Demographic and Clinical Correlates of Breast Cancer Patients with Depression

Ahmed Rady[1,†], Osama Elkholy[1], Heba Abouelwafa[1], Adel Elsheshai[1], Saed Elnoium[2], Ahmed Mohammed[3]

ABSTRACT

Background and objectives

Breast cancer patients are vulnerable to depression with prevalence varying between 11 and 86% in literature with direct and indirect impact on compliance to treatment, quality of life and response to therapeutic course. Our study aims to identifying the profile of patients with cancer breast whom symptoms exceed normal reactive sadness to depressive manifestation necessitating psychiatric and psychological intervention.

Methods

100 female patients with breast cancer diagnosis were recruited from Alexandria Police Hospital after consenting they were subject to mammogram, laboratory investigations for calcium, alkaline phosphatase, renal, hepatic functions and complete blood picture and thyroid profile. Hamilton Rating Scale and structured demographic data questionnaire was to collect relevant data.

Results

The prevalence of moderate to severe depressive symptoms on HAM-D was 52%, Significant statistical association was found between patients with depressive manifestations and postmenopusal state ($p<0.001$), with widowed and divorced ($p<0.001$), family history of brease cancer ($p<0.001$), advanced cancer staging ($p<0.001$), presence of Infiltrative ductal carcinoma ($p<0.001$) and type of surgery whether lumbectomy or modifies radical mastectomy ($p<0.05$). However the presence of brain metastasis, adjuvant chemotherapy or presence of family history of psychiatric illness didn't show statistical difference.

Conclusion

Depression is a common illness among breast cancer patients with particular vulnerable group among those postmenopausal widowed and divorced with advanced stage having rather infiltrative ductal carcinoma.

Keywords

Breast cancer, Depression, HAM-D, Ductal carcinoma

[1]Department of Psychiatry, Alexandria University School of Medicine, Egypt

[2]Department of Diagnostic Radiology, Alexandria University School of Medicine, Egypt

[3]Department of Psychiatry, Alexandria Police Hospital, Egypt

[†]Author for correspondence: Ahmed Rady, MD29, Nabi Daniel StAlexandria 21131, Egypt, Tel: +2 01282441053; email: dr_ahmed_rady@yahoo.fr

Introduction

Breast cancer patients are vulnerable to depression at all stages of the illness, from appearance of first symptoms, time of diagnosis, during treatment and palliative care. An important challenge to clinicians is to identify the point when normal sadness or distress associated with cancer turns to pathological depressive manifestations with impact on therapeutic compliance and outcome [1]. Depression is often underestimated in breast cancer with prevalence varying between 10% and 25%, though depression was found to be highest at diagnosis, depression during survivorship was not adequately studied. During the follow up care, survivors' psychological needs were often neglected [2]. The use of tamoxifen, an anti-estrogen for treatment of hormone sensitive breast cancer has also been associated with depression [3]. Study of depressive symptoms among patients with breast cancer has been under focus within the therapeutic community. It has been found that depressive symptoms do have negative impact on illness course, response to treatment, compliance with medications, quality of life and even all-cause mortality rate when other covariants are adjusted for statistical reasons [4]. It seems that similar findings are found in patients having diagnosis of Major depressive disorder before discovering their cancer breast. Such consistent findings encouraged many authors to recommend therapeutic approach to depressive symptoms weather antidepressant medications or psychological interventions such as meditation and CBT psychotherapy [5].

From economic perspective, women with breast cancer tended to impose higher costs on health insurance system. Such finding was even tested for racial differences and revealed no difference! Though prevalence of breast cancer tended to be higher among white women compared to black women but prevalence of depression among both races were similar with a near similar increased therapy costs compared to those women with breast cancer that don't fulfill criteria for major depression [6].

In the current study we try to profile breast cancer patients at risk of pathological depressive manifestations in order to raise awareness of an underestimated mental health problem among such vulnerable group.

