

Original Research Article

Relationship between adherence to anti-diabetic medication and depression among patients with diabetes mellitus in three selected Chinese hospitals

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Abstract

Purpose: To determine the relationship between adherence to anti-diabetic medication and depression among patients with diabetes mellitus in three hospitals in Chinese.

Methods: This research utilized a quantitative and descriptive design, and included 200 diabetic patients who fulfilled the inclusion criteria for recruitment through a convenient sampling technique. The study applied Beck's depression inventory II scale for assessment of depression, and a questionnaire for adherence to anti-diabetic medication.

Results: A total of 64 (32 %) participants had diabetes for 6 to 10 years. There was a high level of adherence to anti-diabetic medication in 96 patients (48 %); 74 participants (37 %) had moderate adherence to anti-diabetic medication, while 30 patients (15 %) had low adherence. A majority of the patients (181, 90.5 %) had no depression. Six (6) patients (3 %) had mild mood disturbance, 2 patients (1 %) had borderline clinical depression, while 11 patients (5.5 %) experienced moderate depression. Adherence to anti-diabetic medication was not associated with depression ($p = 0.068$). However, depression was associated with age > 50 years ($p = 0.041$), female sex ($p = 0.043$), long duration of illness (> 5 -years) ($p = 0.048$), and presence of one or more comorbidities ($p = 0.049$).

Conclusion: There was no association between adherence to anti-diabetic medication and depression among diabetic patients.

Keywords: Adherence to anti-diabetic medication, Beck's depression inventory II, Depression, Diabetes mellitus

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INTRODUCTION

The prevalence of diabetes mellitus (DM), a disease which results in high degree of mortality, is on the increase all over the world [1]. It has been estimated that 300 million people will have

DM by the year 2025, and this figure may reach 439 million in the year 2030, with a prevalence of 7.7 % of the world population [2,3]. It has also been estimated that 3.96 million adult diabetic patients will die of the disease each year, and that diabetes will be responsible for 6.8 % of all

mortality cases. Depression is a common comorbidity in a chronic disease such as DM. The prevalence of depression is 1.5 – 2 times higher in patients with type 2 DM than in type 1 diabetics [1].

Diabetes-induced depression is highly prevalent, with significant adverse impact on life and health [1]. Indeed, the combination of depression and type 2 DM is a public health problem [1, 4, 5]. One very important factor for ensuring effective and efficient management of diabetes is adherence to treatment and compliance with medications [6]. There is a high possibility of depression in DM, and factors such as genetic predisposition and disease duration play important roles in its etiology [7]. The associations among depression, diabetes and non-adherence to anti-diabetes treatment have been reported by physicians for several hundred years [1, 4]. Earlier reports have indicated a frequency of major despair 1.6 – 2 times higher in diabetics than in non-diabetic patients in the general population [8]. Moreover, one out of every 10 diabetic patients is affected with high level depression [9]. The degrees of major lifetime depression in type 2 diabetics are between 24 and 29 % [4], and point prevalence is between 10 and 15 % [10].

Diabetes is a major public health concern, and when complicated with depression, it adversely affects the quality of life and increases mortality of patients [1]. Compared with individuals who have only diabetes, patients with comorbid depression have increased disease burden, greater symptoms severity, increased work disability, and poorer adherence to diet, exercise, and anti-diabetic, lipid-lowering and anti-hypertensive medications [11].

A descriptive study was conducted to determine the relationship between adherence to anti-diabetic medication and depression among DM patients. Moreover, the study was carried out to ascertain the association between various factors and depression, with exclusion of level of adherence to anti-diabetic medication as one of the independent variables.

METHODS

Ethical approval and consent to participate

Ethical clearance for the study was received from the ethics committee of Ningxia Hui Autonomous Region Ning'an Hospital Review Board (protocol no. NHACL121420). The purpose of the study was clearly explained to the participants. A written informed consent was obtained from each

of them prior to commencement of the study. For participants under 16 years of age, written informed consents were obtained from their parents or guardians. Confidentiality of the responses was assured and maintained throughout the study. The research was conducted in strict adherence to the laws of China and the 2008 Declarations of Helsinki [12].

