligibility criteria. The means of quantitative variables were compared using Student T-test or Wilcoxon-Whitney test depending on the normality of the data. The association between two qualitative variables was tested using the Chi-square test or the Fisher's exact test. Qualitative variables were described in terms of number of observed values, number of missing data, frequencies and percentages. Quantitative variables were described in terms of number of observed values, number of missing data, mean, standard deviation (SD), median, lower and upper quartile, minimum and maximum. Differences were considered statistically significant when P value was <0.05. No adjustment for multiplicity was performed. Mixed model linear regression was used to provide the estimates of the mean difference between outcomes (ADDQol, DTSQs, HFS-II worry subscale scores), according to treatment subgroups, diabetes control, or comorbidities. The models were adjusted for site and for other variables in the model (patient-level variables, physician-level variables). All analyses were conducted using SAS (version 9.4; SAS Institute).

4. Results

4.1. Study Participants

Investigators have recruited 825 patients who signed the ICF in 91 centers in Lebanon and Jordan. Only 694 (84.1%) patients were eligible for analysis (refer-

ence population, Figure 1).

Patients' age ranged from 22 to 87 years with an average of 57.0 ± 11.0 years. Most of the patients (68.4%) aged between 40 and 60 years, whereas 26.4% of them were older than 65 years and 5.2% younger than 40 years. Other socio-demographic and lifestyle-related data as well as clinical characteristics are reported in Table 1. Over 75% of patients received education about T2DM and

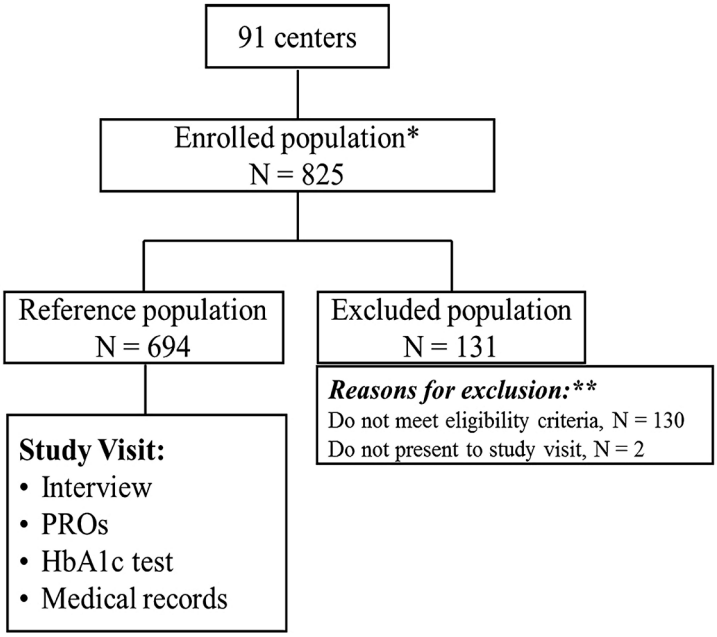

Figure 1. Patients' disposition. *Over 97% of the 825 enrolled patients completed the questionnaires, but scores were only analyzed for the reference population. **One patient could be excluded for more than one reason. HbA1c: glycosylated hemoglobin; PRO: patient-reported outcomes.

Table 1. Patient characteristics.

	Patients number (percentage)	
Socio-demographic data	**N = 694**	
Males	388 (55.9%)	
Holders of secondary school or university degree	501 (72.6%)	
Employed	348 (50.4%)	
Married	590 (85.8%)	
Covered by health insurance	519 (74.8%)	
Lifestyle	**N = 694**	
Regular exercise	301 (43.4%)	
Current alcohol consumption	116 (16.7%)	
Current smoking	192 (27.7%)	
Clinical characteristics	***Range* [*min*; *max*]**	***Mean* (*SD*)**
Weight (Kg)	[47.0; 168.0]	86.6 (17.1)
Height (m)	[1.4; 2.0]	1.7 (0.1)
Body Mass Index (Kg/m^2)	[18.8; 58.8]	30.8 (5.6)
Systolic blood pressure	[90; 190]	131.0 (14.7)
Diastolic blood pressure	[50; 110]	79.4 (9.0)

its complications mostly twice per year. Education and awareness material were mostly provided by the treating physician (498 [92.1%] patients), followed by nutritionists, nurses and pharmacists.