Subjects and Methods

It's a cross sectional observational study where 100 adult female patients with breast cancer consulting outpatient oncology clinic at Alexandria Police Hospital were recruited after explanation of study's purpose and having written consent. No age restriction were imposed, patients having chronic debilitating medical illness, hypothyroidism or taking tamoxifen were excluded. Structured Demographic data questionnaire was applied to participants, blood picture, renal function, hepatic function; electrolytes assessment and brain CT were done. Hamilton Rating Scale for depression HAM-D was passed to screen for depressive symptoms, those showing pathological depressive symptoms were subject to structured clinical Interview for DSM IV-TR to confirm diagnosis of Major Depressive Disorder MDD

Hamilton Rating Scale for Depression HAM-D: is a multiple item questionnaire used to provide an indication of depression and guide to evaluate progress and recovery. The questionnaire is designed for adults and is used to rate severity of depression by probing mood, feeling of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss and somatic symptoms. Initially considered the golden standard for rating depression in clinical research. The original 1960 version contains 17 items to be rated, but four other questions are not added to total score and used to provide additional clinical information. Each item on the questionnaire is scored on a three or five point scale, depending on item, and total score is calculated. Assessment time estimated at 20 min. A score 0-7 is considered normal, score of 20 or higher indicates moderate to severe depression and are often required for entery into clinical trial [7].

■ Statistical analysis

After data collection, they were fed into computer after coding using Statistical Package for Social sciences SPSS version 11.5 for data analysis and tabulation. Descriptive analysis was done, parametric values arithmetic mean, median and standard deviations were calculated, Chi square test was used as non-parametric testing tool. Type one statistical error was set<0.05

Results

■ Descriptive statistics

Age ranged from 21 to 74 with mean 47.32 ± 13.37, 58% were menopausal. As for marital status they were single, married, widowe and divorced 12%, 72%, 14% and 2% respectively

0.66% of our sample had a positive family history for breast cancer and 18% had positive family history for psychiatric illness, 8% had positive family history for depression. As regards staging 2%, 42%, 46% and 10% were those having stage I, II, III and IV respectively. 18% were receiving chemotherapy. 6% had brain metastasis on scanner radiology. 18% had lumbectomy versus 36% had modified radical mastectomy. Histopathological subtyping of tumor was 20% fibroadenomatous dysplasia and 80% infiltrative ductal carcinoma.

The mean total score for HAM-D was 14 ± 4.99 with distribution according to intensity of depressive symptoms as shown in **Table 1**.

■ Inferential statistics

Different demographic and clinical parameters have shown significant association with presence of depressive symptoms as shown in **Table 2**.

Among the sample 54 have undergone surgical intervention either modified radical mastectomy or lumbectomy, those who had the former had more intense depressive symptoms with significant statistical difference **(Table 3)**.

Our study didn't show association between intensity of depression and positive family history of psychiatric disorder, presence of brain metastasis or use of adjuvant chemotherapy (p>0.05)

Discussion

Depression among breast cancer patients is prevalent and underestimated with wide range of variability according to sample size, selection criteria, screening tool as well as ethnic background. Depression not only affects the quality of life but also compromises compliance

Table 1: The mean total score for HAM-D was 14 ± 4.99 with distribution according to intensity of depressive symptoms.

Hamilton Scale for depression HAM-D	No. (N=100)	%
No depression	14	14
Mild depression	32	32
Moderate depression	34	34
Severe depression	20	20
Total HAM-D score ranged 6-24 with mean 14 ± 4.99		

Table 2: Different demographic and clinical parameters have shown significant association with presence of depressive symptoms.

	Hamilton Depression Rating Scale HAM-D				Statistical test
	Normal N=14	Mild N=32	Moderate N=34	Severe N=20	
Premeopausal (N=42) Postmeopausal (N=58)	12 2	10 22	14 20	6 14	X^2=13.7[*]
Single (N=12) Married (N=72) Widowed (N=14) Divorced (N=2)	10 4 0 0	2 28 2 0	0 30 2 2	0 10 10 0	X^2=54.4[*]
+ve family history for breast cancer N=34 -ve family history for breast cancer N=66	0 14	10 22	10 24	14 6	X^2=19.2[*]
Stage I (N=2) Stage II (N=42) Stage III (N=46) Stage IV (N=10)	0 12 2 0	0 22 10 0	2 8 22 2	0 0 12 8	X^2=52.7[*]
Infiltrative ductal carcinoma (N=80) Fibroadenomatous dysplasia (N=20)	4 10	24 8	32 2	20 0	X^2=28.6[*]
+ve history of recurrence (N=20) -ve history for recurrence (N=80)	0 14	2 30	10 24	8 12	X^2=14.1[*]
***P<0.05**					

Table 3: Intense depressive symptoms with significant statistical difference.