Study population

This study was conducted at the Ningxia Hui autonomous region's Ning'an Hospital, Yinchuan, Ningxia, China; The Hainan Province Anning Hospital, Haikou, Hainan, China, and the Hainan People's Hospital, Haikou, Hainan, China. This research was designed in line with descriptive research workflow. Diabetic patients receiving treatment who fulfilled the inclusion criteria during the data collection period were recruited as participants in the study.

Sample size

Based on prevalence of depression among diabetic patients, the calculated sample size for the study was 200. It was hypothesized that at least 10 % of diabetic patients had mild or higher depression. Moreover, 80 % power ($\beta = 0.2$), 5 % type-I error ($\alpha = 0.05$), and 95 % of confidence limit were used for sample size calculation. A non-probability convenience sampling technique was employed for choosing the DM patients (diabetic patients were selected based on ease of recruitment).

Sampling criteria

Inclusion criteria

The included participants were outpatients who were diagnosed with DM and were receiving treatment at the institutes, DM patients willing to participate in the study, and DM patients able to read Chinese and English languages.

Exclusion criteria

Patients with acute illnesses and/or psychiatric problem, and patients with any pre-existing depressive disorders, were excluded.

Background variables

Data regarding socio-demographic variables (age, sex, education, occupation, diet, and exercises) and clinical variables (duration of illness, type of drugs used for treatment, duration of treatment, frequency of drugs, comorbidities (hypertension, bronchial asthma and renal

failure); family history of diabetes, and current complications) were collected from hospital records of patients.

Diabetic medication adherence questionnaire

The questionnaire contained 8 items based on the Institutional Protocol for Medical Adherence (not published). The total score was based on patients' responses to eight simple, yes-or-no questions. Yes was scored '1', while No was scored '0'. High scores indicate high degree of adherence. Scores less than 6 were classified as low adherence, while scores of 6 and 7 indicated medium adherence. A score of 8 was classified as high adherence.

Beck's depression inventory II

Beck's depression inventory (BDI) II contains 21 multiple-choice, self-report inventory questions. The minimum score obtainable is 0, while the maximum is 63. The cutoff for depression is 20 [13]. The scoring of BDI II is as follows: 1 – 10 = normal; 11 - 20 = mild mood disturbances; 20 - 25 = borderline clinical depression; 25 - 30 =

moderate depression; 31- 40 = severe depression, and > 40 = extreme depression [14].

Statistical analysis

Statistical analysis was done with SPSS v25.0 IBM Corporation, Armonk, New York, USA. Chi-square test of Independence was used to analyze data. Univariate and multivariate analyses were used to determine the association between background variables and depression. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Study population

A total of 215 DM patients who were being managed at the institutes declared their willingness to participate in the study. Ten (10) patients had acute illness, while 5 patients had psychiatric problems. These 15 DM patients were excluded from the study. A total of 200 patients with DM were eventually enrolled in the study (Figure 1).

