

The Impact of B12 Vitamin and Folate Deficiency on Depression Levels in Breast Cancer Patients

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ABSTRACT

Objective: This study aims to investigate the impact of B12 vitamin and folate deficiency on depression levels in breast cancer patients.

Material and Methods: A total of 99 breast cancer patients were included in the study, and sociodemographic data, treatment information, and lifestyle factors were recorded. Depression levels were evaluated using the Beck Depression Inventory, and B12 and folate levels were measured through laboratory tests. Statistical analyses were performed using the SPSS software, and the Mann-Whitney U test was used.

Results: Patients who smoked and used alcohol had significantly higher depression scores ($p=0.009$ and $p=0.028$, respectively). Additionally, patients with low B12 vitamin levels had significantly higher depression scores ($p=0.036$). Similarly, patients with folate deficiency also had higher depression scores ($p=0.015$).

Conclusion: This study demonstrates that B12 and folate deficiency can increase depression levels in breast cancer patients. Correcting B12 and folate levels in the management of depression may help improve the quality of life and positively influence the treatment process. Regular monitoring of B12 and folate levels and providing necessary treatment and support are essential in clinical practice.

Keywords: Vitamin B12, Folate, Depression, Breast cancer

INTRODUCTION

Breast cancer is the most common type of cancer among women worldwide and represents a significant health concern, especially in developed countries (1). Treatments and lifestyle changes associated with breast cancer can impact patients' physical and psychological well-being (2). This situation reduces the quality of life for patients and paves the way for the emergence of psychological issues, particularly depression (3).

Depression is a frequently observed condition among breast cancer patients, adversely affecting their quality of life (3). Various factors can influence the development of depression, with biochemical factors holding significant importance (4). Two factors that play a role in the biochemical mechanism of depression are deficiencies in vitamin B12 and folate (also known as folic acid) (4). Insufficiency of B12 and folate can lead to an increase in homocysteine levels, which in turn can cause neurotransmitter imbalances and contribute to depression (5). Furthermore, deficiencies in B12 and folate can affect brain functions and nervous system health, resulting in cognitive impairments and a worsening of depressive symptoms (6,7).

This study investigates the impact of B12 and folate deficiencies on depression levels in breast cancer patients. The findings from this research are considered crucial, as correcting B12 and folate levels in managing depression may enhance the quality of life and positively influence the treatment process for breast cancer patients.

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Additionally, this study was conducted to determine the relationship between B12 and folate deficiencies and depression levels and how this association interacts with other potential factors (e.g., age, gender, socio-economic status). The results obtained from this study could provide significant insights for healthcare professionals and breast cancer patients, aiding in developing new strategies to improve patients' quality of life and mitigate the effects of depression.

MATERIAL and METHODS

This study is designed as a prospective and observational research, aiming to examine the relationship between depression and the levels of vitamin B12 and folate in breast cancer patients. The present study was conducted strictly following the principles outlined in the Declaration of Helsinki. Ethical approval for the study was obtained from the appropriate ethics committee, and all participants provided informed consent before participating in the study. The study was conducted with the approval of the Ethics Committee of X University School of Medicine (Ethics Committee Number: 2021-514-208-3), and written informed consent was also obtained from the patients.

Participants:

Ninety-nine female patients between the ages of 18 and 65 years, diagnosed with breast cancer and undergoing treatment at a city hospital in Istanbul, were included in the study. The median time between diagnosis and interview of the patients participating in our study was 25 months (minimum 15 - maximum 84). The participating patients had no pre-existing neuropsychiatric disorders, alcohol dependency, drug addiction, or any diseases related to B12 vitamin or folate deficiency.

Data Collection:

The sociodemographic and clinical data of the patients were collected from hospital records and through face-to-face interviews with the patients. These data include sociodemographic factors such as age, education level, marital status, occupation, and income level; treatment methods applied, such as radiotherapy, chemotherapy, and hormone therapy; and lifestyle factors like physical activity levels, dietary habits, and smoking status (Table 1).

The depression levels of the patients were assessed using the Beck Depression Inventory (BDI), which is a 21-item measurement administered through face-to-face interviews. The BDI scores range from 0 to 63, with higher scores indicating more severe levels of depression.

Venous blood samples were taken from the patients to measure the levels of vitamin B12 and folate using spectrophotometric methods.

Statistical Analysis:

Descriptive statistics, Mann-Whitney U test, correlation analysis, and multiple regression analysis were utilized to analyse the obtained data. A significance level of $p < 0.05$ was considered for all analyses. All statistical analyses were conducted using the SPSS software (Version 22; SPSS, Inc. Chicago, IL).

RESULTS

This study undertook a comprehensive evaluation of the included 99 breast cancer patients, assessing their demographic and clinical characteristics, as well as their B12 vitamin and folate levels, in correlation with their depression status.

The participants were categorized into distinct depression groups, with 58.6% experiencing minimal depression (scores ranging from 0 to 9), 24.2% facing mild depression (scores between 10 and 16), 13.1% encountering moderate depression (scores from 17 to 29), and 4% reporting severe depression (scores between 30 and 63). These depression levels are presented in Table 2. Regarding B12 vitamin levels, the study identified that 24.2% of the participants had low levels, while 75.8% exhibited normal or high levels. Similarly, for folate levels, 28.3% of the participants displayed low levels, while 71.7% showed normal folate levels.

