



Original research

Relation between diabetes related distress and glycemic control: The mediating effect of adherence to treatment



Amel Fayed, Faten AlRadini*, Ruba Mohammed Alzuhairi, Afrah Eid Aljuhani, Hana Rashid Alrashid, Manal Mohsen Alwazae, Nuha Ramadan Alghamdi

Department of Clinical Sciences, College of Medicine, Princess Nourah Bint Abdulrahman University, Riyadh 11671, PO Box 84428, Saudi Arabia

ARTICLE INFO

Article history:

Received 10 September 2021
Received in revised form 3 December 2021
Accepted 4 December 2021
Available online 23 December 2021

Keywords:

Diabetes related distress
Adherence to treatment
Glycemic control
Mediating effect
Saudi Arabia

ABSTRACT

Aims: Diabetes related distress (DRD) is a negative emotional reaction to stresses associated with diabetes mellitus (DM) and its management. This study estimated the burden of DRD and self-reported adherence to treatment (SRAT) among patients with DM and investigated their relationship with glycemic control. **Methods:** A cross sectional study of consented 157 diabetics was conducted using the 17-item Diabetes Distress Scale (DDS). It measures distress at four subscales: Emotional Burden (EB), Physician-related (PD), Regimen-related (RD) and Interpersonal Distress (ID). SRAT was assessed using Morisky's scale. Glycemic control was assessed using the most recent HbA1c results. Multivariable linear regression analysis was used for adjustment of confounders and bootstrap Confidence Interval was used to test for the occurrence of mediating effect.

Results: Average age was 44.5 ± 16.0 years, 65% were females, 79% had type 2 DM and nearly 55% has had DM for more than 7 years and the average HbA1c was $8.9 \pm 2.2\%$. Clinically significant DRD was reported by 37% of the participants, EB and RD in 40.8%, PD in 46.5%, and ID among 32.5%. Younger patients showed higher level of stress compared to older participants and patients with type 1 DM showed higher level of stress in all DRD domains. Only 46% of patients were defined as having satisfactory SRAT and improvement of SRAT significantly enhanced the glycemic control ($r = -0.32$, $p < 0.01$). DRD and low SRAT negatively correlated with HbA1c; increasing the DRD by one point may increase the HbA1c on average by 0.41 (C.I. 0.02–0.80) and will indirectly raise the HbA1c by 0.24 (C.I. 0.04–0.47) through the mediating effect of low SRAT.

Conclusion: DRD and low SRAT are commonly reported among DM patients and both are indirectly correlated. The mediating effect of low SRAT highlights the clinical role of DRD and clarifies the process by which distress affect the outcome of DM management.

© 2021 The Authors. Published by Elsevier Ltd on behalf of Primary Care Diabetes Europe. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Diabetes Mellitus (DM) is one of the most common chronic disease in the world and living with DM requires comprehensive management such as medical treatment, diet control and lifestyle modification to achieve an acceptable level of glycemic control and hence, avoid short- and long term-complications [1]. The prevalence of DM is progressively increasing globally. The World Health

Organization (WHO) and the International Diabetes Federation reported that in 2019, approximately 54.8 million adults aged 20–79 years, or 12.8% of the regional population in the Middle East and North Africa have DM – with another alarming figure indicating that up to 1 out of 4 Saudis has DM [2,3].

Living with DM is considered stressful as patients need to follow a special lifestyle in their daily diet, physical activity, drug adherence and blood sugar monitoring [4]. Achieving an acceptable level of glycemic control does not depend merely on the clinical management of DM but it is rather influenced by the degree of stress that patients with DM face [1]. This stress has been mostly associated with risk for poor outcomes, including DM onset and complications [1].

Diabetes-related distress (DRD) is commonly referred to as patient's concerns about the burden of DM and its complications,

List of Abbreviations: DM, Diabetes Mellitus; KSA, Kingdom of Saudi Arabia; DRD, Diabetes Related Distress; DDS, Diabetes Distress Scale; EB, Emotional Burden; PD, Physician related distress; RD, Regimen related distress; ID, Interpersonal distress; HbA1c, Glycosylated Hemoglobin; SRAT, Self-reported adherence to treatment.

* Corresponding author.

E-mail address: faalradini@pnu.edu.sa (F. AlRadini).

perception of support, emotional burden and in accessing proper medical care and advice [5]. The Diabetes-Distress scale (DDS) is one of the most validated instruments used in assessing DDS and the four distress-related domains: “emotional burden (EB), physician-related distress (PD), regimen related (RD) distress subscale and diabetes related interpersonal distress (ID)” [5]. The DDS is a 17-items questionnaire which measures different aspects of DM-specific distress to support the clinician and patients in recognizing where interventions might be helpful [6].

DM can be well controlled via good adherence to treatment – oral hypoglycemic and insulin-, and following a diet and lifestyle modifications [7]. Unfortunately, the average adherence to long-term therapy for chronic diseases does not exceed 50% in developed countries, moreover, the adherence to lifestyle modification and proper diet is much lower than adherence to treatment [7]. This poor adherence is reflected clearly on the DM control as measured by glycosylated hemoglobin (HbA1c) which reflects not only the current glycemic status but also predicts its short- and long-term complications [8].

Understanding the relation between DRD, adherence to treatment and glycemic control can help clinicians in providing comprehensive care to their patients rather than depending on the HbA1c alone as an indicator for DM control. However, studies that attempts to clarify the mechanism through which DRD can influence glycemic control of DM patients are limited and poorly understood. Several descriptive studies have demonstrated that high DRD is associated with poor glycemic control and poor behavioral self-management skills like eating unhealthy diet, physical inactivity, and poor medication adherence [9–14]. Similarly, other studies have shown that poor behavioral self-management of DM is associated with poor glycemic control [15,16]. Thus, how these factors interact or are linked in the causal pathway remain unclear. For example, it has been argued that the occurrence of DRD may lead to poor behavioral self-management of DM leading to poor glycemic control [17,18]; while others argue that DRD affects glycemic control directly through physiological mechanisms [19,20]. Moreover, others researchers argue that patients with DM who had poor glycemic control may develop low motivation for undertaking lifestyle changes like healthy diet, exercise etc, which in turn may lead to high DRD. Some previous studies suggest that these constructs may interact in a bidirectional manner over time [20,21]. However, a randomized controlled trial exploring the relationship between DRD, self-management and glycemic control concluded that the interrelationships between these constructs are complex and are likely to follow multifaceted pathways [22].