Type of Surgery (N=54)	Hamilton Depression Rating Scale HAM-D				Statistical test
	Normal N=6	Mild N=18	Moderate N=16	Severe N=14	
Modified Radical Mastectomy (N=36) Lumbectomy (N=18)	2 4	12 6	8 8	14 0	X^2=13.3[*]
***P<0.05**					

with anticancer treatment, associated with prolonged hospitalization and may have negative effect on prognosis and even survival. Among patients with breast cancer, depression has been reported to be related to a significantly reduced chance of survival over 5 years [8].

In agreement with our study that reveals 32% with mild symptoms and 54% moderate to severe symptoms of depression, Sharma and colleagues found 93.4% prevalence of depression among breast cancer, 29.2%, 60% and 4.2% mild, moderate and severe depression respectively [9]. Chinese study revealed prevalence of 26% and half of them fulfilled diagnostic criteria for major depression. Some authors showed lower prevalence of depression 11.5%, 64.3% of them had mild depression using shortened beck depression inventory [10]. The great variation in these results could be attributed to difference in methodology, ethnicity, and time between diagnosis and screening for depression as well as screening scales. However, those findings reflect a high prevalence of depression among women with breast cancer regardless ethnic background.

As for age group as categorized into pre and postmenopausal, authors highlighted that menopausal state has significantly associated with depression in breast cancer patients since estrogen acts as cholinergic agonist and increases norepinephrine activity, those multiple modulations suggest that estrogen may have an antidepressant like effect and enhances neurotransmitter activity [11]. Other authors didn't find any effect of age or menopausal state on depression [12], some authors even found, in contrast to our study, that younger age being more associated with depression [13]. However lot of other demographic and tumor related factors may come with confusion biais effect on results explaining such variability. Though some authors attribute higher prevalence of depression among postmenopausal to the pharmacological antidepressant effect of estrogen but contrary results in other studies have been attributed to psychological impact on younger age with higher rates of anger and poor acceptance of having cancer in their young age [12,13].

Our study revealed higher prevalence of depression among widowed and divorced patients with high significance (p<0.001), some authors came with results in agreement with ours like Chen et al. [10]. On the other hand, Carvalho group found no association between depression and marital status [12].

Such difference in results may be attributed to ethnic and cultural background variability as well as age range of samples. Such finding can be explained by lack of marital social support which normally serves as a clinically positive attribute that improves outcome to treatment.

Carvalho group found +ve family history of breast cancer to have no association with depression but highlighted a significant association between +ve family history of psychiatric disorders and depression. Both results are the opposite of our results [12]. A difference that can be explained by sample size and screening scales used in various studies. Presence of family history may convey persistent cognitive negative thoughts related to collective punishment and insecurity.

As for tumor correlates, our study found higher depression rates with advanced stage, infiltrative ductal carcinoma histopathological subtype and +ve history for recurrence. Our results come in agreement with studies carried out by different authors and can be attributed to poor prognosis and higher recurrence rate and poor quality of life with such tumor correlates of severity and poor outcome [14]. These results also explain the association between intensity of depression and type of surgical intervention practiced, since lumbectomy is rather preserved for mild cases with early stages. Though the presence of brain metastasis that should theoretically categorize tumor as being more advanced, our study failed to show any association between presence of brain metastasis and depression, in agreement with results revealed by many authors [15,16] which may be attributed to the small sample size of patients having brain metastasis in our sample

Finally, as regards effect of preoperative adjuvant chemotherapy, though our study showed no association with depression which reflects replication of previous authors [12]. Some other research groups found chemotherapy use to be correlated with less depressive symptoms and attributed their findings to the fact that responders to chemotherapy showed improvement of their depressive symptoms due to diminished lumb size and reduced pain and manifestations directly related to space occupying lesion though of chemotherapy adverse effects [17].

