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PREVALENCE OF DEPRESSION IN IRANIAN WOMEN WITH BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

INTRODUCTION. Depression is a debilitating disease that is highly prevalent among cancer patients. Various studies in Iran have reported different prevalence. This systematic review and meta-analysis was conducted to estimate the overall prevalence of depression in Iranian women with breast cancer.

MATERIAL AND METHODS. In this study, published articles in Persian and English were collected without time limit. Keyword searches for depression, depressive disorder, dysthymic disorder, major depressive disorder, breast cancer, breast neoplasm, and Iran and all of their potential combinations were performed in Scientific Information Database (SID), MagIran, PubMed, Scopus, Web of Science databases. The heterogeneity between studies was assessed using the Q-Cochrane test and, given the significant heterogeneity, a random-effects model was used to estimate the overall prevalence of depression. Data were analyzed using STATA version 11 software.

RESULTS. The analysis of 22 selected articles with a total sample size of 3,082 showed that the overall prevalence of depression in women with breast cancer was 49.98% (95% confidence interval: 48.43-52.52). The prevalence of depression in Region 1 in the country was (28%; 95% confidence interval: 25.53-52.55) and in other regions, it was (63.79% with 95% confidence interval of 61.82-76.76). The highest and the lowest prevalence of depression were related to BDI (69.33%; 95% confidence interval: 67.19-71.48) and HADS (26.43%; 95% confidence interval: 23.14-29.72), respectively.

CONCLUSIONS. Half of the Iranian women with breast cancer had depression. Given the overlap of physical symptoms of cancer with depression, identifying at-risk patients for controlling and providing therapeutic interventions seems necessary.

Keywords: *depression, breast cancer, prevalence, systematic review, meta-analysis, Iran*

INTRODUCTION

Breast cancer is the most common cancer in women worldwide and in 2012 about 1.2 million new cases were identified (1). In 2016, breast cancer accounted for one-fourth of all cancers in women (2). Studies have shown that 76 percent of all common cancers in Iran are breast cancer, with a total of 40,000 breast cancer cases in Iran, and more than 7,000 patients added annually (3).

Cancer is a scary diagnosis, and cancer patients suffer more emotional and psychological stress than

the general population (4). Because of its importance, emotional distress has been recognized as the sixth vital symptom in cancer care (5), which has a negative impact on adherence to their medical treatments and is associated with decreased quality of life and increases risk of death (6).

Developing breast cancer and receiving treatment have notorious effects on self-image and sexual intercourse, so it is a traumatic experience for many women and many of them develop psychological reactions such as denial, anger, fear of the disease process and treatment (7). Fear and concern about death and recurrence, body image disorder, changes in femininity, sexuality and attractiveness are factors that make patients susceptible to psychological distress such as depression, which may remain years after diagnosis and treatment (8). Depression is associated with pain, fatigue, decreased quality of life, anxiety, suicidal thinking, and decreased survival (9). Depression may disrupt adherence to treatment and may adversely affect the disease process, leading to increased length of hospital stay and medical costs (10).

Various studies conducted in Iran have reported different results. The results of two recent meta-analysis studies conducted on 9 and 18 studies showed that the prevalence of depression in Iranian women with breast cancer was 44% and 46.8%, respectively (11, 12). Given the flaw in the search process in those studies and that all existing studies were not analyzed, there was a need to provide accurate statistics on the prevalence of depression in women with breast cancer. Because health care decisions about depression control and interventions will be based on the results of these studies, inaccurate statistics can lead to incorrect decisions. The aim of this study was to estimate the prevalence of depression in Iranian women with breast cancer.

MATERIAL AND METHODS

This systematic review and meta-analysis study was conducted to estimate the prevalence of depression in Iranian women with breast cancer based on the PRISMA guidelines (13). Inclusion criteria were: using standard tools for measuring depression, articles published in Farsi and English, access to the full text of the articles. Articles of low methodological quality (high-risk bias), interventional, review and qualitative articles and letter to the editor were excluded from the analysis.

Search strategy. Initially, internal database of Scientific Information Database (SID), MagIran and external databases of Google Scholar, Scopus, Web of Science, and PubMed were searched by two researchers independently and without time limitation.

They searched the keywords: "depression", "depressive disorder", "major depressive disorder", "dysthymic disorder", "breast cancer", "breast neoplasm" and "Iran" and their combination. The sources and discussion of the articles were reviewed for access to other articles.