In the Kingdom of Saudi Arabia (KSA), DM-related micro- and macrovascular complications have been studied [23]. However, the psychological impact or distress associated with DM is not widely studied among Saudis suffering from DM [24–26]. Nevertheless, there are no studies that assessed the relation between DRD, adherence to treatment and HbA1c among patients with type 1 and type 2 DM. In this study, we aimed to explore DRD and adherence to treatment among patients with DM and to investigate their relationship with glycemic control.

2. Material and methods

2.1. Study design and subjects

This study is a cross-sectional study of a purposive sample of 157 patients with DM recruited in waiting areas at a tertiary hospital in Riyadh, KSA. The data was collected from the outpatient ward of the hospital. Patients with DM who were attending the outpatient services department and who were clinically diagnosed as diabetic patients were invited to participate in the study.

2.2. Inclusion criteria

Eligible patients of the study were adults at least 18 years of age and less than 99 years old; outpatients who had a confirmed diagnosis of DM for at least one year, and were attending follow up clinic for DM regularly.

2.3. Exclusion criteria

The patients who were excluded from the study are those who were not able to complete the survey because they had severe illness or complications from their DM, and patients who were having difficulty in understanding the questions being posed by the survey.

2.4. Sampling procedure and sample size

The study utilized purposive sampling. Therefore, all eligible patients attending the outpatient DM clinic from December 2020 to March 2021 were invited to participate in the survey. Therefore, all eligible consecutive consenting patients with DM during the study period completed the survey in a private room in the clinic.

Sample size calculation was based on data derived from previous literature showing that the correlation between depressive mood and adherence to treatment is intermediate ($r = 0.15-0.25$) [27]. Using G-Power program for calculating the minimal sample size, with 95% level of significance ($\alpha = 0.05$) and a power of 80% ($\beta = 0.2$), the minimal sample size needed was 89. We recruited 157 patients with DM to compensate for the missing data in HbA1c readings.

2.5. Data collection tool

Data collection tool was a validated pre-tested questionnaire. This questionnaire was composed of different sections assessing various domains.

- 1 Sociodemographic data: This included age, sex, marital status and average monthly income of the family.
- 2 Second section was about the medical history of the DM and presence or absence of comorbidities; duration and type of DM, type and frequency of medication, family history of DM, other comorbid conditions and history of DM complications.
- 3 The third section included DDS composed of 17 questions that evaluated diabetes related problems over the last one month [5,6]. The DDS-17 has four distinct subclasses of diabetes-related distress i.e., EB (5 items), PD (4 items), RD (5 items), and ID (3 items). The responses to each item in the questionnaire were rated on a 6-point Likert scale as follows (1, not a problem; 2, a slight problem; 3, a moderate problem; 4, somewhat serious problem; 5, a serious problem; and 6, a very serious problem). The cutoffs for low, moderate, and high distress was a mean score of: <2, between 2–2.9, and high distress: ≥ 3 respectively [5,6]. The DDS-17 was translated from English to Arabic, both forward and backward translations were carried out. Its reliability was tested using Cronbach's Alpha and was excellent (Cronbach's Alpha = 0.91). In this study, patients were considered to have no clinically relevant DRD if their scores were less than 2.9, if they scored 3 or more, they were considered as having clinically significant distress level.
- 4 Self-reported adherence to treatment (SRAT) was measured using Morisky Medication Adherence Scale (MMS-8); this is a validated tool for evaluation of SRAT [28]. The tool consists of eight questions. The response options are “yes” or “no” for items 1 through 7 and item 8 has a five-point Likert response scale. Each “no” response is rated as 1 and each “yes” response is rated as 0 except for item 5, in which each “yes” response is rated as 1 and each “no” response is rated as 0. For Item 8, the code (0–4)

has to be standardized by dividing the result by 4 to calculate a summated score. Total scores on the MMAS-8 range from 0 to 8, with scores of 8 reflecting high adherence, 7 or 6 reflecting medium adherence, and <6 reflecting low adherence. Permission to use the scale was granted by Donald Morisky, the copyright holder of the instrument. Also, after translation and piloting, its reliability was tested by Cronbach's Alpha which was very good and was excellent (Cronbach's Alpha = 0.69).

5 Lastly, we reviewed laboratory work-up of each patient to assess the most recent HbA1c (maximally within the last 3 months before the survey) of each patient. Overall, 77 of the patients did not have a recent HbA1c.

2.6. Statistical analysis

Descriptive statistics in terms of means, standard deviations were used to describe the studied sample. Analysis of quantitative data by *t*-test and association of categorical variables by chi-square test were conducted. Pearson's correlation coefficient was used to test correlations between quantitative variables.

The normality of DRD and HbA1c scores was assessed using a visual inspection of graphs. These were found to be normally distributed. Group means were evaluated using the analysis of variance (*t*-test where appropriate). Multivariable linear regression analysis was performed with DRD scores as the outcome variable and HbA1c and SRAT as predictor variables. Variables with clinical importance (age and sex) and those with univariate $p < 0.3$ were included as the explanatory variables using the Enter method. Multicollinearity was assessed using the variance inflation factor. Statistical mediation effect was assessed using structural equation modelling using the PROCESS macro for SPSS [29]. The model was adopted considering HbA1c as an outcome, DRD as a predictor and SRAT as a mediator. We hypothesized that the effect of DRD upon HbA1c can be explained partially by the SRAT. The effect of DRD on HbA1c was measured by total effect (sum of direct and indirect effect of DRD on HbA1c), and the mediating effect was measured by the indirect effect of DRD on HbA1c via SRAT. Statistical significance of mediating effect was tested using percentile bootstrap Confidence Interval (C.I.) approach where 5000 samples were randomly generated from the data set to create the CI. *P*-value less than 0.05 was considered statistically significant.