4.2. Medical History

Most patients were either overweight (237 [39.5%]) or obese (335 [48.4%]). Average systolic blood pressure (BP) was 131.0 ± 14.7 mmHg and average diastolic BP was 79.4 ± 9.0 mmHg, indicating an overall well-controlled BP in T2DM patients. Renal function was also assessed and serum creatinine levels showed an average of 97.3 ± 106.1 μmol/L for 573 patients. Most of the patients (85.2%) had their serum creatinine levels below 106.1 μmol/L, and only 14 patients (2.4%) above 353.7 μmol/L. Values for urinary albumin levels as well as the albumin-creatinine ratio were not conclusive for the reference population as they were only collected in 117 and 162 patients, respectively, showing a suboptimal screening for albuminuria by physicians. Patients' lipid profile and liver function tests are displayed in Table 2.

4.3. History of Diabetes and Treatment Patterns

The majority of patients had a family history of diabetes, mostly from their maternal side (62.7% out of 582 patients). Patients had had diabetes for less than five years (32%), for five to nine years (25%), and for over nine years (43%). Most of the patients (70.1%) practiced SMBG at a rate of 15.7 ± 14.1 times per month. At least one hypoglycemia event within the last year prior to the study visit was reported by 201 (29.0%) patients and the average number was 8.3 ± 14.1 hypoglycemia events per patient per year. All 694 patients of the reference population were taking anti-diabetes medications, 510 (73.5%) received exclusively oral antidiabetics (OADs) and 28 (4.0%) received only injectable medications, while 156 (22.5%) received a combination treatment of OADs and injectable medications. Figure 2 summarizes treatment pattern of patients on oral medications; over 40% of patients on OADs were treated with a combination of two medications (Figure 2(A)), mainly metformin combined with either sulfonylurea or with a dipeptidyl peptidase 4 (DPP-4) inhibitor (Figure 2(B)).

Injectable medications mainly included insulin and only one patient was treated with a glucagon-like peptide 1 (GLP-1) receptor agonist. Table 3 displays

Table 2. Lipid profile and liver function tests.

Lipid profile (***Mean values ± SD***)	
Total cholesterol	4.7 ± 1.4 mmol/L
Low-density lipoprotein-cholesterol	2.7 ± 1.0 mmol/L
High-density lipoprotein-cholesterol	1.1 ± 0.3 mmol/L
Triglycerides	2.0 ± 1.1 mmol/L
Liver function tests (***Mean values ± SD*** [***range***])	
Alanine transaminase	28.9 ± 15.4 IU/L [5.0; 174.0]
Aspartate transaminase	27.1 ± 16.7 IU/L [8.0; 140.0]

Table 3. Treatment pattern for all patients in the reference population.

	Reference population N = 694
OADs alone	**510 (73.5%)**
One treatment	**114 (22.4%)**
Metformin	100 (87.7%)
Other	14 (12.3%)
Two treatments	**216 (42.4%)**
Metformin + DPP-4 inhibitor	128 (59.3%)
Metformin + Sulfonylurea	67 (31.0%)
Other	21 (9.7%)
Three treatments	**151 (29.6%)**
Metformin + Sulfonylurea + DPP-4 inhibitor	96 (63.58%)
Metformin + DPP-4 inhibitor + SGLT2 inhibitor	21 (13.9%)
Other	34 (22.5%)
Four treatments	**29 (5.7%)**
Metformin + Sulfonylurea + DPP-4 inhibitor + Thiazolidinediones	15 (51.7%)
Metformin + Sulfonylurea + DPP-4 inhibitor + SGLT2	12 (41.4%)
Other	2 (6.9%)
Injectables alone	**28 (4.0%)**
One treatment	**23 (82.1%)**
Premixed insulin	19 (82.6%)
Basal insulin	3 (13.0%)
GLP-1 receptor agonist	1 (4.4%)
Two treatments	**5 (17.9%)**
Basal insulin + prandial insulin	3 (60.0%)
Basal insulin + premixed insulin	2 (40%)
OADs + injectables	**156 (22.5%)**
Two treatments	**37 (23.7%)**
Metformin + premixed insulin	17 (46.0%)
Metformin + basal insulin	6 (16.2%)
Metformin + GLP-1 receptor agonist	6 (16.2%)
Other	8 (21.6%)
Three treatments	**64 (41.0%)**
Metformin + DPP-4 inhibitor + basal insulin	16 (25.0%)
Metformin + DPP-4 inhibitor + premixed insulin	12 (18.8%)
Metformin + sulfonylurea + basal insulin	8 (12.5%)
Other	28 (43.8%)
Four or more treatments	**55 (35.3%)**
Metformin + DPP-4 inhibitor + sulfonylurea + basal insulin	18 (32.7%)
Metformin + DPP-4 inhibitor + sulfonylurea + premixed insulin	6 (10.9%)
Other	31 (56.4%)

DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide; OADs, oral antidiabetics; SGLT2, sodium-glucose cotransporter 2.

details of the treatment patterns followed by all patients of the reference population. It is worth noting that 20 patients (2.9%) were prescribed non-drug therapies, mainly herbal preparations.

Over 80% of patients were also being treated for other conditions. Most concomitant medications were HMG CoA reductase inhibitors (72.4%), angiotensin receptor blockers (39.3%), platelet aggregation inhibitors (32.9%) beta-blocking agents (21.2%), and angiotensin-converting enzyme inhibitors (13.0%).

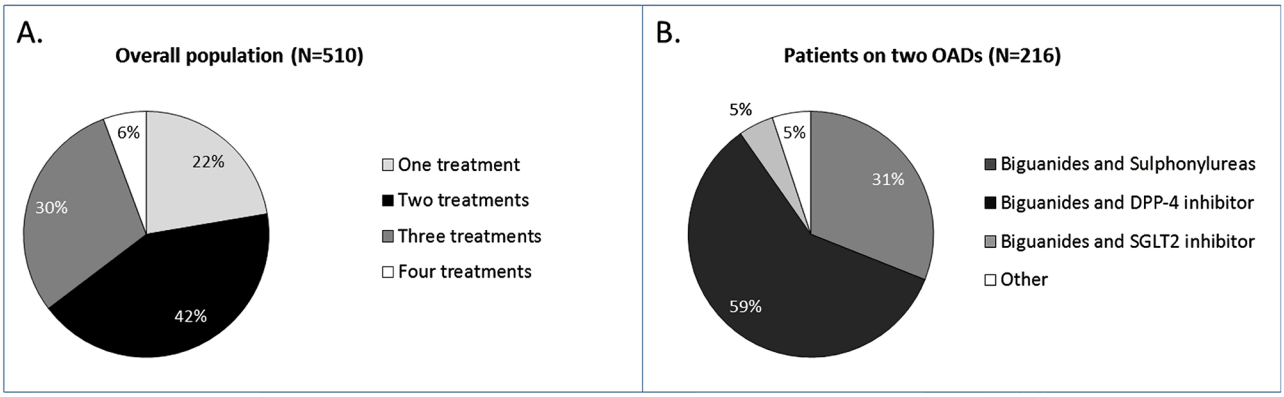

Figure 2. Treatment pattern of study patients treated with oral medication. (A) Percentages of patients receiving one or a combination of oral antidiabetic treatments. (B) Treatment pattern of patients receiving a combination of two oral antidiabetic treatments. DPP-4, dipeptidyl peptidase-4; SGLT2, sodium-glucose cotransporter 2.

4.4. HbA1c Target Achievement

Physicians set targets for HbA1c values, on a case-by-case basis, ranging from 5.0% (31 mmol/mol) to 10.0% (86 mmol/mol). The average HbA1c target set by physicians was of 6.8% ± 0.5% (51.3 ± 5.4 mmol/mol) for all patients. Physician-set targets were reached by 268 (38.6%) patients, and 245 (35.3%) patients reached the absolute HbA1c target of 7.0% (53 mmol/mol). The three main reasons for failing to reach HbA1c targets were poor adherence to diet and/or physical exercise recommendations (85.9%), poor adherence to SMBG practice (48.8%), and failure of the current antidiabetic treatment regimen (38.7%). On average, HbA1c values decreased by 0.5% ± 1.5% (5.2 ± 17.0 mmol/mol) in the period extending between 12 months and one month prior to the study visit. Upon comparing HbA1c target achievement among treatment subgroups, results showed that 43.0% of patients treated with OADs reached the HbA1c target set by their physicians, whereas 28.9% of those treated with a combination of OADs and injectable medications achieved their target, and only 14.3% of patients on injectable medications were able to achieve the HbA1c target set by their physicians. The difference between these treatment subgroups was statistically significant ($P < 0.001$).

