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The prevalence of comorbid depression in patients with diabetes: A meta-analysis of observational studies

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ABSTRACT

Depression is one of the most common psychiatric disorders in patients with diabetes, which can exacerbate and accelerate adverse diabetes complaints by reducing self-care behaviors and medication adherence. The purpose of this study is to estimate the prevalence of depression in Iranian patients with diabetes. The search was conducted in the databases of Scientific Information Database (SID), MagIran, PubMed, Scopus, Web of Science, and Google Scholar. The following keywords and their possible combinations were used: depressive disorder, major depressive disorder, dysthymic disorder, diabetes mellitus and Iran. Heterogeneity between studies was examined with I^2. The data were analyzed using the meta-analysis method and random-effects model with Stata version 11.0. The analysis of 37 selected articles with a total sample size of 7849 indicated that the overall prevalence of depression in Iranian patients with diabetes was 54% (95% CI: 47.32–60.70). In addition, the prevalence of depression in women (56.25%; 95% CI: 48.83–63.68) was higher than that of men (41.05%; 95% CI: 32.74–49.36). The results showed that there was no relationship between the prevalence of depression and publication year (0.249), sample size ($p = 0.529$), and mean age of the subjects ($p = 0.330$). More than half of the patients with diabetes suffer from depression. Identification and treatment of these patients can be an important step in controlling and delaying the diabetes complication.

Contents

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1. Introduction

Diabetes is the most common chronic metabolic disease that has become a global epidemic. About 200 million people worldwide suffer from diabetes and are expected to reach 592 by 2035 [1]. The prevalence of diabetes in Iran is 7.7%, which is predicted to double by 2025 [2]. Due to micro- (retinopathy, nephropathy, and neuropathy) and macrovascular complications (cardiovascular disease, cerebrovascular disease, and stroke), the mortality rate for diabetic patients is twice that for non-diabetic patients [3]. Diabetes is the cause and cause of 30% of kidney failure and 12% of blindness in the world [4]. Diabetic patients are susceptible to psychiatric disorders due to short-term and long-term complications of the disease, daily injections of insulin, regular blood glucose monitoring, physical complications, hospitalization and diabetes-related constraints [5].

Depression is the most common psychiatric disorder that is more common in diabetic patients than in the general population [6]. More than 300 years ago, Thomps Willis, a British physician, pointed out the link between diabetes and depression, suggested that diabetes was the result of "sadness or long sorrow" [7]. Depression is characterized by low levels of energy, reduced energy, feeling guilty, difficulty concentrating, anorexia, thoughts of death and suicide, sleep disturbances, and functional impairment [4]. The results of various studies have shown that depression is associated with a decrease in quality of life, poor self-care, reduced treatment compliance, and impaired glycaemic control [8–11]. Also, diabetic patients with depression have twice the risk of death than do those without depression [12]. A meta-analysis that combined the results from 10 studies reported that the mortality rate of depressed diabetic patients was 1.5 times higher than non-depressed diabetic patients [13].

Both depression and diabetes are associated with morbidity and mortality, and when these two diseases coincide, the risk for developing comorbidities, poor blood glucose control, complications and complaints, and cost of the disease increases [14,15]. Many studies have examined the prevalence of depression among patients with diabetes, reported different results. A review of the literature showed that the prevalence of depression among Iranian patients with diabetes varied between 13.7% and 87% [5,16]. Considering the fact that the essential step in planning to control this problem among diabetic patients is the accurate identification of the situation, we conducted this study with the aim of estimating the prevalence of depression in Iranian patients with diabetes.