3. Results

A total of 166 patients were invited to participate in the survey and 157 of them completed the survey, giving a response rate of (94.6%). Table 1 shows the characteristics of the studied sample. The participants have an average age of 44.4 ± 15.9 years with the majority 103 (65.6%) aged between 30 and 60 years. There was a predominance of females 103 (65.6%) and Saudi patients 141(89.8%). Only 10 (6.4%) of the patients were illiterate whilst more than 33% of them had university or higher education. The patients were asked their perception regarding their household income meeting their needs, about 70% of the participants believed that their income was enough or even more than enough because they have some savings.

Seventy-nine percent of the patients had type 2 DM, and the patients have had their DM illness for an average of 9.3 ± 7.8 years and receiving on average 1.9 ± 1.1 antidiabetic medications per day. The mean fasting blood sugar of the patients was 172 ± 83.5 mg/dl and their average HbA1c was 8.9 ± 2.3 . Only 15 (18.8%) of the participants were controlled as defined by having HbA1c less than 7% while 28.7% reported no diabetic complications.

Clinically significant DRD was reported by 60 (38.2%) of the participants. EB and RD were each reported by 64 (40.8%) of the

Table 1
Characteristics of the study sample.

Variables	Frequency (%)
Age (in years)	44.4 ± 15.9
Less than 30	35 (22.3)
30–60	103 (65.6)
More than 60	19 (12.1)
Gender	
Male	54 (34.4)
Female	103 (65.6)
Nationality	
Saudi	141 (89.8)
Non-Saudi	16 (10.2)
Marital status	
Married	99 (63.1)
Not married	58 (36.4)
Educational level	
Illiterate	10 (6.4)
Secondary/diploma	95 (60.5)
University or higher	52 (33.1)
Economic level	
Currently in debt	23 (14.6)
Not enough	25 (15.9)
Enough	63 (40.1)
Enough and save	46 (29.3)
Type of diabetes	
Type 1	33 (21.0)
Type 2	124 (79.0)
Level of glycaemic control (HbA1c level) ^a	
4–6.49	13 (16.3)
6.5–8.49	22 (14.0)
8.5–10.49	23 (14.6)
10.5–12.49	18 (11.5)
12.5 or more	4 (2.5)
Controlled DM (HbA1c <7)	15 (18.8)
Uncontrolled DM (HbA1c ≥7)	65 (81.3)
Diabetes complications	
No complications	45 (28.7)
Cardiac	21 (13.4)
Ophthalmological	55 (35.0)
Renal	12 (7.6)
Diabetic foot	26 (16.6)
Number of DM complications	
None	45 (28.7)
One or two complications	93 (59.2)
Three or more complications	19 (12.1)
Diabetes related distress	
DRD	60 (38.2)
EB	64 (40.8)
RD	64 (40.8)
ID	51 (32.5)
PD	73 (46.5)
Self-Reported Adherence to treatment (SRAT)	
Bad	86 (54.8)
Good	57 (36.3)
Very good	14 (8.9)

DRD: Diabetes related distress, EB: Emotional Burden, PR: physician related distress, RR: Regimen related distress, ID: Interpersonal distress.

^a Missing 77 readings.

patients, PD by 73 (46.5%), and ID among 51 (32.5%). About 45% of the patients were defined as having satisfactory SRAT.

Table 2 shows relation between DRD and its domain with various characteristics of the participants. Younger patients steadily show higher level of stress compared to older participants and this trend reached statistical significance in RR ($p < 0.05$). Patients with type 1 DM showed higher levels of stress in all DRD domains and they significantly suffered from RR more than those with type 2 DM (60.6 versus 35.5%, $p < 0.05$). DRD and its domains were noticed

Table 2
Relation between diabetes related distress and patients' characteristics.