Selection of studies and extraction of information. Two researchers independently screened the title and abstract of the articles and then reviewed the full text of the articles according to the inclusion criteria. They then extracted the required information such as first author, year of publication, mean age of the samples, sample size, study location and depression measurement tools. Any disagreements were resolved through consultation.

Quality assessment. Two researchers independently reviewed the methodological quality of the articles based on 10 items from the ESTROBE checklist. These items included title, abstract, goals, hypotheses, research environment, inclusion criteria, sample size, statistical methods, descriptive data, interpretation of findings, research limitations, and research funding (14). Higher scores represented the higher quality of articles. Based on the scores obtained, the articles were divided into three categories of poor (score 4 and lower), average (4 to 7) and good (above 7).

Statistical analysis. In this systematic review and meta-analysis, we calculated the point estimate and 95% confidence interval for the prevalence of depression with respect to the binomial distribution. The heterogeneity between studies was assessed by Cochran's Q test with a significance level less than 0.1 and I^2 statistic. Based on I^2 index, the heterogeneity was classified into three categories of less than 25% (low heterogeneity), 25% to 75% (moderate heterogeneity) and more than 75% (high heterogeneity). Because heterogeneity was high among selected studies (98.1%), the pooled prevalence was estimated using the random effects model. Sensitivity analysis was used to ensure the stability of the results, so that each time a study was excluded from the meta-analysis, the effect of that study on the overall prevalence of depression was examined. Subgroup analysis and meta-regression analysis were used to investigate the potential source of changes affecting the prevalence of depression. Subgroup analysis by country's geography (Region 1/other regions) and type of depression screening tool (BDI, HADS, DASS-42, Zung) and univariate regression analysis to examine the relationship between depression and mean age, year of publication, score The quality of papers and sample size of the selected studies were used. Publication bias was inspected visually with funnel plots and analyzed with Egger's method (15). Data analysis was performed using Stata version 11 software.

RESULTS

Selection of studies. A total of 925 articles were found by searching the national and international databases. After removing duplicate studies, the title and abstract of the remaining 912 non-duplicate articles were reviewed. At the screening stage, 845 unrelated articles were excluded from the analysis and the full texts of 67 articles were read. The rest of the articles were reviewed for eligibility and 45 other studies were excluded. The process of selecting and screening articles based on PRISMA's steps is presented in the following flowchart (Figure 1).

Characteristics of selected studies. Finally, 22 articles with a sample size of 3,082 were included in the analysis. The mean age of the samples was 47.7 years. The studies were from 2000 to 2018. Half of the studies were conducted in Region 1 and the other half in other regions of the country. Symptoms of depression were assessed in 12 studies using the BDI tool and in 6 studies by the HADS tool. The sample size ranged from 42 to 297 individuals. In terms of methodological quality, 16 studies were at a good level and 6 were at a moderate level. Further details are presented in Table 1.

