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Original Article

Obesity Mediates the Effect of Past and Current Mental Health on Diabetes Treatment Outcomes

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Abstract

Background: Anxiety and depression (A&D) are common among patients with diabetes (DM). We assessed the mediatory effect of obesity on the pathway between past and current mental health (as measured by A&D) on self-care DM treatment adherence and DM treatment failure.

Methods: We used data collected in two rounds (2009-12, 2014-2018) of a population-based cohort study in Kerman, Iran (KERCADRS). By a random cluster sampling approach, 5900 residents of Kerman aged 15 to 75 yr were recruited to the study to measure demographic characteristics, body measures (to calculate BMI), adherence to DM treatment, and symptoms for A&D (Beck questionnaires). Fasting blood also collected for biochemical tests and glycemic control (as an indicator for treatment failure). We used path analysis and Structural Equation Modeling (SEM) for analysis.

Results: We analyzed data for 264 patients with diabetes who attended in both study rounds. While only 5.7% reported not adherence to DM treatment, 67.9% had diabetes treatment failure. Past mental health had a significant positive association with HbA1c (standard beta coefficient for total effect =0.148, *P*=0.044), of which 42% was indirect effect through obesity. Current mental health had a positive association with current no adherence to diabetes treatment (standard beta coefficient for total effect=0.077, *P*=0.001).

Conclusion: Our study showed an important indirect path from A&D to diabetes treatment failure outcome which mediated by obesity. Screening for A&D symptoms and treating those as well as obesity among patients with diabetes may improve glycemic control.

Keywords: Obesity; Mental health; Diabetes mellitus; Treatment outcomes

Introduction

Diabetes Mellitus (DM) is now among the top ten causes of death in adults worldwide, with a prevalence estimated at 9.3% (i.e., 463 million people) in 2019, and in rise to 700 million (51% increase) by 2045 (1). In Iran, the DM prevalence ranged from 2.3% (2) to 14.1% (3). Diabetes

suboptimal glycemic control also reported among 60% of diabetic patients in Iran (4). Thus, the prevalence of complications like diabetic foot ulcer (3%), cardiovascular disease (33%), retinopathy (36%), neuropathy (38%) and nephropathy (43%) in Iranian patients with type 2 DM reported higher than the global rates (5).

Comorbidities are common among Iranians living with diabetes. Obesity was reported among 42.4% of men and 52.0% of women in Iran diagnosed with diabetes (6). Mental health disorders also reported to be frequent among general population (Anxiety: 25.4% moderate, 22.7% severe; Depression: 5.5% moderate, 0.4% severe) (7), and much higher among people with DM (Anxiety: 62%, Depression 59%) (8). Overweight and obesity also reported to be frequent among people with anxiety (42.3%) and people who had depressive symptoms (38.9%) (7). More importantly, 79% of people with DM who had depressive symptoms, and 75.5% of those with anxiety had suboptimal glycemic control (4). The mechanism of the effect of underlying mental health conditions on diabetic control outcome is not clear.

Anxiety and depression are common among people living with diabetes, but their direct and indirect effect on DM outcomes through obesity has not been studied yet. In this study, we used data from a cohort study to assess the mediatory effect of obesity on the pathway between past and current mental health (as measured by anxiety and depression) on self-care DM treatment adherence and also DM treatment failure (as measured by glycemic control level). Our null hypothesis was that "obesity does not mediate the pathway between past and current mental health on self-care DM treatment adherence and also on DM treatment failure".

Methods

We used data collected in two rounds of a population-based cohort study in Kerman, Iran, called Kerman Coronary Artery Disease Risk factor Study (KERCADRS). The first round recruited 5900 residents of Kerman City between 2009 and 2012 who aged 15 to 75 yr old (9). Twenty-four eligible individuals were invited to the study from families who resided in 250 randomly selected zip codes of Kerman. Study social workers assessed the eligibility, and briefly descried the study to eligible individuals about the aims, procedures, risks and benefits of participating in the study, and were asked to provide the informed consent, at each household during field visits and invited them to visit the study clinic. They were asked to fast about 12 h before their visit. The second round of the study was conducted between 2014 and 2018 using the same procedures and measures.

The study protocol and procedures were all reviewed and approved by Kerman Medical University Ethic committee (Ethic codes IR.KMU.REC.1388.139 & IR.KMU.REC.1392.405 for phase 1 and 2 respectively).