Patient characteristics	ED n(%)	PR n(%)	RR n(%)	ID n(%)	DRD n(%)
Age					
Less than 30	18(51.4)	18(51.4)	21(60.0)	14(40.0)	17(48.6)
30–60	40(38.8)	47(45.6)	40(38.8)	35(34.0)	39(37.9)
More than 60	6(31.6)	8 (42.1)	3(15.8)*	2(10.5)	4(21.1)
Gender					
Males	20(37.0)	23(42.6)	19(35.2)	18(33.3)	19(35.2)
Females	44(42.7)	50(48.5)	45(43.7)	33(32.0)	41(39.8)
Nationality					
Saudi	57(40.4)	66(46.8)	59(41.8)	46(32.6)	55(39.0)
Non-Saudi	7(43.8)	7(43.8)	5(31.3)	5(31.3)	5(31.3)
Social level					
Dept	9(39.1)	14(60.9)	11(47.8)	10(43.5)	11(47.8)
Not enough	11(44.0)	13(52.0)	7(28.0)	4(16.0)	8(32.0)
Enough	28(44.4)	28(44.4)	28(44.4)	22(34.9)	24(38.1)
Enough and save	16(34.8)	18(39.1)	18(39.1)	15(32.6)	17(37.0)
Education					
Illiterate	4(40.0)	5(50.0)	3(30.0)	2(20.0)	3(30.0)
School	39(41.1)	48(50.5)	32(44.2)	31(32.6)	40(42.1)
University/higher	21(40.4)	20(38.5)	8(40.0)	18(34.6)	17(32.7)
Marital status					
Married	38(38.4)	45(45.5)	35(35.4)	33(33.3)	34(34.3)
Single	17(45.9)	18(48.6)	20(54.1)	13(35.1)	16(43.2)
Divorced/widow	9(42.9)	10(47.6)	9(42.9)	5(23.8)	10(47.6)
Type of Diabetes					
Type 1	15(45.5)	17(51.5)	20(60.6)	12(36.4)	15(45.5)
Type 2	49(39.5)	56(45.2)	44(35.5)*	39(31.5)	45(36.3)
Complications of DM					
No complication	12(26.7)	16(35.6)	15(33.3)	12(26.7)	11(24.4)
One or two complications	41(44.1)	44(47.3)	39(41.9)	34(36.6)	39(41.0)
Three or more complications	11(57.9)*	13(68.4)*	10(52.6)	5(26.3)	10(52.6)*
Controlled DM					
Controlled (<7)	4(26.7)	4(26.7)	5(33.3)	3(20.0)	4(26.7)
Uncontrolled 7+	34(52.3)	32(49.2)	34(52.3)	23(35.4)	32(49.2)
Adherence to treatment					
Poor	41(47.7)	42(48.8)	47(54.7)	36(41.9)	39(45.30)
Good	19(33.3)	26(45.6)	16(28.1)	15(26.3)	18(31.6)
Very good	4(28.6)	5(35.6)	1(7.1)*	0(0.0)*	3(21.4)
EB	–	53(82.8)*	51(79.7)*	38(59.4)*	55(85.9)*
PR	53(72.6)*	–	52(71.2)*	40(54.8)*	55(75.3)*
RR	51(79.7)*	52(81.3)*	–	42(65.6)*	53(82.8)*
ID	38(74.5)*	40(78.4)*	42(82.4)*	–	41(80.4)*

p – value based on Chi-square test. EB: Emotional Burden, PR: Physician Related Distress, RR: Regimen Related Distress, ID: Interpersonal Distress, DRD: Diabetes Related Distress, HbA1c: glycosylated haemoglobin.

* = p < 0.05.

more seriously among patients who suffer from more complications especially in ED, PR and DRD. Additionally, poor level of SRAT was significantly associated with higher level of stress particularly RR and ID. DRD and all its domains were insignificantly associated with gender, economic level, marital status, education, type or duration of diabetes ($p > 0.05$). Moreover, patients who suffer from one sub-type of distress are significantly more likely to endure other distresses.

Table 3 displays the relation between SRAT and different domains of DRD. Patients suffering from any DRD significantly reported less adherence to treatment scores. Meanwhile, indirect correlation between SRAT and all domains of DRD was prominent as reported by the negative Pearson's correlation coefficients and the significant P-value. The negative correlation was also confirmed between the HbA1c level and the SRAT; the better adherence score, the lower level of HbA1c ($r = -0.32$, $p = 0.003$).

In univariate analysis (Table 4), patients who had poor adherence rate had a significantly higher DRD score (3.02), compared to those with good (2.44) and very good (2.04) adherence rates ($p = 0.001$). Also, higher levels of HbA1c level was significantly related to the higher DRD scores ($p = 0.04$). Patients who are below 30 years old had higher DRD scores compared to older individuals, but the difference was not statistically significant ($p = 0.09$). Similarly, patients who had one or more DM complications had higher

Table 3
Relation between Self-Reported Adherence to Treatment and Diabetes Related Distress.

	Adherence to treatment mean \pm SD	p-value	Pearson's Correlation coefficient	p-value
EB		0.002	–0.32	<0.001
Yes	4.4 \pm 2.2			
No	5.1 \pm 1.8			
PR		0.123	–0.30	<0.001
Yes	4.8 \pm 2.2			
No	4.5 \pm 1.9			
RR		<0.001	–0.41	<0.001
Yes	4.0 \pm 2.1			
No	5.8 \pm 1.7			
ID		<0.001	–0.33	<0.001
Yes	4.2 \pm 2.0			
No	5.5 \pm 1.9			
DRD		0.001	–0.38	<0.001
Yes	4.3 \pm 2.3			
No	5.5 \pm 1.8			
HbA1c		0.032	–0.32	0.003
Controlled (<7)	5.9 \pm 1.6			
Uncontrolled 7+	4.5 \pm 2.2			

Emotional Burden, PR: Physician Related Distress, RR: Regimen Related Distress, ID: Interpersonal Distress, DRD: Diabetes Related Distress, HbA1c: glycosylated haemoglobin.

Table 4
Univariate analysis of factors associated with higher DRD score.

Variables	Mean DRD score	F (t) statistics	p-value
Age (in years)		2.43	0.09
Less than 30	3.03 (±1.13)		
30–60	2.70 (±1.25)		
More than 60	2.30 (±0.78)		
Sex		0.19	0.67
Male	2.67 (±1.21)		
Females	2.76 (±1.19)		
Nationality		0.24	0.63
Non-Saudi	2.74 (±1.21)		
Saudi	2.59 (±1.10)		
Marital status		0.38	0.54
Married	2.68 (±1.23)		
Not married	2.80 (±1.13)		
Educational level		0.30	0.74
Illiterate	2.47 (±1.18)		
Secondary/diploma	2.77 (±1.22)		
University or higher	2.70 (±1.15)		
Economic level		0.53	0.66
Currently in debt	2.95 (±1.34)		
Not enough	2.59 (±1.22)		
Enough	2.78 (±1.18)		
Enough and save	2.62 (±1.13)		
Type of diabetes		1.19	0.28
Type 1	2.93 (±1.24)		
Type 2	2.67 (±1.18)		
HbA1c level		0.16	0.69
Controlled DM	2.74 (±1.24)		
Poorly controlled DM	2.86 (±1.33)		
HbA1c Level (continuous)		2.38	0.04
Number of DM complications		2.57	0.08
None	2.41 (±1.14)		
One or two complications	2.81 (±1.22)		
Three or more complications	3.05 (±1.12)		
Adherence to treatment (SRAT)		7.08	0.001
Bad	3.02 (±1.24)		
Good	2.44 (±1.07)		
Very good	2.04 (±0.86)		

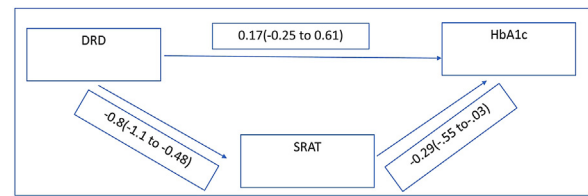
p-value based on Analysis of variance (ANOVA).