4.5. Patients' QoL and Treatment Satisfaction

To evaluate the QoL and treatment satisfaction of patients, PRO scores were determined according to the ADDQoL and DTSQ questionnaires as well as the HFS-II worry survey. Out of the 694 patients in the reference population, 8 (1.2%) did not complete the ADDQoL questionnaire, 15 (2.2%) did not complete the DTSQ questionnaire, and 19 (2.7%) did not complete the HFS-II worry survey. Average weighted impact score for the ADDQoL questionnaire ranged for 685 patients from −8.8 to 0.5 with a mean of −3.1 ± 1.9. The range boundaries of the score values of the ADDQoL questionnaire are −9 to +3, where −9 indicates utter dissatisfaction and +3 indicates full satisfaction. The score of the ADDQoL first item ranged from −3.0 to 3.0 with a mean of 1.1 ± 1.1, and the

score of the second item from −3.0 to 1.0 with a mean of −1.7 ± 0.9. Patients' answers to these two items are detailed in Table 4. Overall, around 25% of patients described their current QoL as below good, and close to 90% thought that if they did not have diabetes, their QoL would improve to different extents.

Patients scored a mean of 27.6 ± 6.9 (with a range of 1 to 36) on the DTSQ, which evaluates treatment satisfaction. DTSQ questionnaire score values can range from 0 to 36, where 0 indicates complete dissatisfaction with the treatment and 36 full satisfaction. Therefore, an average score of 27.6 ± 6.9 suggests that patients' remained not fully satisfied about their treatment scheme. When patients were asked in the DTSQ questionnaire about the frequency at which they felt their blood glucose levels were unacceptably high or unacceptably low, the average scores of their answers were 2.8 ± 1.8 and 2.0 ± 1.8, respectively, on a scale from 0 to 6, 0 indicating "none of the time" and 6 indicating "most of the time".

The average score of the HFS-II worry subscale was 20.5 ± 17.8, on a scale going from 0 (no worry whatsoever) to 72 (extreme worry). The calculated score shows that patients remain far from having no worries at all and are still afraid of hypoglycemia.

4.6. Factors Influencing Patients' QoL and Treatment Satisfaction

PRO scores were then compared among different treatment patterns, HbA1c target achievement status and comorbidities. Mean differences between these groups were calculated after adjusting for patients' characteristics. Table 5 compares the QoL, treatment satisfaction, and worry of hypoglycemia of patients on injectable and OADs and those on injectable medication to patients on OADs only. Compared to orally treated patients, a statistically significant decrease was noted in ADDQoL scores for the subgroup of patients treated with injectable

Table 4. Patients' answers to the first two items of the ADDQoL questionnaire.

	Reference population **N = 694** N (%)
Item 1: evaluation of the general QoL	**N = 685**
Excellent	59 (8.6%)
Very good	179 (26.1%)
Good	282 (41.2%)
Neither good nor bad	124 (18.1%)
Bad	32 (4.7%)
Very bad	5 (0.7%)
Extremely bad	4 (0.6%)
Item 2: if I did not have diabetes, my QoL would be…	**N = 685**
Very much better	126 (18.4%)
Much better	315 (46.0%)
A little bit better	164 (23.9%)
The same	77 (11.2%)
Worse	3 (0.4%)

ADDQoL: Audit of Diabetes-Dependent Quality of Life; QoL: Quality of Life.

Table 5. PRO score outcomes in patients on injectables and injectables with OADs compared to patients on OADs alone and in patients on different OAD treatment patterns.