2. Method

2.1. Search strategy

To identify the relevant studies, two authors (MSP and ZM) independently searched Scientific Information Database (SID), MagIran, PubMed, Scopus, Web of Science, and Google Scholar using the search terms, depressive disorder, major depressive disorder and dysthymic disorder, diabetes mellitus combined with Iran. National databases are not sensitive to Boolean operators (the search is not possible as a combination of keywords), so the search was performed as a single word. As a result, a large number of articles were obtained from national databases, many of which were irrelevant. Then titles and abstracts of retrieved articles were screened for relevance to exclude studies that were clearly irrelevant. Finally, the full text of the remaining articles was also read to ensure whether the studies met our inclusion criteria. Furthermore, the reference lists of selected articles were reviewed to access more relevant articles.

2.2. Inclusion and exclusion criteria

In this meta-analysis, we included the observation articles published in Persian or English. Qualitative studies, interventional studies, and review studies were excluded. Since there is no comprehensive database for grey literature in Iran, we did not include conference abstracts, theses, books, or book sections.

2.3. Data extraction

The required information such as name of first author, publication year, sample size, location of the study, age of subjects, region, type of diabetes, and the prevalence of depression was extracted by two independent researchers (TN and SK). In the case of disagreement, the main author (RGG) made the final decision. The methodological quality of the articles was evaluated based on the selected items of the STROBE checklist (titles and abstracts, goals and hypotheses, setting, inclusion and exclusion criteria, sample size, statistical methods, descriptive data, interpretation of findings, research limitations, and funding) [17].

2.4. Statistical analysis

In this systematic review and meta-analysis, we calculated the point estimate and 95% confidence interval (CI) for the prevalence of depression with respect to the binomial distribution. The heterogeneity between the studies was investigated by Cochran Q test with a significant level less than 0.1 and I^2statistic. Based on I^2 statistic, heterogeneities were divided into three classes less than 25% (low heterogeneity), 25%–75% (moderate heterogeneity) and more than 75% (high heterogeneity) [18]. Because heterogeneity was high among selected studies, the pooled prevalence was estimated using the random effects model. To ensure the stability of the results, a sensitivity analysis was performed by omitting one study at each turn. We used a subgroup analysis (region, type of diabetes) and meta-regression (age, sample size, and publication year) to explore sources of heterogeneity. We also assessed the publication bias with the funnel plot based on the Egger's regression test. Data analysis was performed the statistical software Stata v11 (Stata Corporation, College Station, TX, USA).

3. Results

Database searching using the method described led to the retrieval of 987 articles. In the identification and screening stage, 913 irrelevant articles were excluded, and the full texts of the remaining articles were read. Out of 72 articles, 35 were excluded for various reasons. Finally, 37 papers were analyzed according to the PRISMA statement [19] (Fig. 1)

The total sample size was 7849. The smallest and largest sample size was 80 and 514, respectively. Out of 37 selected studies, only 3 studies had strong methodological quality, and 34 articles had