DRD scores compared to those without any complications, but the difference was also not statistically significant ($p = 0.08$). In multivariable linear regression analysis (Table 5), having one or more complications significantly predicted higher DRD scores ($p = 0.01$), while very good adherence rates were inversely related to higher DRD scores ($p = 0.002$).

Fig. 1 shows the mediating effect of SRAT on the relation between DRD and HbA1c. The total effect of DRD on HbA1c was 0.41 (C.I. is 0.02 to 0.80) meaning that increasing the DRD by one point can increase the HbA1c on average by 0.41%. Additionally, there was a significant indirect effect of DRD on the HbA1c level through SRAT, (0.24, C.I. = 0.04–0.47) indicating that increasing the DRD by one point will increase the HbA1c by 0.24% through the mediating effect of SRAT (Table 6).

Table 5
Multivariate linear regression analysis of factors associated with higher DRD score.

Variables	β	95% C.I.	F test	p-value	R^2
Constant	2.26	1.13–3.40	3.94	<0.001	0.13
Older age category	-0.30	-0.76 to 0.17	-1.27	0.21	
Female sex	0.03	-0.36 to 0.41	0.15	0.89	
Type 2 DM	0.15	-0.47 to 0.77	0.48	0.63	
One or more complications	0.38	0.08–0.67	2.53	0.01	
Very good adherence level	-0.46	-0.75 to -0.17	-3.09	0.002	



DRD: Diabetes related distress, SRAT: Self-reported adherence to treatment, HbA1c: glycosylated haemoglobin

Fig. 1. Mediating effect of Self-reported Adherence to treatment (SRAT) in the relation between Diabetes Related Distress (DRD) and HbA1c.

Table 6
Effect of diabetes related distress on HbA1c level.

Effect	β	95% C.I.	p-value	R^2
Total	0.41	0.02–0.80	0.04	0.05
Indirect (mediating through SRAT)	0.24	0.04–0.47	0.04	
a (DRD and SRAT)	-0.81	-1.14 to -0.48	<0.01	0.23
b (SRAT and HbA1c)	-0.29	-0.54 to -0.03	0.03	0.11

4. Discussion

The current study revealed that a considerable proportion of a sample of Saudi patients with DM are suffering from clinically significant DRD and poor SRAT. Both parameters were positively associated with advancement of age. No other sociodemographic factors or diabetes-related attributes were significantly associated with DRD or SRAT except the number of diabetes complications. DRD and SRAT negatively correlated with HbA1c; increasing the DRD by one point may directly increase the HbA1c on average by 0.17 and will indirectly raise the HbA1c by 0.24 through the mediating effect of SRAT.

The prevalence of clinically significant DRD among our patients was 38.2% which was higher than the findings of a similar local study that showed 25% prevalence of moderate to high DRD [25]. Other international studies conducted from USA [30,31], and Malaysia showed higher DRD prevalence, 56%, 51% and 49.2%, respectively [32]. The difference in the reported figures can be explained by the differences in demography of the studied samples, type of DM and frequency of associated complications.

In our study, younger age was significantly associated with DRD. This is comparable to other studies that demonstrated a significant correlation between DRD with age [25,32]. Older age patients showed less level of distress that can be predicted as they already suffer from other comorbidities, nevertheless, younger patients are not used to being sick or experienced in the management of chronic diseases compared to their peers. Living with DM requires the patient to be committed to many daily regimens that are not expected to be easily tolerated by younger adults as reflected by the prominent differences in RR domain.

Patients with diabetic complications were found to have more clinically significant DRD, mainly ED and PR domains. These findings are expected due to the high burden of diabetic complication with possible frequent hospital visits and admissions. The signifi-

cant association between DRD and diabetic complications was also reported in other researches [25].

Gender, economic level, marital status, level of education and duration of DM were all found to be insignificant factors in relation to DRD. The relation between DRD and these factors revealed inconsistent findings in previous studies [25,26,30,32]. Overall, in studies among rural African American women and Asian patients, there was an insignificant association between their demographic characteristics and DRD [30,32]. In contrast, there are other studies who found a significant relationship between the DDS score and low income, unemployment, gender with higher rates among females [25].

DRD prevalence was studied mainly among patients with Type 2 DM as it was believed that distresses faced by both groups are substantially different. In this study, we have assessed DRD prevalence in type 1 DM and type 2 DM patients. We found that DRD prevalence was 36.3% among patients with type 2 DM and 45.5% in type 1 DM. It comes as no surprise, given that living with type 1 DM requires adherence to daily doses of insulin adjusted all the time according to glucose level along with frequent glucose monitoring furthermore the younger age of type 1 DM patients can add to their distress.

Relation between DRD and glycemic control have been reported inconsistently by various studies [31–34]. In one study [32], conducted among 700 Asian patients with type 2 DM, the prevalence of DRD was 49.2% and no significant relation was detected between DRD and HbA1c. Gonzalez et al., in 2016 showed that 46.2% of type 2 DM patients had clinically significant diabetes distress and defined negative correlation between emotional distress and HbA1c [33]. Similarly, Fisher et al., concluded that DRD significantly affects HbA1c [31]. In a prospective analysis of the relation between DRD and HbA1c, DRD was found to be able to predict future HbA1c and drug adherence [34].