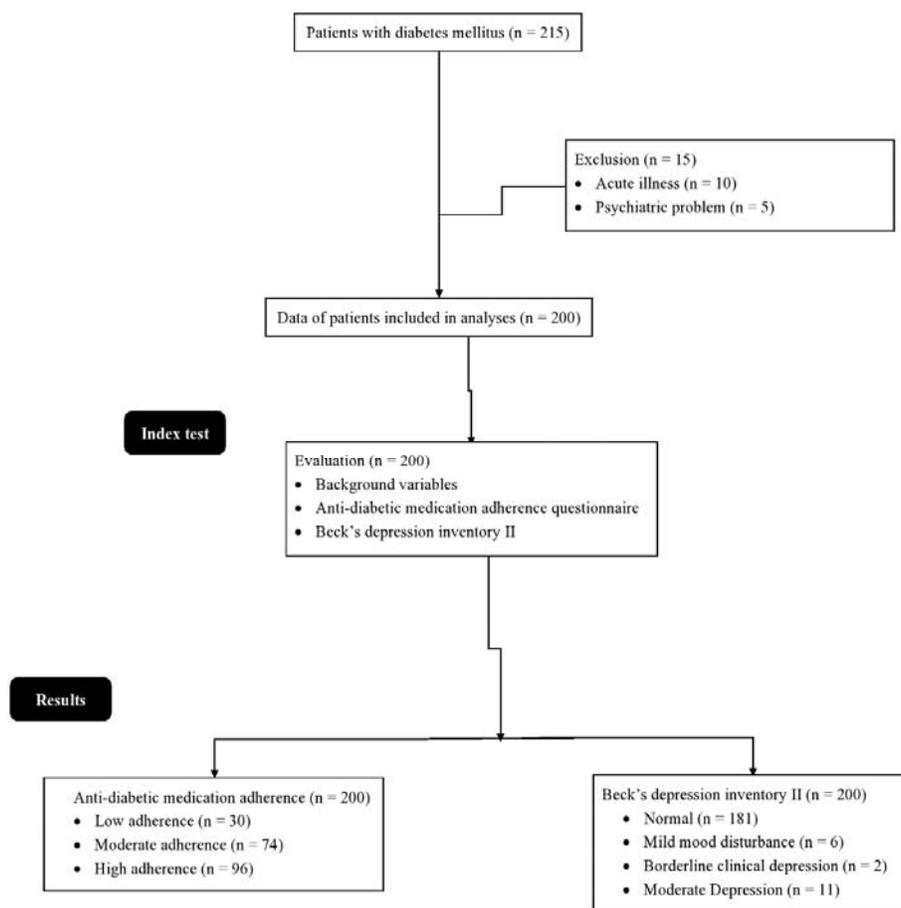


Figure 1: Flow diagram of the study

Socio-demographic characteristics

In this study, 73 of the enrolled patients (36.5 %) were within the age group of 61–70 years; 140 (70 %) were female, 72 (36 %) had secondary education, 124 (62 %) were housewives, 160 (80 %) did not follow diabetic diet, while 143 (71.5 %) used regular exercise. These data are shown in Table 1.

Table 1: Socio-demographic characteristics of patients (n = 200)

Variable	Frequency (%)	
Age (years)	10–20	1 (0.5)
	21–30	3 (1.5)
	31–40	5 (2.5)
	41–50	24 (12)
	51–60	59 (29.5)
	61–70	73 (36.5)
	71–80	34 (17)
	81–90	1 (0.5)
Sex	Male	60 (30)
	Female	140 (70)
Education	No formal education	67 (33.5)
	Primary education	46 (23)
	Secondary education	72 (36)
	Higher education	7 (3.5)
	Graduate	5 (2.5)
Occupation	Professional qualification	3 (1.5)
	Retired	24 (12)
	Employed	16 (8)
	Coolie	33 (16.5)
	Housewife	124 (62)
Diet control	Politician	2 (1)
	Student	1 (0.5)
	Yes	40 (20)
Exercise	No	160 (80)
	Yes	57 (2.8)
	Yes	143(71.5)

Clinical conditions of the patients

The study results indicated that 64 participants (32 %) had DM for 6 to 10 years, 146 (73 %) were on oral anti-diabetic drugs, 49 (24.5 %) had been on treatment for 6 -10 years, 199 (99.5 %) were taking oral hypoglycemic drugs twice a daily, 97 (48.5 %) had hypertension, 137 (68.5 %) had no family history of DM, while 179 (89.5 %) did not have complications (Table 2).

Responses to questionnaire on adherence to anti-diabetic medication

Majority of the participants returned positive responses to the items in the adherence questionnaire, indicating adherence to anti-diabetes medication. These results are presented in Table 3. The results showed that 96 participants (48 %) had high level of adherence to anti-diabetic medication, 74 participants (37%)

had moderate adherence to anti-diabetic medication adherence, while 30 patients (15%) had low adherence to anti-diabetic medication. These results are presented in Figure 2.

Table 2: Clinical conditions of patients

Variable	Frequency (%)	
Duration of illness	<1 year	5 (2.5)
	1–5 years	31 (15.5)
	6–10 years	64 (32)
	11–15 years	48(24)
	16–20 years	35 (17.5)
	21–25 years	9 (4.5)
	26–30 years	6 (3)
	31–35 years	1 (0.5)
Route of the antidiabetic drugs	36–40 years	1 (0.5)
	Oral	146 (73)
Duration of treatment	Injectable	1 (0.5)
	Oral & Injectable	43 (21.5)
	<1 year	5 (2.5)
Frequency of the drugs	1–5 years	31 (15.5)
	6–10 years	63 (31.5)
	11–15 years	49 (24.5)
	16–20 years	35 (17.5)
	21–25 years	8 (4)
Comorbidities	26–30 years	6 (3)
	31–35 years	2 (1)
	36–40 years	1 (0.5)
	Twice in a day	199 (99.5)
	Thrice in a day	1 (0.5)
Family history of diabetes	Hypertension	97 (48.5)
	Bronchial asthma	5 (2.5)
	Hypertension & Renal failure	1 (0.5)
	Hypertension & bronchial asthma	2 (1)
Current complication	No comorbid illness	95 (47.5)
	Yes	63 (31.5)
	No	137 (68.5)
No complication	Neuropathy	14(7)
	Retinopathy.	7(3.5)
	Nephropathy	0 (0)
	No complication	179 (89.5)