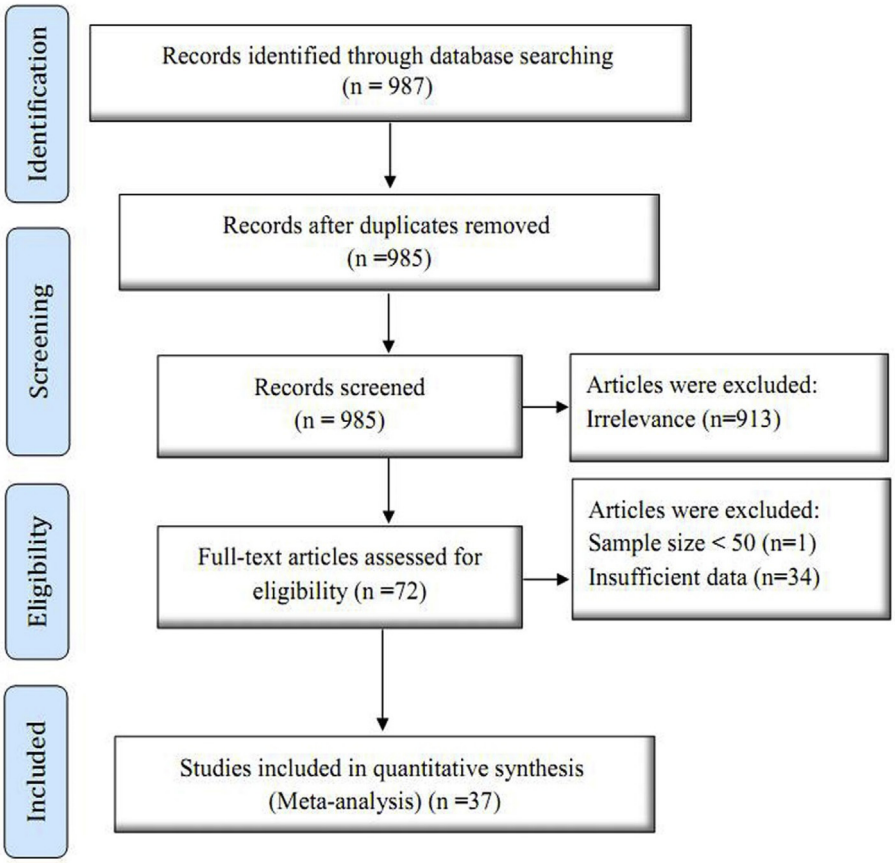

Fig. 1. The screening and selection of articles in accordance with PRISMA statement.

moderate methodological quality. More details are provided in Table 1.

To investigate whether all relevant articles on depression in Iranian patients with diabetes were published and included in this study, publication bias was used. Results showed that publication bias was not significant (P = 0.618) (Fig. 2).

The pooled prevalence of depression in patients with diabetes was 54% (95% CI: 47.32–60.70) (Fig. 3). Also, the prevalence of depression in women (56.25%; 95% CI: 48.83–63.68) was higher than that of men (41.05%; 95% CI: 32.74–49.36).

The subgroup analysis showed that the highest and lowest prevalence of diabetes was related to region 2 (68.36%; 95% CI: 60.36–76.35) and 3 (41.38%; 95% CI: 35.42–47.33), respectively. Further details are summarized in Table 2.

The results of the meta-regression showed that there was no relationship between the prevalence of depression and publication year (0.249), sample size (p = 0.529), and mean age of the subjects (p = 0.330). The results of the sensitivity analysis indicated that the exclusion of any study alone did not have an impact on the overall prevalence of depression (Fig. 4).

4. Discussion

This systematic review and meta-analysis was conducted to estimate the prevalence of depression among Iranian patients with diabetes. Although Khalighi et al. (2019) had already studied depression in Iranian patients with diabetes; various mistakes in this research (lack of proper screening for the articles) could distract the actual estimate of the prevalence of depression. For example, they had incorrectly included a study that had been done on patients with cardiovascular disease (Tajfard et al. study). The findings were also not fully documented, which could be confusing readers Healthcare decisions are made based on the findings of these studies, so using wrong results can affect decision making [51]. The results showed that more than half of the patients with diabetes (54%) suffered from depression. Similar to our findings, the results of various studies have shown that the prevalence of depression in diabetic patients in Palestine, China, and Mexico was 40.2%, 43.6% and 47.2%, respectively [14,52,53]. In the study of Khan et al. (2019), the prevalence of depression in Tanzanian patients with diabetes was 87%, which is more than the reported incidence in Iran [54]. In summary, all of these studies have shown that depression is prevalent in patients with diabetes, and the reason for the slight differences in results can be attributed to the demographic characteristics and clinical features of these patients. Regarding the high prevalence of depression in patients with diabetes and the adverse effects of depression on diabetes, clinical guidelines have recommended that all patients with diabetes be screened for depression [12].

It is still unclear whether diabetes increases the risk of depression or that depression increases the odds of diabetes. Although the relationship between these two chronic conditions is clear, the nature of the relationship is still unclear. Golden believes there is a bi-directionally associated between diabetes and depression [55]. Chronic stress associated with depression leads to hypercortisolemia, obesity, and eventually metabolic syndrome. Depression is also associated with increased levels of glucocorticoids, catecholamines and growth hormone, which can lead to

Table 1
Characteristics of the included articles in the meta-analysis.