Meta-analysis of depression. The prevalence of depression in women with breast cancer in Iran was 49.98% (95% confidence interval: 48.43-52.52) (Figure 2). The results of the subgroup analysis showed that the prevalence of depression based on the BDI tool was 33.69% (95% confidence interval: 19.67-48.71) and 43.26% with the HADS tool (95% confidence interval: 14.23-72.29). Four studies also used the DASS-42 and Zung tools, with a prevalence of depression of 90.31% (95% confidence interval: 88.34-91.28). Of the 22 analyzed studies, 11 were in the Region 1 and the remaining 11 were in the other regions of the country. The prevalence of depression in Region 1 of the country (28% with 95% confidence interval: 25.53-30.49) was lower than in other regions of the country (63.79% with 95% confidence interval: 61.82-76.76).
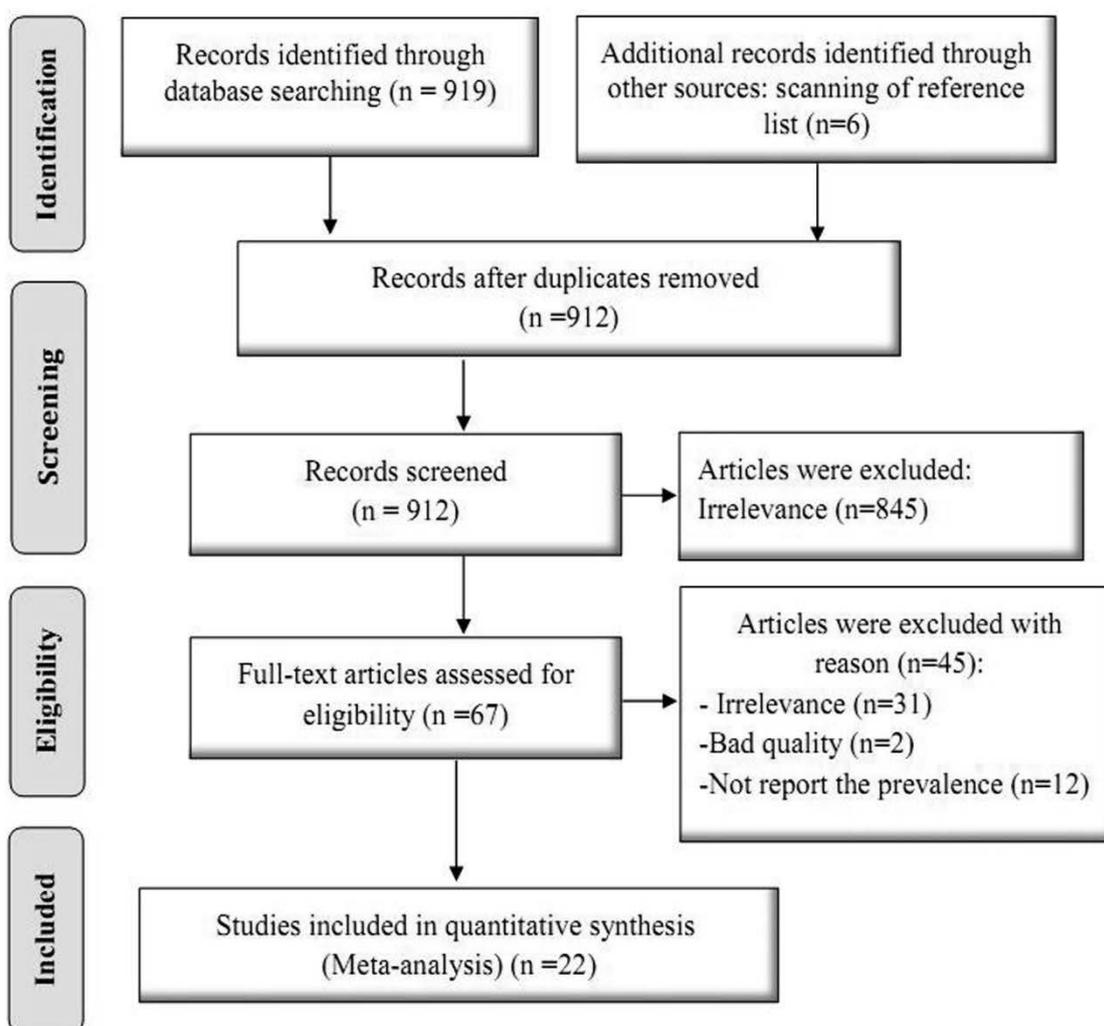
Figure 1. Screening process and selection of articles

Table 1. The main characteristics of the studies included in the present systematic review and meta-analysis