	ADDQoL		DTSQ		HFS-II	
PRO scores compared to patients on OADs						
In patients on injectables only	−1.06 *		−2.24		+7.81 *	
In patients on injectables and OADs	−0.67 **		−1.69 *		+2.22	
PRO scores in patients on different OAD patterns						
Metformin + DPP-4 inhibitors	−2.66	P < 0.05	28.7	P < 0.01	15.2	P = 0.06
Metformin + Sulfonylureas	−3.15		25.6		20.4	

ADDQoL: Audit of diabetes dependent quality of life, DPP-4: dipeptidyl peptidase 4, DTSQ: Diabetes treatment satisfaction questionnaire, HFS-II: Hypoglycemia fear survey-II, OAD: Oral antidiabetics, PRO: Patient-reported outcome.*, P < 0.01; **, P < 0.001.

medication (−1.1) (P = 0.0031) and for those treated with OADs and injectable medications (−0.7) (P < 0.001), irrespective of patients' characteristics or physicians' specialty. As far as treatment satisfaction was concerned, a statistically significant decrease (−1.7) was noted in DTSQ scores of patients treated with OADs and injectable medications compared to patients treated with only OADs (P = 0.0097). Concerning HFS-II worry survey scores, they were higher in patients treated with injectable medication only (+7.81) when compared to those treated with OADs (P = 0.0053).

Among patients treated with OADs, ADDQoL scores showed that those treated with a combination of metformin and DPP-4 inhibitors, scoring −2.7 ± 1.7, were more satisfied than those treated with metformin and sulfonylureas, scoring −3.2 ± 1.5 (P = 0.039). The DTSQ questionnaire also showed a better QoL reported by patients treated with metformin and DPP 4 inhibitors who scored 28.7 ± 6.1 compared to those treated with metformin and sulfonylureas who scored 25.6 ± 7.2 (P = 0.002), and it was clear that the perception of hyperglycemia frequency was lower when patients were treated with metformin and DPP-4 inhibitors (P = 0.007). HFS worry survey revealed results pointing in the same direction as the previous questionnaires and showing that patients treated with metformin and DPP4-inhibitors attributed a lower effect of diabetes on their QoL than those treated with metformin and sulfonylureas, visible by respective scores of 15.2 ± 15.9 and 20.4 ± 19.0. However, this difference was not statistically significant (P = 0.060).

On the other hand, ADDQoL questionnaire, DTSQ questionnaire and HFS-II worry subscale scores were all significantly different in patients achieving their HbA1c target compared to those who did not achieved it (−0.6 [P = 0.0016], −2.5 [P < 0.001] and +3.3 [P = 0.0071], respectively). However, comorbidities did not seem to majorly impact PRO scores. Indeed, only three conditions are suggested to have a certain effect on patients' perceptions. Genitourinary infection compromised patient satisfaction, with a decreased DTSQ score (−2.0; P = 0.02), diabetic retinopathy was associated with enhanced anxiety, reflected by an increase in HFS-II worry scale survey score (+3.3; P = 0.04), and chronic kidney disease reduced QoL, as revealed by a decrease in the ADDQoL score (−0.4; P = 0.04).

5. Discussion

This observational study aimed at evaluating the QoL and treatment satisfaction of patients with T2DM treated with oral or injectable antidiabetic medications in Jordan and Lebanon. Data showed that over 85% of patients were overweight or obese, which is in agreement with the general association of obesity with metabolic disorders, in particular T2DM [12] [13]. Average blood pressure and liver enzyme levels were within normal ranges. Laboratory screening for nephropathy was suboptimal, as data for urinary albumin levels and for the albumin creatinine ratio was missing for over 50% of the patients, highlighting a gap in the screening for nephropathy. Nephropathy screening is essential for a comprehensive approach to T2DM management, since it might indicate diabetes progression or onset of diabetes-induced kidney disease [14] [15] [16]. Patients had had diabetes for about 9 years prior to this study and most of them self-monitored their glucose levels and received education about diabetes on a regular basis, suggesting success in engaging patients in their diabetes management. In fact, SMBG practice and physician-provided guidance about disease and its complications are both known to reduce disease burden and improve prognosis and QoL [15] [17] [18], despite reported discomfort from frequent finger pricks [18].