In the current study, poor SRAT was reported by nearly 55% of the participants while 36.4% of them had good SRAT and only 8.9% showed very good level of SRAT. These findings are higher than other national reports; good adherence was reported by Saudi researchers to range from 23% to 35% [35]. These figures are sub-optimal when compared to the target of good adherence of DM patients to be around 80% in order to assure an adequate level of glycemic control [36]. The differences in the reported level of adherence to treatment is variable probably because different tools were used to measure adherence to treatment.

Participants reporting higher level of DRD had the lowest SRAT and, correspondingly, demonstrated higher HbA1c values. These results agree with those revealed by many researchers who also demonstrated a significant relationship between DRD and adherence to medications [30,31,37]. Another recent study from KSA identified nonadherence to treatment as an independent risk factor for uncontrolled DM [38].

Reaching a satisfactory level of HbA1c is assumed to be achieved by proper adherence to treatment and many studies demonstrated the relation between adherence to diabetes treatment and good glycemic control. However, many psychological factors are considered to affect the adherence to treatment such as depressive disorders, DRD, self-efficacy, emotional distress, and many other concerns [39]. The present study adds to the current body of evidence for this strong relation between adherence to treatment, glycemic control and various DRD domains.

This study clarified the interaction between DRD, SRAT and glycemic control where SRAT was a mediating factor explaining the negative effect of DRD on HbA1c. Patients who were overwhelmed by their distress may simply stop medications and their glycemic control may worsen [6]. In addition, patients may intentionally stop taking their medication if they have concerns about the efficacy or side effects of the drugs while they may comply with their medica-

tion if they receive proper and clear encouraging instructions from their physicians [40].

Although logically and clinically accepted, uncontrolled HbA1c is mostly treated by intensifying medications, the situation may be completely different among distressed patients. The inhibitory effect of DRD on the medication adherence can mask the expected beneficial effect of more medications and tighter control of diabetes. These findings signify the importance of managing DRD to consequently improve the adherence to treatment that can result in better control of diabetes. Many studies tested various interventions to alleviate the DRD and their findings are encouraging as DRD appeared very responsive to various interventions among different patients with DM [4,41–43]. Furthermore, beyond lowering the burden of DRD, these interventions were found to be effective even in improving long term complications of DM [4,41–43].

Although there were several strengths in the present study, it has some limitations. One of the limitations is the cross-sectional nature of the study design; therefore, the potential for causality in the relationships between DRD, SRAT and HbA1c cannot be determined. Second, purposive sampling was used to recruit the study participants from a single tertiary health facility. Therefore, the findings of the study may not be generalizable to the whole country. Third, adherence rates were assessed using self report by the patients. This may be prone to self-report bias. Another limitation was missing 77 readings of HbA1c which might have underestimated the effect of DRD on glycemic control; however, the minimum sample size required to test the correlation between DRD and HbA1c was exceeded in the current study.

5. Conclusions

DRD and low SRAT are commonly reported among patients with DM and both are indirectly correlated. SRAT was found to be mediating the negative DRD's effect on glycemic control in the Saudi population, hence, these findings highlight the clinical role of DRD and SRAT and help provide better understanding of the process by which distress can affect the outcomes of DM management. The implications of this study for policy suggests that addressing DRD in patients with DM may improve management outcomes through improvement in their SRAT. Therefore, mechanisms for the identification and diagnosis of DRD among DM patients in the study population is strongly recommended.

Ethics approval and consent to participate

A written informed consent was used in this study. The patients were invited to the study & a clear description of the study objectives was given. Also, participation was completely voluntary with participant full choice to withdraw at any time of the research. The study was approved from the Institutional Review Board at Princess Nourah Bint Abdulrahman University (Approval letter number 16-0038).

Consent for publication

Not applicable.

Availability of data and material

Data are available on reasonable request from the primary investigator (AF) after approval from the Institutional Review Board at Princess Nourah Bint Abdulrahman University.

Competing interests

All authors declared no conflicts of interests

Funding

This study is funded by Princess Nourah bint Abdulrahman University Researchers Supporting Project (number PNURSP2022R21) Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia.

CRedit authorship contribution statement

Amel Fayed: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing - review & editing. **Faten AlRadini:** Data curation, Formal analysis, Methodology, Validation, Writing - original draft. **Ruba Mohammed Alzuhairi:** Investigation, Methodology, Writing - review & editing. **Afrash Eid Aljuhani:** Investigation, Methodology, Writing - review & editing. **Hana Rashid Alrashid:** Investigation, Methodology, Writing - review & editing. **Manal Mohsen Alwazae:** Investigation, Methodology, Writing - review & editing. **Nuha Ramadan Alghamdi:** Investigation, Methodology, Writing - review & editing.

Acknowledgments

We would like to thank all participants of this study for participation in our study, and we extend our gratitude to Dr. Ghadeer Alsheikh for supporting the research team.