Author	year	Mean age	Sample size	Instrument	Location	Prevalence (%)	Quality score
Keihanian (16)	2018	52.35	100	BDI	Ramsar	45	8
Heidarirad (17)	2018	38.40	200	BDI	Sanandaj	81	9
Tadayon (18)	2018	-	114	BDI	Dezful	61.40	8
Motamadi (19)	2016	46.94	50	BDI	Tehran	62	8
Mehrabani (20)	2016	55.91	260	DASS-42	Neyshabour	51.28	8
Shakeri (21)	2016	47.60	98	BDI	Kermanshah	95.90	8
Heydarheydari (22)	2015	46.27	275	BDI	Kermanshah	41	8
Nikbakhsh (23)	2014	59.04	46	HADS	Babol	65	8
Musarezaie (24)	2014	46.10	297	DASS-42	Isfahan	34.50	10
Derakhshanfar (25)	2013	47.05	111	BDI	Hamedan	61.30	8
Mashhadi (26)	2013	45.80	42	BDI	Zahedan	76.20	8
Heidari Gorji (27)	2012	52.48	63	BDI	Tehran	60.30	7
Taghavi (28)	2011	46.43	240	BDI	Isfahan	65	7
Vahdaninia (29)	2010	47.20	167	HADS	Tehran	22.2	8
Didehdar Ardebil (30)	2009	43.81	60	BDI	Babol	50	7
Ranjbar Kochaksarayi (31)	2006	46	100	Zung	Tabriz	42	7
Montazeri (32)	2005	48.20	177	HADS	Tehran	29.37	8
Montazeri (33)	2004	46.60	243	DSM-IV	Tehran	16	8
Haghighat (34)	2003	45.70	112	HADS	Tehran	32	7
Ramezani (35)	2001	47.53	120	BDI	Kerman	40.80	9
Montazeri (36)	2001	45.40	56	HADS	Tehran	14	7
Montazeri (37)	2000	47.20	151	HADS	Tehran	22	8
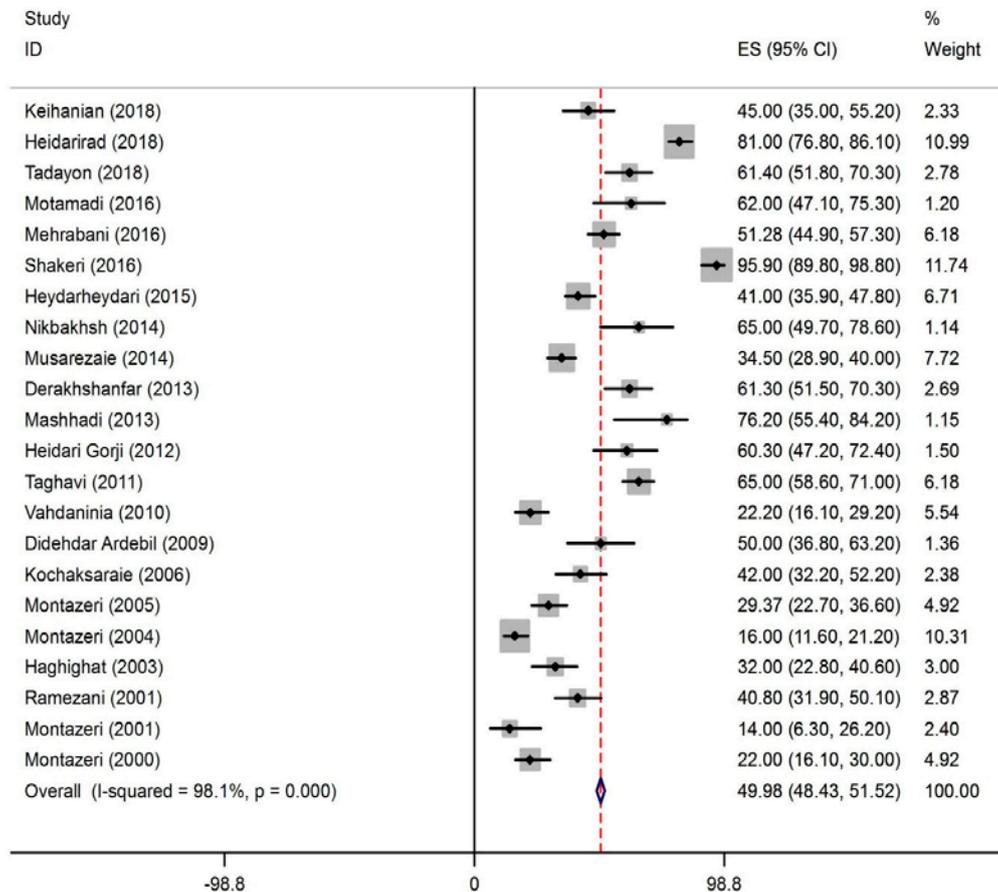
Figure 2. Prevalence of depression and its 95% confidence interval in women with breast cancer based on the random-effects model. The middle point of each line represents the prevalence of depression in each study and the rhombic form of the prevalence of depression for all studies in Iran.

Meta-regression findings. The results showed that there was a significant relationship between the prevalence of depression and the year of publication ($p = 0.306$), but there was no relationship between the prevalence of depression and the mean age of patients, quality score and sample size. (Figure 3).