To assess the QoL and treatment satisfaction of T2DM patients, study participants filled the ADDQoL, the DTSQs and the HFS-II worry scale survey, which are established tools for such assessments [19] [20] [21], and used worldwide as powerful and reliable indicators [22]-[29]. These three tools are used in the present study for the first time in the region, and although they were all validated, bias might be inevitable while using them, since patients usually visit their physician more often if they have a poor QoL than if they were satisfied. Results indicate a negative impact of T2DM on the patients QoL and a suboptimal satisfaction with their diabetes treatment with a non-negligible extent of worry and anxiety among T2DM patients, highlighting a gap in diabetes management in terms of patient comfort.

Over 35% of patients were at their HbA1c target, which positively affected their satisfaction scores. In particular, a decrease in the ADDQoL and DTSQs satisfaction scores and an increase in the HFS-II worry subscale survey were noted in patients failing to achieve HbA1c target of 7%. While most of the comorbidities had no significant effect on patients' satisfaction, PRO scores showed that, when it comes to treatment patterns, patients treated only with OADs were significantly more satisfied and less anxious, compared to those treated with injectables only or with injectables combined to OADs. Of note, physicians in this study reported reluctance at prescribing more aggressive antidiabetic treatments to prevent hypoglycemia and patients not achieving their HbA1c targets seemed more "worried" than their counterparts. The literature indeed links fear of hypoglycemia with suboptimal glycemic control [30].

With the increase of T2DM burden in the world in general, and in Lebanon and Jordan in particular [2] [3], it is of utmost importance to ensure compre-

hensive management of the disease while managing glycemia and assessing patients' satisfaction in order to ensure patients are motivated and engaged in their care plan. While this study showed that OADs have a better impact on the general well being of patients, a gap remains in the management of the disease reflected by suboptimal scores. The study suggests that, when possible, health care providers should rely more on oral medications, favoring those known to induce fewer side effects, and in particular those with a lower risk of causing hypoglycemia and those supporting better weight control. Sodium glucose cotransporter-2 (SGLT2) inhibitors might provide such advantages but their clinical use in this study was minimal probably due to the limited availability of this treatment option when the study was conducted. SGLT2 inhibitors are the most recent addition to the therapeutic options available for the treatment of T2DM, only becoming available after the introduction of incretin-based therapies, DPP-4 inhibitors and GLP-1 receptor agonists. These agents have potential advantages with regard to their weight loss promoting effect, low risk of hypoglycemia, reduction in BP, and improved cardiovascular and renal profiles. Because their mechanism of action is independent of the severity of insulin resistance and β-cell failure, they are effective in all individuals with T2DM as long as the estimated glomerular filtration rate is higher than 45 - 60 mL/min/1.73 m^2. The American Association of Clinical Endocrinologists and American College of Endocrinology guidelines [31] recommend multiple agents as second line treatment in patients inadequately controlled on metformin, starting with GLP-1 receptor agonists and SGLT2 inhibitors. The ultimate rank in guidelines for the novel agents will be strongly influenced by the results of ongoing cardiovascular and renal outcome trials, novel combination studies, comparative efficacy and cost compared with older, "more established", but less effective agents when long-term glycemic control is at stake. Recently, the use of SGLT2 inhibitors was positively associated with T2DM patients' satisfaction [25].

Limitations to this study include a lack in the clinical auditing of laboratory values, which could provide more insight on the reality of T2DM patients' health status. Moreover, the cross-sectional design only allows describing patient satisfaction and extent of worry at one point in time; hence the relevance of launching a study with longitudinal design to follow patients' attitudes and QoL over time, with a potential for treatment adjustment and glycemic response.

6. Conclusion

The simplify study was carried out to evaluate the QoL and treatment satisfaction of patients with T2DM treated with oral and/or injectable antidiabetic medications in Jordan and Lebanon. PRO scores for 3 different questionnaires, ADDQoL, DTSQ, and HFS-II worry subscale, were analyzed and showed that patients on OADs reported better QoL, higher treatment satisfaction and less fear from hypoglycemia than those on injectable medication alone or injectable and OADs. The study also highlights gaps in diabetes management, in particular

suboptimal nephropathy screening, as well as the need for a more comprehensive approach to T2DM management and selection of medications that would support weight control and a lower hypoglycemia incidence.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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