The main focus of this study was to investigate various factors that could influence the levels of depression among breast cancer patients. The results indicated that depression scores were statistically significantly higher in patients who smoked, consumed alcohol, underwent axillary dissection, and had low B12 levels or folate deficiency. Specifically, the depression scores of patients who smoked ($p = 0.009$) and those who used alcohol ($p = 0.028$) were found to be higher compared to patients without these habits. Additionally, patients who underwent axillary dissection had higher depression levels ($p = 0.029$) compared to those who underwent sentinel dissection. Furthermore, patients with low B12 levels ($p = 0.036$) and those with folate deficiency ($p = 0.015$) also exhibited higher depression scores compared to patients without these deficiencies.

Table 1. Sociodemographic characteristics and clinical data of the patients.

Sociodemographic/Clinical Characteristics	No. of Patients	Percentage (%)
Marital status		
Married	79	80,6
Single	7	7,1
Widowed	13	13,2
Educational level		
No formal schooling	10	10,1
Primary/ secondary school	53	53,5
High school	26	26,3
University	10	10,1
Menopausal status		
Premenopausal	53	53,3
Postmenopausal	46	46,5
Gave birth before		
Yes	83	83,8
No	16	16,2
Smoking status		
Non-smoker	74	74,4
Smoker	25	25,3
Alcohol use		
Non-drinker	88	88,9
Drinker	11	11,1
Other diseases		
No	61	61,1
Yes	38	38,4
Family history of breast cancer		
No	51	51,1
Yes	48	48,5
Operation type		
Mastectomy	33	33,3
Breast conserving surgery	65	65,7
Axillary lymph node dissection	32	32,3
Sentinel lymph node dissection	66	66,7

Table 2: Number and percentage distribution of patients according to their depression levels

Depression level (score)	Number of patients (n)	Percentage (%)
Minimal (0-9)	58	58,6
Light (10-16)	24	24,2
Medium (17-29)	13	13,1
Severe (30-63)	4	4

DISCUSSION

This study aimed to examine the impact of various factors, including vitamin B12 and folic acid deficiency, smoking and alcohol use, and axillary dissection, on depression levels in breast cancer patients. The results revealed that low vitamin B12 and folic acid levels, as well as smoking, alcohol consumption, and axillary dissection, were associated with higher levels of depression in these patients.

Similar findings have been reported in other studies within the literature. For instance, Ulusoy et al. (7) observed higher depression levels in patients with low vitamin B12. Similarly, Maunsell et al. found that patients who underwent axillary dissection experienced elevated depression levels compared to those who underwent sentinel dissection (8).

Although more respectful and of multidisciplinary competence, the different surgical approaches could still have a negative psychological and emotional impact, including perception of one's body image. Overall body image perception appears to be better after conservative breast surgery than mastectomy, regardless of whether reconstructive surgery is performed. But a panel of breast cancer surgeons disagreed, confirming that overall body image perception may likely be influenced by unknown factors other than surgical techniques and cosmetic results. However, patients who underwent axillary dissection may have been more prone to depression due to the perception that their disease was at a more advanced stage compared to patients who underwent sentinel lymph node dissection.

In our study, this also yielded statistically significant results. Additionally, axillary dissection may have increased this negative effect by causing an increase in long-term arm edema and arm pain.

The literature consistently supports the impact of smoking and alcohol use on depression levels, which aligns with the findings of this study. Burgess et al. (9) demonstrated higher depression levels in breast cancer patients who smoked, while Holahan et al. (10) showed that depression levels were elevated in patients who used alcohol. The results of this study underscore the significance of factors such as vitamin B12 and folic acid deficiency, smoking and alcohol use, and axillary dissection in potentially increasing depression levels among breast cancer patients. Managing these factors is of utmost importance in improving the overall quality of life for patients. Additionally, it underscores the significance of considering depression as a pivotal element in the treatment process. By addressing these factors proactively, healthcare providers can better support breast cancer patients in coping with depression and improving their well-being throughout their treatment journey.

The distribution of participants based on depression levels in this study aligns with similar studies in the literature, indicating consistent trends. For instance, Ganz et al. (11) reported a depression prevalence of 41.5% among breast cancer patients, which closely corresponds to the combined rates of mild, moderate, and severe depression levels observed in this study (41.3%). These parallel findings strengthen the validity of the current study's results and reinforce the notion that depression is a common concern among breast cancer patients. Understanding the prevalence of depression in this context is essential for healthcare professionals to provide appropriate support and interventions to enhance the psychological well-being of patients throughout their cancer journey. Recognizing the similarities in the distribution of depression levels, healthcare providers can refine their strategies to more effectively address the emotional needs of breast cancer patients.