The publication bias diagram was used to check whether all articles on depression in women with breast cancer were published and included in the study. The results showed that publication bias was not significant ($P = 0.540$). (Figure 4).
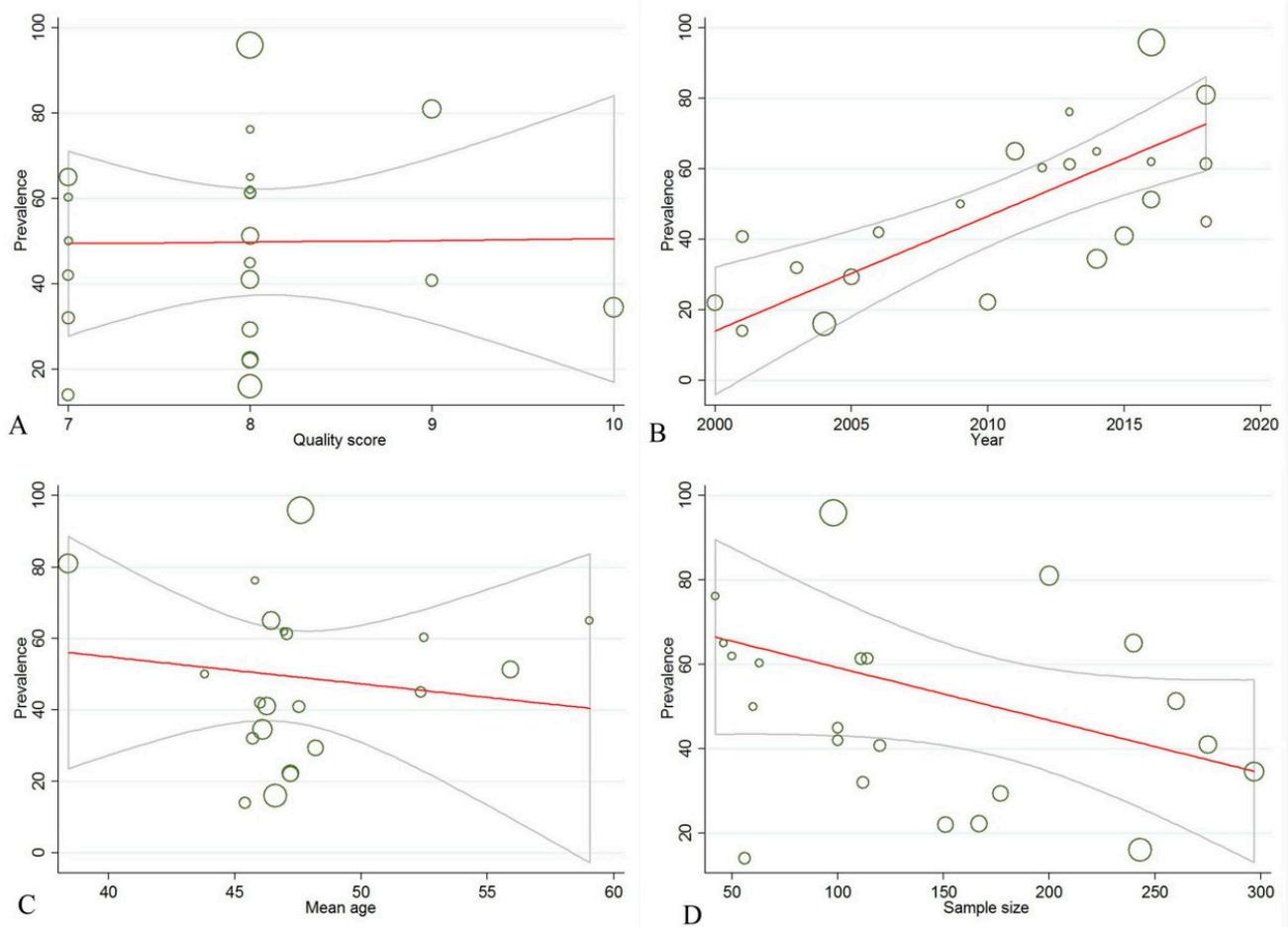
Figure 3. Meta-regression results. Correlation between the prevalence of depression and quality of papers (A), year of publication (B), the mean age of samples (C) and sample size (D).
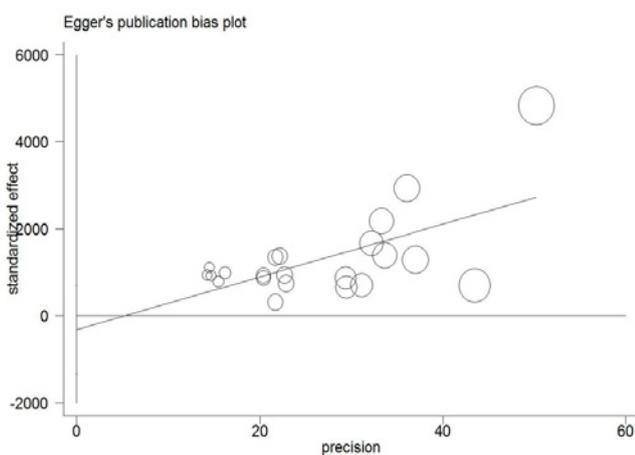
Figure 4. Publication bias