References

- [1] M.E. Hilliard, J.P. Yi-Frazier, D. Hessler, A.M. Butler, B.J. Anderson, S. Jaser, Stress and A1c among people with diabetes across the lifespan, *Curr. Diab. Rep.* 16 (2016) 67, <http://dx.doi.org/10.1007/s11892-016-0761-3>.
- [2] International Diabetes Federation. IDF Diabetes Atlas; 9th Edition, IDF; https://www.diabetesatlas.org/upload/resources/material/20200302.133351_IDFATLAS9e-final-web.pdf [Accessed; 2/11/2021].
- [3] A. Alwin Robert, M.A. Al Dawish, Microvascular complications among patients with diabetes: an emerging health problem in Saudi Arabia, *Diab. Vasc. Dis. Res.* 16 (2019) 227–235, <http://dx.doi.org/10.1177/1479164118820714>.
- [4] B. Karlsen, B. Oftedal, E. Bru, The relationship between clinical indicators, coping styles, perceived support and diabetes-related distress among adults with type 2 diabetes, *J. Adv. Nurs.* 68 (2012) 391–401, <http://dx.doi.org/10.1111/j.1365-2648.2011.05751.x>.
- [5] W.H. Polonsky, L. Fisher, J. Earles, et al., Assessing psychosocial distress in diabetes: development of the diabetes distress scale, *Diabetes Care* 28 (2005) 626–631, <http://dx.doi.org/10.2337/diacare.28.3.626>.
- [6] L. Fisher, R.E. Glasgow, J.T. Mullan, M.M. Skaff, W.H. Polonsky, Development of a brief diabetes distress screening instrument, *Ann. Fam. Med.* 6 (2008) 246–252, <http://dx.doi.org/10.1370/afm.842>.
- [7] World Health Organization, *Adherence to Long-Term Therapies: Evidence from Action*, World Health Organization, Geneva, 2003, Available from: <http://whqlibdoc.who.int/publications/2003/9241545992.pdf> [Accessed 19 August 2021].
- [8] Standards of medical care in diabetes-2017: summary of revisions, *Diabetes Care* 40 (2017) S4–S5, <http://dx.doi.org/10.2337/dc17-S003>.
- [9] S. Tsujii, Y. Hayashino, H. Ishii, Diabetes Distress and Care Registry at Tenri Study Group, Diabetes distress, but not depressive symptoms, is associated with glycaemic control among Japanese patients with type 2 diabetes: Diabetes Distress and Care Registry at Tenri (DDCRT 1), *Diabet. Med.* 29 (2012) 1451–1455, <http://dx.doi.org/10.1111/j.1464-5491.2012.03647.x>.
- [10] J.E. Aikens, Prospective associations between emotional distress and poor outcomes in type 2 diabetes, *Diabetes Care* 35 (2012) 2472–2478, <http://dx.doi.org/10.2337/dc12-0181>.
- [11] I.A. Kretchy, A. Koduah, T. Ohene-Agyei, V. Boima, B. Appiah, The association between diabetes-related distress and medication adherence in adult patients with type 2 diabetes mellitus: a cross-sectional study, *J. Diabetes Res.* 2020 (2020), 4760624, <http://dx.doi.org/10.1155/2020/4760624>.
- [12] Y. Hu, L. Li, J. Zhang, Diabetes distress in young adults with type 2 diabetes: a cross-sectional survey in China, *J. Diabetes Res.* 2020 (2020), 4814378, <http://dx.doi.org/10.1155/2020/4814378>.
- [13] K.A. Wolde, G.M. Wondim, Diabetic distress among diabetic patients in the referral hospital of Amhara Regional State, Ethiopia, *Int. Q. Community Health Educ.* 40 (2) (2020) 105–114, <http://dx.doi.org/10.1177/0272684x19857580>.
- [14] D. Umpierre, P.A. Ribeiro, C.K. Kramer, et al., Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis, *JAMA* 305 (2011) 1790–1799, <http://dx.doi.org/10.1001/jama.2011.576>.
- [15] M.K. Rhee, W. Slocum, D.C. Ziemer, et al., Patient adherence improves glycemic control, *Diabetes Educ.* 31 (2005) 240–250, <http://dx.doi.org/10.1177/014571705274927>.
- [16] M.F. Peyrot, Theory in behavioral diabetes research, *Diabetes Care* 24 (2001) 1703–1705, <http://dx.doi.org/10.2337/diacare.24.10.1703>.
- [17] M. Peyrot, J.F. McMurry Jr., D.F. Kruger, A biopsychosocial model of glycemic control in diabetes: stress, coping and regimen adherence, *J. Health Soc. Behav.* 40 (1999) 141–158.
- [18] C.L. Hanson, S.W. Henggeler, G. Burghen, Model of associations between psychosocial variables and health-outcome measures of adolescents with IDDM, *Diabetes Care* 10 (1987) 752–758, <http://dx.doi.org/10.2337/diacare.10.6.752>.
- [19] C. Lloyd, J. Smith, K. Weinger, Stress and diabetes: a review of the links, *Diabetes Spectr.* 18 (2005) 121–127, <http://dx.doi.org/10.2337/diaspect.18.2.121>.
- [20] S.H. Golden, M. Lazo, M. Carnethon, et al., Examining a bidirectional association between depressive symptoms and diabetes, *JAMA* 299 (2008) 2751–2759, <http://dx.doi.org/10.1001/jama.299.23.2751>.
- [21] B. Mezuk, W.W. Eaton, S. Albrecht, S.H. Golden, Depression and type 2 diabetes over the lifespan: a meta-analysis, *Diabetes Care* 31 (2008) 2383–2390, <http://dx.doi.org/10.2337/dc08-0985>.
- [22] D. Hessler, L. Fisher, R.E. Glasgow, L.A. Strycker, L.M. Dickinson, P.A. Arean, U. Masharani, Reductions in regimen distress are associated with improved management and glycemic control over time, *Diabetes Care* 37 (3) (2014) 617–624, <http://dx.doi.org/10.2337/dc13-0762>.
- [23] M.A. Al Dawish, A.A. Robert, R. Brahm, et al., Diabetes mellitus in Saudi Arabia: a review of the recent literature, *Curr. Diabetes Rev.* 12 (2016) 359–368, <http://dx.doi.org/10.2174/1573399811666150724095130>.
- [24] A. Alzahrani, A. Alghamdi, T. Alqarni, R. Alshareef, A. Alzahrani, Prevalence and predictors of depression, anxiety, and stress symptoms among patients with type II diabetes attending primary healthcare centers in the western region of Saudi Arabia: a cross-sectional study, *Int. J. Ment. Health Syst.* 13 (2019) 48, <http://dx.doi.org/10.1186/s13033-019-0307-6>.
- [25] M.O. Aljuaid, A.M. Almutairi, M.A. Assiri, D.M. Almalki, K. Alswat, Diabetes-related distress assessment among Type 2 diabetes patients, *J. Diabetes Res.* 2018 (2018), 7328128, <http://dx.doi.org/10.1155/2018/7328128>.
- [26] A.D. Alkhatami, M.A. Alamin, A.M. Alqahtani, W.Y. Alsaed, M.A. Alkhatami, A.H. Al-Dhafeeri, Depression and anxiety among hypertensive and diabetic primary health care patients. Could patients' perception of their diseases control be used as a screening tool? *Saudi Med. J.* 38 (2017) 621–628, <http://dx.doi.org/10.15537/smj.2017.6.17941>.
- [27] J.L. Grenard, B.A. Munjas, J.L. Adams, M. Suttrop, M. Maglione, E.A. McGlynn, W.F. Gellad, Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis, *J. Gen. Intern. Med.* 26 (10) (2011) 1175–1182, <http://dx.doi.org/10.1007/s11606-011-1704-y>.
- [28] D.E. Morisky, A. Ang, M. Krousel-Wood, H.J. Ward, Predictive validity of a medication adherence measure in an outpatient setting, *J. Clin. Hypertens.* 10 (2008) 348–354, <http://dx.doi.org/10.1111/j.1751-7176.2008.07572.x>.
- [29] A.F. Hayes, *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*, Guilford Press, New York, NY, US, 2013.
- [30] D.M. Cummings, L. Lutes, K. Littlewood, et al., Regimen-related distress, medication adherence, and glycemic control in rural African American women with type 2 diabetes mellitus, *Ann. Pharmacother.* 48 (2014) 970–977, <http://dx.doi.org/10.1177/1060028014536532>.
- [31] L. Fisher, R.E. Glasgow, L.A. Strycker, The relationship between diabetes distress and clinical depression with glycemic control among patients with type 2 diabetes, *Diabetes Care* 33 (2010) 1034–1036, <http://dx.doi.org/10.2337/dc09-2175>.
- [32] B.-H. Chew, R. Vos, S. Mohd-Sidik, G.E. Rutten, Diabetes-related distress, depression and distress-depression among adults with type 2 diabetes mellitus in Malaysia, *PLoS One* 11 (2016), e0152095, <http://dx.doi.org/10.1371/journal.pone.0152095>.
- [33] J.S. Gonzalez, N.S. Kane, D.H. Binko, A. Shapira, C.J. Hoogendoorn, Tangled up in blue: unraveling the links between emotional distress and treatment adherence in type 2 diabetes, *Diabetes Care* 39 (2016) 2182–2189, <http://dx.doi.org/10.2337/dc16-1657>.
- [34] J.E. Aikens, Prospective associations between emotional distress and poor outcomes in type 2 diabetes, *Diabetes Care* 35 (2012) 2472–2478, <http://dx.doi.org/10.2337/dc12-0181>.
- [35] A.M. Alqarni, T. Alrahbani, A.A. Qarni, H.M.A. Qarni, Adherence to diabetes medication among diabetic patients in the Bisha governorate of Saudi Arabia - a cross-sectional survey, *Patient Prefer. Adherence* 13 (2018) 63–71, <http://dx.doi.org/10.2174/PPA.S176355>.
- [36] M.S. Kirkman, M.T. Rowan-Martin, R. Levin, et al., Determinants of adherence to diabetes medications: findings from a large pharmacy claims database, *Diabetes Care* 38 (2015) 604–609, <http://dx.doi.org/10.2337/dc14-2098>.
- [37] L. Fisher, J.T. Mullan, P. Arean, R.E. Glasgow, D. Hessler, U. Masharani, Diabetes distress but not clinical depression or depressive symptoms is associated with glycemic control in both cross-sectional and longitudinal analyses, *Diabetes Care* 33 (2010) 23–28, <http://dx.doi.org/10.2337/dc09-1238>.
- [38] M.J. Alramadan, D.J. Magliano, T.H. Almgib, et al., Glycaemic control for people with type 2 diabetes in Saudi Arabia - an urgent need for a review of management plan, *BMC Endocr. Disord.* 18 (2018) 62, <http://dx.doi.org/10.1186/s12902-018-0292-9>.
- [39] S.Y. Chen, H.C. Hsu, R.H. Wang, Y.J. Lee, C.H. Hsieh, Glycemic control in insulin-treated patients with type 2 diabetes: empowerment perceptions and diabetes