First Author	Year	Sample size		Place	Type	Tool	Prevalence		
		Total	M/F				Total	Male	Female
Mansori [20]	2019	514	133/381	Khorramabad	II	BDI	46.3	36.8	49.6
Haji-Arabi [4]	2018	145	54/91	Semnan	II	BDI	76.6	–	–
Soudagar [21]	2018	200	50/147	Bandar Abbas	I & II	DASS-21	31.3	–	–
Eskandari [22]	2017	202	55/147	Sari	II	GHQ	25.4	–	–
Ahrari [23]	2015	200	56/144	Gonabad	II	BDI	64	–	–
Derakhshanpour [24]	2015	330	117/213	Gorgan	II	BDI	58.2	68.8	61.5
Kalantari [25]	2014	90	27/63	Rasht	II	BDI	37.8	33.3	39.7
Behrouz [26]	2014	210	100/110	Kermanshah	II	Scl-90	56	62	49
Palizgir [27]	2013	184	–	Tehran	II	BDI	71	56.1	78
Parham [28]	2013	116	36/80	Ghom	II	BDI	70.7	26.7	74.4
Harooni [29]	2013	403	120/283	Chadegan	II	BDI	60	53.3	62.4
Baradaran [30]	2013	185	89/96	Tehran	I & II	DDS	43.2		
Sajjadi [5]	2012	80	–	Hamadan	II	GHQ-28	13.7	–	–
Rahimian Boogar [31]	2012	254	–	Tehran	II	PHQ-9	25	–	–
Khamseh [32]	2011	185	89/96	Tehran	II	Interview	43.2	–	–
Khamseh [32]	2011	185	89/96	Tehran	II	PHQ-9	47.6	–	–
Khamseh [32]	2011	185	89/96	Tehran	II	CES-D	61.6	–	–
Ghafari [33]	2010	100	50/50	Golestan	I & II	BDI	–	58.8	76.2
Yekta [34]	2010	167	56/111	Urmia	II	BDI	43.4	37.8	45.9
Kasiri Dolat-abadi [35]	2010	383	114/269	Isfahan	II	BDI	72	21.4	56.5
Nikbakht [36]	2009	100	21/79	Bandar Abbas	I & II	BDI	50	–	–
Mazloomy [37]	2008	100	29/71	Yazd	II	BDI	64	48.3	70
Mousavi [38]	2008	100	39/61	Shahroud	II	BDI	78	32	75.4
Mahmodi [39]	2008	227		Dehaghan	I & II	BDI	77	–	–
Salehi [40]	2007	134	42/92	Arak	II	Hamilton	11	24	15.2
Nejati Safa [41]	2007	100	32/68	Tehran	I & II	HADS-D	28	–	–
Khamseh [42]	2007	206	–	Tehran	I & II	BDI	71.8	–	–
Ranjbar [43]	2007	100	–	Shiraz	I & II	BDI	71.4	–	–
Shamsaei [44]	2006	384	–	Hamedan	I & II	BDI	72.2	–	–
Noroozinejad [45]	2006	309	–	Ahwaz	I & II	BDI	72.2	–	–
Behnam [46]	2005	450	–	Semnan	II	BDI	71.6	57.3	79.2
Larijani [47]	2003	375	153/222	Tehran	I & II	BDI	31.8	–	–
Sepehrmanesh [48]	2003	300	78/222	Kashan	I & II	BDI	53.3	41	57.7
Sepehrmanesh [48]	2003	300	78/222	Kashan	I & II	Interview	–	32	47.3
Rahnama [49]	2002	96	–	Mashhad	II	BDI	70	–	–
Taziki [50]	2001	150	47/103	Gorgan	I & II	BDI	34	36.7	66
Abdollahyan [16]	2000	100	21/69	Mashhad	II	Scl-90R	87	–	–