Incidence of depression among patients

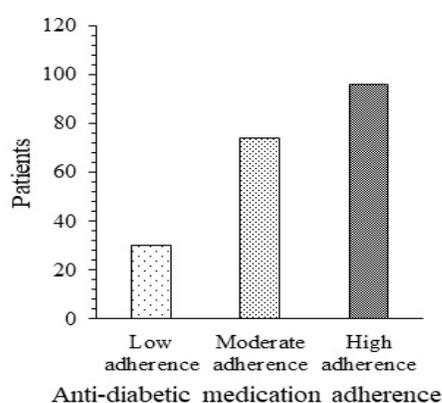
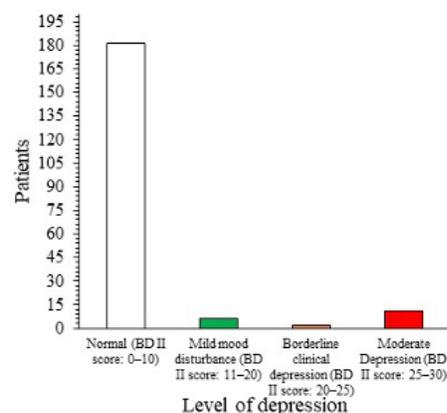
Beck's depression inventory II was used to determine the percentage distribution of depression among the DM patients. The results in Figure 3 show that most of the respondents (181, 90.5 %) did not have depression. Only 6 participants (6 %) had mild mood disturbance, while the numbers of patients with borderline clinical depression and moderate depression were 2 (1 %) and 11 (5.5 %), respectively.

Risk factors for depression

Table 4 shows that there was no association between adherence to anti-diabetic medication and depression among DM patients ($p = 0.068$).

Table 3: Responses to anti-diabetic medication adherence questionnaire

S/N	Item	Frequency (%)
1	Did not forget to take medication	137 (68.5)
	Forgot to take medication	63 (31.5)
2	Did not make mistake in medication	151 (75.5)
	Mistake in medication	49 (24.5)
3	Did not stop taking medication	176 (88)
	Stopped taking medication	24 (12)
4	Did not forget to take medication while traveling	112 (56)
	Forgot to take medication while traveling	88 (44)
5	Took medication on the previous day	127 (63.5)
	Did not take medication on the previous day	73 (36.5)
6	Did not stop the medication when symptoms were under control	177 (88.5)
	Stopped medication when symptoms were under control	23 (11.5)
7	Taking medication is convenient	163 (81.5)
	Taking medication is inconvenient	37 (18.5)
8	Did not experience difficulty in remembering to take medication	172 (86)
	Experience difficulty in remembering to take medication	28 (14)

**Figure 2:** Degrees of patients' adherence to anti-diabetic medication**Figure 3:** Levels of depression in enrolled patients

Univariate analysis showed that depression was associated with age > 50 years ($p = 0.021$), female sex ($p = 0.023$), absence of exercise ($p = 0.026$), long duration of illness (> 5 years) ($p = 0.029$), and presence of one or more comorbid

illnesses ($p = 0.042$). In addition, multivariate analysis revealed that depression was associated with age > 50 years, female sex, long duration of illness (> 5 years), and presence of comorbidities (Table 5).