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Furthermore, the findings of this study align with similar depression levels reported in other studies in the literature. For instance, the study conducted by Burgess et al. (9) found signs of depression in 37% of breast cancer patients, which closely matches the combined rates of mild, moderate, and severe depression levels observed in this study. The consistent conclusion that depression is prevalent among breast cancer patients and warrants consideration during treatment is in harmony with the existing literature. It highlights the importance of addressing the psychological well-being of patients as an integral part of their cancer care.

Regarding the impact of factors such as education level, having children, number of children, menopause status, and age on depression, the findings of this study present some differences and similarities when compared to other studies. Notably, the study by Lorant et al. (12) revealed a higher risk of depression in individuals with lower education levels, which contrasts with the lack of significant impact of education level observed in this study.

Similarly, the study by Freeman et al. (13) reported higher depression levels in postmenopausal women compared to

premenopausal women, differing from the findings of this study regarding menopause status. Additionally, Kessler et al. (14) suggested that depression risk is higher at younger ages and decreases with increasing age, which is not reflected in the results of this study.

These discrepancies can be attributed to various factors, such as differences in study design, sample size, measurement methods, and cultural and socio-economic factors. Each study's unique context and methodology may contribute to varying outcomes when investigating the impact of these factors on depression levels. For a comprehensive understanding of depression in breast cancer patients, it is crucial to review the collective evidence from multiple studies, taking into account both commonalities and variations while considering various influencing factors. By doing so, healthcare professionals can develop more tailored and effective strategies for addressing depression and supporting the overall well-being of breast cancer patients.

The limitations of this study are related to the sample size, geographical location, and socio-economic diversity of the patients. To increase the generalizability of the study, larger sample sizes and multicenter studies involving participants from different regions are needed. Furthermore, more detailed data collection and analysis methods are required to control for other potential factors that may influence the study's outcomes, such as sleep patterns, stress levels, and genetic factors.

CONCLUSION

This study sheds light on the diverse factors influencing depression levels among breast cancer patients. By considering lifestyle changes, correcting nutrient deficiencies, and providing psychological support, healthcare professionals can offer more effective interventions and treatment approaches. Ultimately, this holistic approach holds the potential to enhance patients' quality of life and positively influence their overall treatment journey.

Highlights

- Breast cancer's prevalence and its physical and psychological effects underscore the need to address patients' mental well-being.
- Depression frequently emerges among breast cancer patients, potentially linked to biochemical factors and treatments.
- Vitamin B12 and folate deficiencies may contribute to depression through homocysteine-related neurotransmitter imbalances.
- The study's multifaceted approach identifies correlations between depression and factors like smoking, alcohol use, surgery type, and vitamin deficiencies.
- Insights enhance healthcare strategies, emphasizing tailored interventions to manage both psychological and physiological aspects of breast cancer patients' well-being.

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018 Nov;68(6):394–424.
2. Ganz PA. Psychological and social aspects of breast cancer. *Oncology (Williston Park)*. 2008 May;22(6):642–6, 650; discussion 650, 653.
3. Massie MJ. Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr*. 2004;(32):57–71.
4. Bottiglieri T. Homocysteine and folate metabolism in depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2005 Sep;29(7):1103–12.
5. Gilbody S, Lewis S, Lightfoot T. Methylene tetrahydrofolate reductase (MTHFR) genetic polymorphisms and psychiatric disorders: a comprehensive review. *Am J Epidemiol*. 2007 Jan 1;165(1):1–13.
6. Reynolds EH. Folic acid deficiency and its neurological consequences. In 2014. p. 927–43.
7. Ulusoy IS, Horasanli B, Kulaksizoglu S. The correlation between vitamin B12 and vitamin D levels and self-reported cognitive complaints in individuals with initial episode major depressive disorder. *Dusunen Adam: The Journal of Psychiatry and Neurological Sciences*. 2021;34:64–72.
8. Maunsell E, Brisson J, Deschênes L. Psychological distress following initial breast cancer treatment: Identifying potential risk factors. *Cancer*. 1992 Jul 1;70(1):120–5.
9. Burgess C, Cornelius V, Love S, Graham J, Richards M, Ramirez A. Depression and anxiety in women with early-stage breast cancer: A five-year observational cohort study. *BMJ*. 2005 Mar 26;330(7493):702.
10. Holahan CJ, Moos RH, Holahan CK, Brennan PL. Social context, coping strategies, and depressive symptoms: An expanded model with cardiac patients. *J Pers Soc Psychol*. 1997 Apr;72(4):918–28.
11. Ganz PA, Desmond KA, Belin TR, Meyerowitz BE, Rowland JH. Predictors of sexual well-being in women after a breast cancer diagnosis. *J Clin Oncol*. 1999 Aug;17(8):2371–80.
12. Lorant V, Deliège D, Eaton W, Robert A, Philippot P, Ansseau M. Socio-economic disparities in depression: A meta-analysis. *Am J Epidemiol*. 2003 Jan 15;157(2):98–112.
13. Freeman EW, Sammel MD, Lin H, Nelson DB. Associations of hormones and menopausal status with depressed mood in women with no prior history of depression. *Arch Gen Psychiatry*. 2006 Apr;63(4):375–82.
14. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005 Jun;62(6):593–602.