First, 10 ml blood was collected to measure fasting blood sugar (FBS), cholesterol, triglyceride and HbA1C. Second, participants had breakfast and visited by the study general physician for taking medical history for diseases and medications, and medical exam (including blood pressure). Third, demographics characteristics and other body measures like height and weight were collected by a trained interviewer. Finally, a trained interviewer conducted the interview and completed the Persian versions of the Beck questionnaires for depression and anxiety. We did not assess the reliability and validity of the depression and anxiety scales among our study participants because both scales were validated among Iranian population in the past as follows:

Depression: The Beck Depression Inventory (BDI) is a standard tool for screening the severity of depression. This questionnaire consists of 21 questions. The total score (min 0, max 63) is obtained by scoring each question in a Likert scale of 0 to 3. The total scores of (0-15), (16-30), (31-46) and (47-63) were considered as non-depressive, mild, moderate, and severe depression, respectively (7). BDI has been translated into Persian and standardized. The Persian BDI

showed to be a reliable tool (with Cronbach's alpha 0.87 and repeatability coefficient 0.74). Moreover, the concurrent validity of BDI was assessed and confirmed by comparison with Automatic Thoughts Questionnaire (10).

Anxiety: The Beck Anxiety Inventory (BAI) is a standard tool for screening the severity of anxiety. This questionnaire consists of 21 questions, each score between 0-3 (Likert scale). The total score ranges from 0 to 63. The severity of anxiety defined as four categories: 0-7: anxiety-free, 8-15: mild, 16-25 moderate, 26-63 severe (7). BAI has been translated into Persian and standardized. Kaviani et al., showed the reliability of the Persian BAI as excellent (Cronbach's alpha of 0.92 and reproducibility coefficient of 0.83). Moreover, Intraclass correlation of BAI questionnaire with clinical specialist evaluation showed high validity (correlation coefficient of 0.72) (11).

Obesity: We measured obesity by calculating body mass index (BMI) based on height and weight of participants. BMI scores (Kg/M^2) are categorized to underweight (below 18.5), normal (18.5 - 24.9), overweight (25.0 - 29.9), and obese (30.0 and above) (7). We grouped BMI into two groups: normal (bellow 25.0) and overweight/obese (25.0 and above).

Diabetes diagnosis and treatment outcomes: we identified diabetes mellitus (DM) in participants by looking at self-reported medical history for diagnosis of DM or taking pill or insulin for treatment. Among individuals with DM, we measured adherence to treatment by self-reported use of DM medications (pill or insulin) at the time of study. Treatment failure was assessed by HbA1c, which is a reliable indicator of average blood glucose level over the last 3 months - a higher score (HbA1c > 7%) is an indicator of uncontrolled DM or treatment failure (4).

Analysis

We reported the prevalence of not adherence to DM treatment, and DM treatment failure (HbA1c > 7%) overall and in subgroups defined by demographic characteristics, past (study round 1) and current (study round 2) obesity (i.e., normal vs. overweight/obese), and past and current mental health (i.e., anxiety and depression). The differences in the subgroup for these two outcomes were assessed by Chi Square test.

Both anxiety and depression status were measured two times in our study; the first measurement was in round 1, and the second measurement was in round 2. We called the measurements in round 1 as "past" mental health status, and measurement in round 2 as "present" mental health status. We used structural equation model (SEM) (12) for analysis the pathways between past and current mental health (i.e. anxiety and depression) to not adherence to DM treatment and DM treatment failure. We used path diagrams to build the SEM model and then estimate the beta coefficients for each path using the data. Both anxiety and depression scores were used as observed variables for an underling mental health condition (a latent variable not measured directly in our study).

We used comparative fit index (CFI = 1.0 treatment failure, CFI = 1.0 not adherence: 1 and above means good fit (12)) standardized root mean squared residual (SR = 0.05 treatment failure, SR = 0.04 not adherence: 0.08 and less means good fit (12)), and coefficient of determination (R^2 = 0.85 treatment failure, R^2= 0.86 not adherence: 0.9 and above means good fit (12)) to assess the goodness-of-fit for the two models.

Then, we used "estat teffects, standardized" command in Stata to estimate the direct, indirect and total effect of past and current mental health on study outcomes (treatment failure and not adherence to DM treatment) through past and current obesity. We analyzed data and made the SEM model and all post estimation in Stata v.15.1 (StataCorp LLC, Texas, USA).