Table 4: Association of depression with anti-diabetic medication adherence

Drug compliance	Depression		Chi-square	P-value
	Normal	Depression		
Number of included patients in study	187	13		
Low adherence	30	0	5.391	0.068
Medium adherence	72	3		
High adherence	85	10		

Table 5: Association of depression with background variables among participants

Variable	Odds ratio	95% confidence interval	P
Age (>50 years vs <50 years)	1.234	0.469–0.985	0.041
Sex (female vs male)	1.567	0.567–0.875	0.043
Exercises (no vs yes)	0.896	0.442–0.887	0.056
Duration of illness (>5 years vs <5 years)	1.256	0.354–0.987	0.048
Comorbid illness (presence vs absence)	1.222	0.359–0.976	0.049

An odds ratio more than 1 ($p < 0.05$) was considered significant. Data of normal patients ($n = 181$) were considered as reference standard. Significant, i.e., associated with depression

DISCUSSION

The study found that 146 (73 %) patients were on oral anti-diabetic drugs once or twice daily. Majority of the patients preferred treatment with oral hypoglycemic drugs. There was high level of medication adherence with oral medication [15]. Thus, physicians are advised to prescribe oral hypoglycemic agents for DM patients so as to ensure high level of adherence to anti-diabetic medication. It was found that 48, 37 and 15 % of the patients had high, moderate, and low adherence, respectively, to anti-diabetic medication. These findings are similar to those obtained earlier in a retrospective cohort study [15] and in cross-sectional studies [16,17]. In these studies, the diabetic patients had high level of adherence to anti-diabetic medication.

Majority of the participants did not have depression. The findings of this study are in agreement with results obtained in a cross-sectional study [4] and in a community-based study [18] which revealed that there was no association between anti-diabetic medication adherence and depression in diabetic patients.

In this study, age < 50 years, female sex, long duration of illness (> 5 years), and the presence of one or more comorbid illnesses were associated with depression. These are independent factors for depression in diabetes patients irrespective of adherence to anti-diabetic medications [19]. The results are consistent with findings in similar studies [4,17,19]. In this study, 105 patients (52.5 %) had comorbid illnesses. Comorbidity is major complication in DM patients [19]. Thus, it is recommended that physicians should consider comorbidities while treating DM patients.

Limitations of the study

There are several limitations in this study. For example, it was a retrospective study, and it lacked randomized trial. The cutoff for depression in BDI II was 20. The BDI was shaped by Aaron T Beck which is a 21 multiple-choice-question, self-report inventory. This inventory is the most widely used psychometric test for measurement of severity of depression. There are three versions of the BDI, first published in 1961 and later revised in 1978. The BDI is widely used as an assessment tool by health care professionals and researchers in a variety of settings, but the value of cutoff varies from country to country [14]. In China, the cutoff for medical samples is 20 [20]. The Morisky adherence questionnaire is a clinical research method used for assessing adherence of patients

to medication [21]. The Morisky scale is a validated medication non-adherence assessment tool. This scale has already been cited in over 70 articles since its publication in 1986, and has since then been validated. However, it was not used in the current study. Although the validated Morisky scale is used to assess the risk of medication non-adherence, there is no single measure accepted as a 'gold standard' for evaluating medical adherence [16]. Therefore, the present study did not use the Morisky adherence questionnaire for medication adherence evaluation among DM patients. There is lack of clarity regarding the assessment of treatment compliance. This should have been assessed using blood glucose levels, HbA1c levels, and the development of complications of diabetes.

Previous studies have shown that depression in patients with diabetes affects the ability for self-care, including dieting, exercise, keeping medical appointments, blood glucose monitoring, and foot care. However, these vital factors were not evaluated in the current study. The internal consistency of each factor and the general scale of BDI II were not assessed using Cronbach's α coefficient. Comorbid medical illnesses and current diabetic complications may be confounding factors associated with depression in diabetic patients, but they were not included in the simple logistic regression analysis.

CONCLUSION

There is no association between adherence to anti-diabetic medication and depression in diabetic patients in the hospitals studied. Old age, female sex, long duration of illness, and presence of one or more comorbidities were independent risk factors for depression among diabetic patients. It is hereby recommended that the relevant authorities publish an institutional protocol for medical adherence for diabetic patients.

DECLARATIONS

Acknowledgement

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Availability of data and materials

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that they have no conflict of interest or any other competing interest regarding this research.

Authors' contributions

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors read and approved the manuscript for publication. Hidong Luo and Yin Lin contributed equally to resources, literature review, data curation, supervision, the investigation, formal analysis, and validation of the study. Jia Li was a project administrator, contributed to conceptualization, literature review, resources, formal analysis, and data curation of the study. Wiguo Xu contributed to the methodology, literature review, and resources of the study, draft, and edited the manuscript for intellectual content. All authors agree to be accountable for all aspects of work ensuring integrity and accuracy.

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