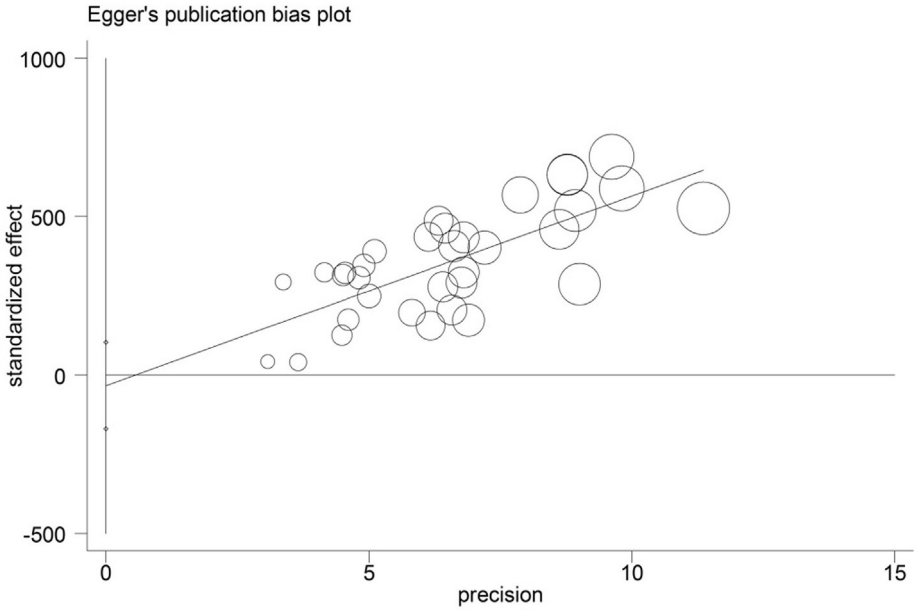

Fig. 2. Publication bias.