Results

Out of 5900 individuals recruited in the first round of the study, 175 were under the age of 15 or older than 75, 148 had missing data on diabetes mellitus (DM), and 4879 had no history of DM or medication for DM, 379 were lost to fol-

low-up and were not visited in the second round of the study, 4 persons had only depression but not anxiety, 66 had missing data on treatment outcomes, and another 51 had missing data on adherence to DM medication. This led to having an analytical sample of 264 individuals for DM treatment adherence outcome, and 249 individuals for treatment failure outcome. Descriptive characteristics, anxiety and depression scores, BMI and HbA1c outcomes of study participants from each study round included in our analysis is presented in Table 1.

Table 1: Descriptive characteristics, exposures and outcomes of study participants in our study (analytical sample=249)

Variable	***Round 1 2009 and 2012***		***Round 2 2014 to 2018***	
	N	Mean ± SD [Min, Max]	N	Mean ± SD [Min, Max]
Age (yr)	249	56.1±7.9 [22, 70]	249	61.2±7.9 [27, 75]
Anxiety score	249	19.1±12.8 [0, 56]	249	10.2±8.7 [0, 45]
Depression score	249	15.9±8.9 [0, 45]	249	11.0±6.9 [0, 43]
Body Mass Index – BMI, Kg/M^2	248	28.2±5.2 [17.3, 54.9]	247	28.8±5.5 [17.1, 54.1]
HbA1c	202	8.5±1.8 [5.2, 13.5]	237	8.2±2.0 [4.7, 15]

Overall, 169 (67.9%) of participants had diabetes treatment failure (Table 2). The frequency of diabetes treatment failure was higher among people at younger age (100.0% to 77.8%), illiterate people (82.1%), those with anxiety in the first round (74.4%). About 69.4% of people with overweight/obesity in the first round, and 69.1% of those with overweight/obesity in the second round of study had diabetes treatment failure.

Only 15 (5.7%) of participants reported not adherence to diabetes treatment (Table 3). The frequency of people with no adherence to diabetes treatment ranged from 0% in people at younger age to 8.6% in those aged 65-74 yr. About 7.2% of people with overweight or obesity in the first round, and 5.9% of those with overweight or obesity in the second round of study reported no adherence to diabetes treatment.

According to the structural model analysis (Fig. 1), past mental health (anxiety and depression) had a significant positive correlation with HbA1c in the past (standard correlation coefficient for total effect =0.148, *P*=0.044). The structural model showed that 58% of this effect was through direct effect (standardized correlation coefficient=0.085) and 42% was indirectly through obesity (standardized correlation coefficient=0.063).