Conclusion

Our study highlights the high prevalence of depressive manifestations among patients with breast cancer that set an alarm to a diagnosis

that necessitate a multidisciplinary management with an important role for mental health professionals. Profiling patients at higher risk for depression among those widowed or divorced, postmenopausal state. Some tumor correlates like history of recurrence, advanced staging, histopathological subtyping as well as surgical intervention practiced in patients are associated with more intense depression, raising awareness alarm to screen for depression among those particular vulnerable group rather than overlooking depression and underestimating it

by considering that as normal reactive sadness

Limitation

Our study is limited by sample size that went smaller with sub-categirization leading to use of nonparametric rather that parametric statistical test. Screening for depression was made using only one psychological scale that was not confirmed by more scaling to confirm consistent sub-categorization into mild, moderate and severe depressive symptoms

References

1. Henderson TO, Amsterdam A, Bhatia S, *et al*. Systematic review: Surveillance for breast cancer in women treated with chest radiation for childhood, adolescent or young adult cancer. *Ann. Intern. Med* 152(1), 444-455 (2010).

2. Allen JD, Savadatti S, Levy AG. The transition from breast cancer 'patient' to 'survivor'. *Psychooncology* 18(1), 71-78 (2009).

3. Strong V, Waters R, Hibberd C, *et al*. Management of depression for people with cancer (SMaRT oncology 1): A randomized trial. *Lancet* 372 (9632), 40-48 (2008).

4. Boyle CC, Stanton A, Ganz PA, *et al*. Improvement of emotion regulation following mindfulness meditation: effect on depressive symptoms and perceived stress in younger breast cancer survivors. *J. Consult. Clin. Psychol* 85(4), 397-402 (2017).

5. Liang X, Margolis K, Hendryx M, *et al*. Effect of depression before breast cancer diagnosis on mortality among postmenapausal women. *Cancer* 123(16), 3107-3115 (2017).

6. Husaini BA, Miller O, Novotny M, *et al*. Racial

similarities in the effects of depression on hospital cost of breast cancer. *Cancer. Res* 77(13), (2017).

7. Hedlund J, Viewig B. The Hamilton Rating Scale for depression: A comprehensive review. *J. Operational. Psychiatry* 10(1), 149-165 (1979).

8. Ravdin PM, Cronin KA, Howlader N, *et al*. The decrease in breast cancer incidence in 2003 in United States. *N. Engl. J. Med* 356(1), 1670-1674 (2007).

9. Sharma A, Zhang J. The prevalence of depression and its predictors among breast cancer patients in Nepal. *Asian. J. Psychiatry* 16(1), 10 (2015).

10. Chen X, Zheng Y, Zheng W, *et al*. Prevalence of depression and its related factors among Chinese women with breast cancer. *Acta. Oncologica* 48(8), 1128-1136 (2009).

11. Fann JR, Thomas-Rich AM, Katon WJ, *et al*. Major depression after breast cancer: A review of epidemiology and treatment. *Gen. Hosp. Psychiatry* 30(2), 112-126 (2008).

12. Carvalho SM, Bezerra IM, Freitas TH, *et al*. The prevalence of major depression in patients with breast cancer. *J. Human. Growth. Dev*

25(1), 68-74 (2015).

13. Mehnert A, Koch U. Psychological comorbidity and health related quality of life and its association with awareness, utilization and need for psychosocial support in a cancer register-based sample of long term breast cancer survivors. *J. Psychosom. Res* 64(4), 383-91(2008).

14. Papoola AO, Adewuya AO. Prevalence and correlates of depressiv e disorders in outpatients with breast cancer in lagos, Nigeria. *Psychooncology* 21(6), 675-679 (2012).

15. Cordes MC, Scerwath A, Ahmed T, *et al*. Distress, anxiety and depression in patients with brain metastasis before and after radiotherapy. *BMC. Cancer* 14(1), 731-736 (2014).

16. Wadasadawala T, Gupta S, Bagul V. Brain metastasis from breast cancer: management approach. *J. Can. Res. Ther* 3(1), 157-165 (2007).

17. Chintamani, Gogne A, Khandelwal R, *et al*. The correlation of anxiety and depression levels with response to neoadjuvant chemotherapy in patients with breast cancer. *JRSM. Short. Rep* 2(3), 15 (2011).