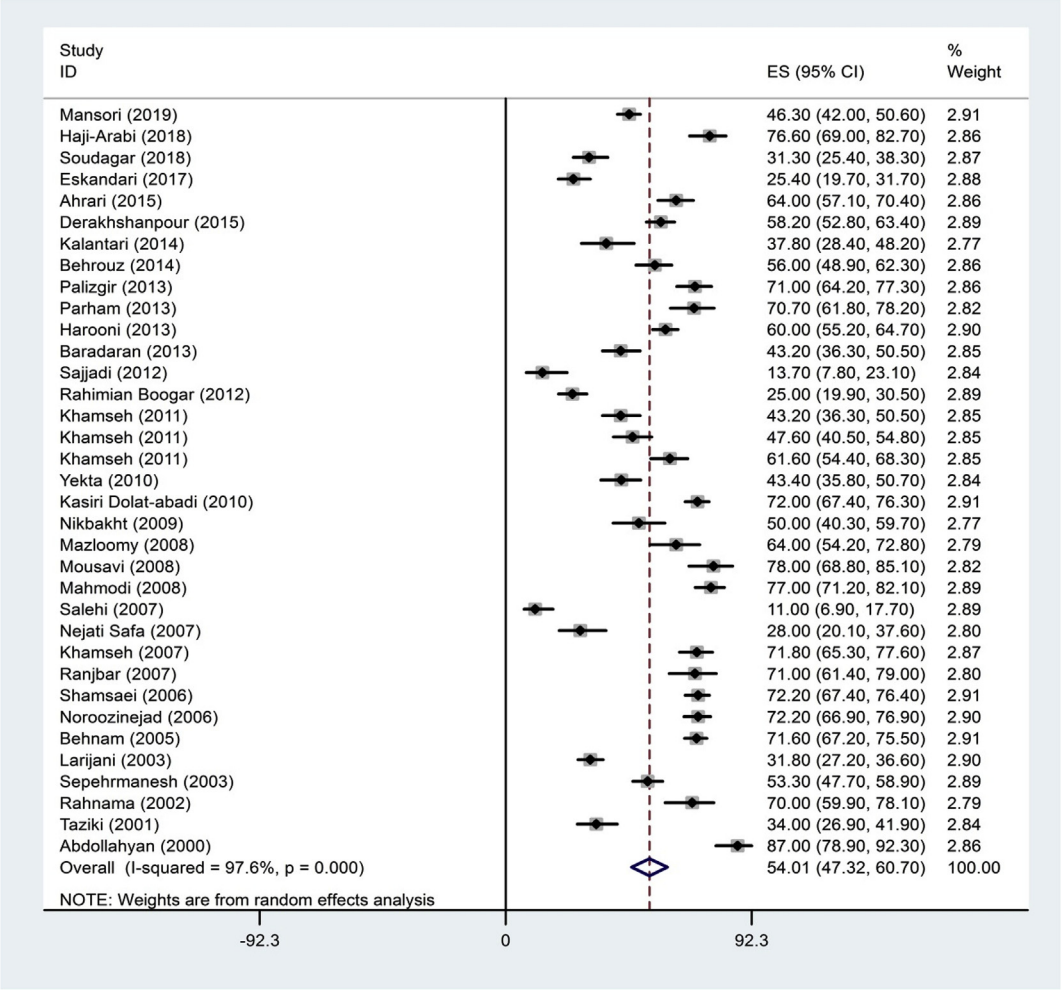

Fig. 3. Forest plot of the prevalence of depression in patients with diabetes. The 95% confidence interval for each study is shown in the form of horizontal lines around the central mean and midpoint of the dotted line represents the mean of the overall score and the lozenge shape shows the confidence interval of the prevalence of this disorder.

Table 2
Prevalence of depression based on subgroups analysis.

Group		Number of study	Prevalence (%)	Confidence level (95%)	Heterogeneity	
					%	p
Tool	Beck	23	61.66	55.74–67.57	95.5	0.001
	Others	12	39.40	26.88–51.92	97.7	0.001
Type of diabetes	II	23	54.51	45.92–63.10	97.7	0.001
	I & II	12	53.06	41.97–64.16	97.4	0.001
Region	Region 1	15	50.66	40.65–60.66	97.5	0.001
	Region 2	6	68.36	60.36–76.35	91.2	0.001
	Region 3	2	41.38	35.42–47.33	–	0.376
	Region 4	5	52.24	34.26–70.21	98.2	0.001
	Region 5	7	53.83	31.68–75.98	98.5	0.001

Region 1: the provinces of Tehran, Alborz, Qazvin, Mazandaran, Semnan, Golestan, and Qom; **Region 2:** the provinces of Isfahan, Fars, Boushehr, Chaharmahal va Bakhtiari, Hormozgan, and Kohkilouyeh va Boyerahamad; **Region 3:** the provinces of Eastern Azarbaijan, Western Azarbaijan, Ardebil, Zanjan, Gilan, and Kurdistan; **Region 4:** the provinces of Kermanshah, Ilam, Hamedan, Markazi, Lorestan and Khouzestan; **Region 5:** the provinces of Khorasan Razavi, Southern Khorasan, Northern Khorasan, Kerman, Yazd, and Sistan va Balouchestan.

insulin resistance and diabetes development [56]. In addition, metabolic abnormalities caused by drugs used to treat depression, unhealthy lifestyle and physical inactivity increase the likelihood of developing diabetes in depressed patients [57,58].