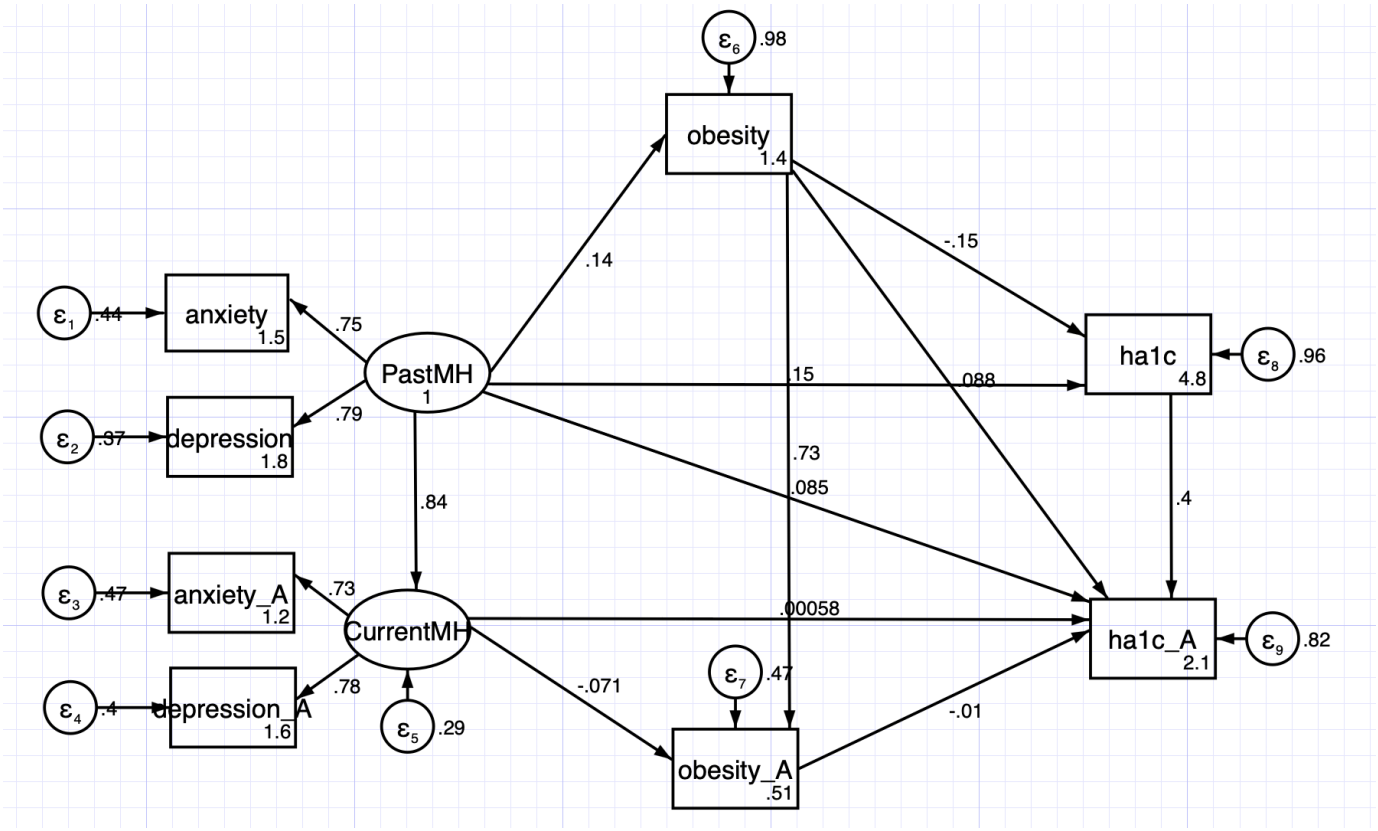
According to the structural model analysis (Fig. 2), past mental health (anxiety and depression) had a non-significant negative correlation with no adherence to diabetes treatment in the past (standard correlation coefficient for total effect= -0.036, *P*=0.582). The current mental health (anxiety and depression) had a positive correlation with current no adherence to diabetes treatment (standard correlation coefficient for total effect=0.077, *P*=0.001). For both past and current mental health effect on no adherence to diabetes treatment, the indirect effects were not statistically significant.

Table 2: Frequency of diabetes treatment failure in subgroups of participants

Subgroups	***Participants***	***n (%) with treatment failure***	***Statistics***
Total	249	169 (67.9)	
Age(yr)			
34-15	3	3 (100.0)	Pearson chi²(5)= 2.5134 *P*=0.774
44-35	2	14 (77.8)	
54-45	18	47 (65.3)	
64-55	72	83 (66.9)	
74-65	124	22 (68.8)	
Gender			
Men	93	62 (66.7)	Pearson chi²(1)= 0.0988 *P*= 0.753
Women	156	107 (68.6)	
Education			
Illiterate	39	32 (82.1)	Pearson chi²(3)= 7.4734 *P*=0.058
Primary to middle	111	71 (64.0)	
High school	57	42 (73.7)	
University	42	24 (57.1)	
Anxiety and depression (round 1)			
Normal	115	73 (63.5)	Pearson chi²(2)= 5.0139 *P* =0.082
Anxiety	117	87 (74.4)	
Anxiety and depression	17	9 (52.9)	
Anxiety and depression (round 2)			
Normal	189	127 (67.2)	Pearson chi²(2)= 0.4144 *P*=0.813
Anxiety	55	39 (70.9)	
Anxiety and depression	5	3 (60.0)	
Physical activity (round 1)			
Mild to sever	142	93 (65.5)	Pearson chi²(1)= 0.8573 *P*=0.354
Low	107	76 (71.0)	
Physical activity (round 2)			
Mild to sever	124	87 (70.2)	Pearson chi²(1)= 0.5939 *P*=0.441
Low	125	82 (65.6)	
Obesity (round 1)			
Normal	68	43 (63.2)	Pearson chi²(1)= 0.8708 *P*=0.351
Overweight or obese	180	125 (69.4)	
Obesity (round 2)			
Normal	56	35 (62.5)	Pearson chi²(1)=0.8640 *P*=0.353
Overweight or obese	191	132 (69.1)	