DISCUSSION

The study, which aimed to estimate the prevalence of depression in Iranian women with breast cancer, revealed that half of the patients suffer from depression. This finding is consistent with the results of the study by Burgess et al., who reported that half of the women with breast cancer had symptoms of depression (38). The latest meta-analysis has shown that the global prevalence of depression in women with breast cancer is 32%, which is lower than the prevalence of depression in Iranian patients (39). The results of this study showed that the prevalence of depression in Iranian women with breast cancer was higher than China (26%) (40) and lower than India (70%) (41). Differences in the prevalence of depression

in these societies can be attributed to demographic characteristics, different studied cases, different screening tools for depression, cultural and behavioral differences in different societies.

In our country, as in other countries, woman's breasts are a symbol of femininity, sex, beauty, baby nutrition, love and motherhood. For this reason, women after breast cancer have severe psychological problems such as impaired body image, reduced self-esteem, loss of femininity and sexual function, anxiety and depression, hopelessness, guilt and shame, fear of relapse, isolation and fear of death experience. Depression is highly prevalent in these patients but, as it is often undiagnosed, remains untreated, leading to exacerbation of patients' physical and psychological problems, affecting patients' quality of life and adherence to treatment (42).

The results of various meta-analyses in Iran reveals that the prevalence of depression in patients with diabetes (43) and rheumatoid arthritis (44) were 54% and 65.5%, respectively that are higher in comparison to breast cancer. The prevalence of depression in women with breast cancer does not appear to be lower than those mentioned, but because these women are reluctant to disclose their depression symptoms, they are less likely to show and report it (45). Oncologists, on the other hand, may not be sufficiently familiar with the symptoms of depression in these women. On the other hand, it is always challenging to diagnose depression in this group of women because of the overlap of depression with physical symptoms of cancer (46).

The prevalence of depression was much lower in Region 1, which covers Tehran (the capital of Iran) and Qazvin, Mazandaran, Semnan, Golestan, Alborz and Qom provinces. The finding may be attributed to the better health care facilities in these areas that identify patients in the early stages of depression. According to the results of this study, the highest and lowest prevalence of depression was related to studies using BDI and HADS tools, respectively, which is consistent with the findings of Gharaei et al. (12). The reason for this finding may be attributed to the psychometric properties of the above instruments. According to the results of the meta-regression, there was no relationship between the prevalence of depression and the mean age of women with breast cancer, which is consistent with the results of the study by Gharaei et al. (12). But there was a significant relationship between the prevalence of depression and the year of publication of the article, with an increasing trend between 2000 and 2018 that could be attributed to progress in identifying patients and recent socioeconomic problems in Iranian society.

One limitation of this study was that some information such as the degree of cancer, the duration of the disease, the duration of the diagnosis, were not reported in the selected studies, which precluded us from further analysis. A further limitation of this study was the non-use of grey literature, as there is no specific database in Iran for the study of dissertations, conferences, and seminars. One of the strengths of this study is its novelty.

The results of this study revealed that half of the Iranian women with breast cancer suffer from depression. Depression as an underlying disease has exacerbated physical and mental problems in these women and severely deteriorates their quality of life. Given the overlap of physical symptoms of breast cancer with depression, identifying at-risk patients for controlling and providing therapeutic interventions seems necessary.

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