The prevalence of depression in women was higher than that of men, which is consistent with studies conducted in China [53], Germany [59]. A study in Bangladesh also found that 29% and 30.5% of men and women with diabetes had depression symptoms [60]. The reason for this finding may be the social inactivity of women and their hormonal changes. Subgroup analysis showed that the prevalence of depression in both diabetic patients was similar. Both types of patients with diabetes are always concerned about

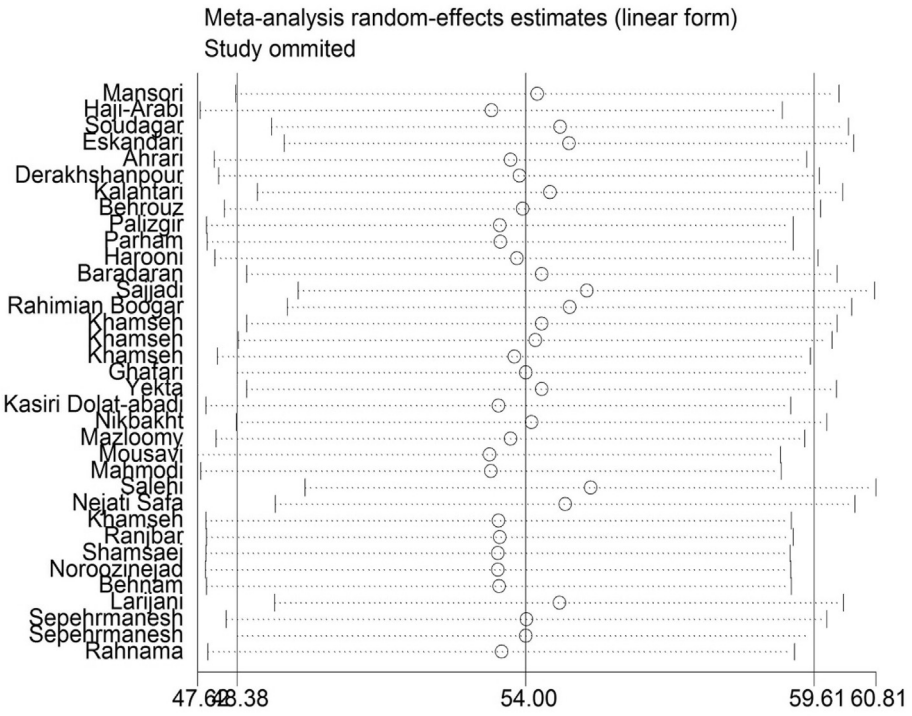

Fig. 4. The sensitivity analysis.

physical complications and diabetes-related constraints, which can affect their mood. Also, the prevalence of depression based on Beck's tool was more than other tools. Given the clear difference between the reported results based on these screening tools, it is recommended that, with respect to the culture and context of the community, appropriate tools be used to investigate depression. Differences in the prevalence of depression in different regions of the country can also be due to cultural differences and socio-economic status of the regions.

The results of meta-regression showed no relationship between the prevalence of depression and the publication year. It seems that the health programs implemented to control depression in these patients were ineffective and need to be reviewed. On the other hand, there was no relationship between the age of the patients and the prevalence of depression. This finding emphasizes that depression affects all diabetic patients of any age and is not limited to a specific age group. One of the limitations of this study was that some of the selected articles had reported incomplete results. The main strength of this study was its comprehensiveness, which provided findings with details.

Depression is prevalent in patients with diabetes, with more than half of them suffering from depression. The presence of depression leads to a reduction in medication adherence and self-care behaviors in these patients and eventually the appearance of diabetic complications that can impose a large financial burden on patients and health systems. It is recommended that the medical team, and especially the nurses, screen all diabetic patients for depression. Identifying patients at risk of depression and its treatment can be an important step in promoting self-care and delaying disease complaints.

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Disclosure (authors)

The authors declare no conflicts of interest.

DDS: Diabetes Distress Scale; **BDI:** Beck Depression Inventory; **HADS:** Hospital Anxiety and Depression Scale; **DES-D:** Center for Epidemiologic Studies Depression Scale; **DASS:** Depression, Anxiety and Stress Scale; **Scl-90:** Symptom Checklist 90; **PHQ-9:** Patient Health Questionnaire; **GHQ:** General Health.

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