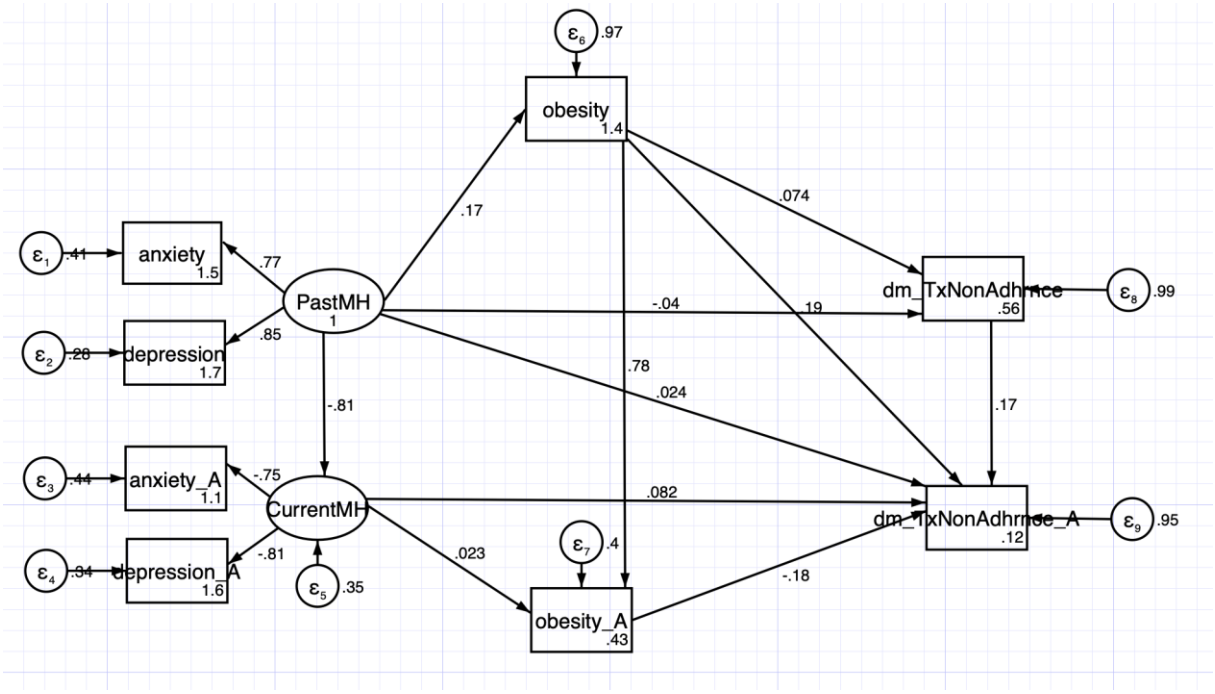
Table 3: Frequency of not adherence to diabetes treatment in subgroups of participants

Variable	*Partic-ipants*	*n (%) with no ad-herence to treat-ment*	*Statistics*
Total	264	15 (5.7)	
Age			
34-15	3	0 (0.0)	Pearson $chi^2(5)$
44-35	18	0 (0.0)	= 4.085
54-45	79	7 (8.9)	*P*= 0.537
64-55	129	5 (3.9)	
74-65	35	3 (8.6)	
Gender			
Men	100	7 (7.0)	Pearson $chi^2(1)$
Women	164	8 (4.9)	= 0.5219
			P=0.470
Education			
Illiterate	44	5 (11.4)	Pearson $chi^2(3)$
Primary to middle	117	6 (5.1)	= 3.673
			P=0.299
High school	60	3 (5.0)	
University	43	1 (2.3)	
Anxiety and depression (round 1)			
Normal	122	7 (5.7)	Pearson $chi^2(2)$
Anxiety	124	7 (5.6)	= 0.002
Anxiety and depression	18	1 (5.6)	*P*= 0.999
Anxiety and depression (round 2)			
Normal	201	12 (6.0)	Pearson $chi^2(2)$
Anxiety	58	3 (5.2)	= 0.3605
Anxiety and depression	5	0 (0.0)	*P*=0.835
Physical activity (round 1)			
Mild to sever	152	10 (6.6)	Pearson $chi^2(1)$
Low	112	5 (4.5)	= 0.5381
			P=0.463
Physical activity (round 2)			
Mild to sever	135	11 (8.1)	Pearson $chi^2(1)$
Low	129	4 (3.1)	= 3.1359
			P=0.077
Obesity (round 1)			
Normal	69	1 (1.4)	Pearson $chi^2(1)$
Overweight or obese	194	14 (7.2)	= 3.1477
			P=0.076
Obesity (round 2)			
Normal	59	3 (5.1)	Pearson $chi^2(1)$
Overweight or obese	203	12 (5.9)	= 0.0579
			P=0.810