- distress as important determinants, *Biol. Res. Nurs.* 21 (2019) 182–189, <http://dx.doi.org/10.1177/1099800418820170>.
- [40] O.O. Shiyanbola, C.M. Brown, E.C. Ward, "I did not want to take that medicine": African-Americans' reasons for diabetes medication nonadherence and perceived solutions for enhancing adherence, *Patient Prefer. Adherence* 12 (2018) 409–421, <http://dx.doi.org/10.2147/PPA.S152146>.
- [41] L. Fisher, D. Hessler, R.E. Glasgow, et al., REDEEM: a pragmatic trial to reduce diabetes distress, *Diabetes Care* 36 (2013) 2551–2558, <http://dx.doi.org/10.2337/dc12-2493>.
- [42] L. Fisher, D. Hessler, W. Polonsky, L. Strycker, V. Bowyer, U. Masharani, Toward effective interventions to reduce diabetes distress among adults with type 1 diabetes: enhancing emotion regulation and cognitive skills, *Patient Educ. Couns.* 102(8)(2019) 1499–1505, <http://dx.doi.org/10.1016/j.pec.2019.03.021>.
- [43] M. Shumway, L. Fisher, D. Hessler, V. Bowyer, W.H. Polonsky, U. Masharani, Economic costs of implementing group interventions to reduce diabetes distress in adults with type 1 diabetes mellitus in the T1-REDEEM trial, *J. Diabetes Complications* 33 (2019), 107416, <http://dx.doi.org/10.1016/j.jdiacomp.2019.107416>.