Past Mental Health	*P*	Standardized Coefficient	% of effect
*direct effect:	0.218	0.085	58
*indirect effect:	0.054	0.063	42
*total effect	0.044	0.148	100
Current Mental Health			
*direct effect:	0.094	0.001	45
*indirect effect:	0.915	0.001	55
*total effect	0.847	0.001	100

Fig. 1: Structural equation model to assess the effect of mental health (anxiety and depression) through obesity on diabetes treatment outcome (HbA1c)



Past Mental Health	*P*	Standardized Coefficient	% of effect
*direct effect:	0.857	0.024	----
*indirect effect:	0.582	-0.060	----
*total effect	0.582	-0.036	100
Current Mental Health			
*direct effect:	0.520	0.082	----
*indirect effect:	0.694	-0.004	----
*total effect	0.001	0.077	100

Fig. 2: Structural equation model to assess the effect of mental health (anxiety and depression) through obesity on not adherence to diabetes treatment

Discussion

Our findings suggested that past mental health status associated with glycemic control and treatment failure outcome in people diagnosed with diabetes; more than 40% of this effect mediated by obesity. Moreover, current mental health status associated with current no adherence to diabetes treatment, which we found no evidence that this effect is being mediated by obesity. While majority of participants self-reported adherence to diabetes treatment, their glycemic control measures showed most failed the DM treatment favorite outcome.

To our knowledge, we are the first to show the mediatory effect of obesity on the association between past mental health and treatment failure in people living with diabetes. Obesity (as measured by waist circumference) have shown to mediate the effects of other factors such as age (SEM Beta Coefficient 0.156, *P*<0.001), family history of diabetes (SEM Beta C. 0.844, *P*=0.001), alcohol intake (SEM Beta C.1.43, *P*=0.001) and weekly fruit diet (SEM Beta C. −0.009, *P*=0.034) on blood sugar level (13). Anxiety and depression (30% or more) are the most common mental health disorders among patients with diabetes (14) 15). Obesity is also very common (42.4% to 52.0%) among patients with dia-

betes (6). Both mental health and obesity showed to have significant adverse effects on health-related quality of life in individuals with diabetes. Early detection of anxiety and depression (15), and screening for obesity and treating those with such co-morbidities can improve the treatment outcomes and quality of life in these patients (16). The mechanism and underlying pathophysiological link between mental health disorders and obesity studied is still under investigation. Higher risk of metabolic syndrome (including obesity) was reported in people diagnosed with schizophrenia (17). People with depression develop obesity at higher odds than people without depression (OR 1.18 to 3.76) (19) and suggested that eating disorder, gender, and other personality disorders moderate the path between depression and obesity (18). Another study showed a bi-directional path, obesity causes depression and vice versa (19). Obesity as a cause of depression was reported in several studies through mechanisms such as functional impairment and disability (20), poorer perceived health lead to poor self-care (21), body image dissatisfaction (22), repeated dieting (23). Depression as cause of obesity also reported in several studies through mechanisms such as increased stress reactivity with hormonal change (24), poor adherence to diet and stressed eating (25), and reduced perceived or actual social support (26). Most of these mechanisms also apply to people who have anxiety disorders.

Our study showed mental health disorder resulted from anxiety and depression associated with sub-optimal self-care of DM (i.e., not adherence to treatment). Association between depression and sub-optimal care in patients with diabetics has been reported in studies from Australia (Adj. OR 2.22, $P<0.001$) (27), China (Beta 5.34, $P=0.000$) (28), United States (Adj. OR 1.9, $P<0.001$) (29). In Netherlands and Australia, participants with DM who had a higher level of anxiety and depression were at higher risk for poor adherence to DM medications for lowering blood glucose (OR=2.49) (30). Similar results also reported from a study on about 100 patients with diabetes in Portugal (31). This highlights the importance of screening of anxiety and depression among diabetic patients.

Our study had three major limitations. About 54% of people with diabetes who participated in the first round of study did not participate in the second study. The effect of excluding these people from the analysis is unclear. Although we used standard questionnaires to measure depression, anxiety and adherence to DM treatment, they all were measured based on self-report and therefore may subject to measurement error. Due to the small number of people with depression alone, it was not possible to separate the effect of depression from anxiety due to the small sample size.

Conclusion

This study showed an important indirect path from anxiety and depression to diabetes treatment failure outcome which mediated by obesity. Screening for anxiety and depressive symptoms and treating them as well as obesity among patients with diabetes may improve glycemic control and so treatment outcomes.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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