

## Childhood Psychological Trauma and Psychiatric Comorbidity in Patients with Breast Cancer

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### ABSTRACT

**Background:** Most patients with breast cancer experience some psychosocial distress. These increased levels of distress increase the risk of depression and anxiety with subsequent adverse effect on compliance to cancer treatment. In patients with breast cancer, childhood trauma is associated with higher levels of fatigue, stress and psychological distress and has a significant impact on patients' reaction and adjustment to cancer diagnosis.

**Objective:** The aim of this study was to detect psychiatric comorbidity and impact of childhood trauma in patients with breast cancer and study their relations with tumor grading and histopathological characteristics.

**Patients and Methods:** In this cross-sectional study, we recruited 150 patients diagnosed with breast cancer. Participants were females aged 18 years or older. Patients with history of another cancer, comorbid serious medical condition, in their investigation phase of cancer diagnosis or those who refused to participate in the study were excluded. The tools applied to participants were the Symptom Checklist 90 Revised and Childhood Trauma Questionnaire.

**Results:** 113 patients (75.3%) had psychiatric comorbidity; somatization was the most common psychiatric comorbidity (58.7%) followed by depression (40.7%). Patients reported severe to extreme childhood trauma in domains of physical neglect (28%), physical abuse (22.7%), emotional neglect (7.3%), emotional abuse (18%) and sexual abuse (2%). Patients with psychiatric comorbidity had more grade III and IV in tumor grading. Patients with grade IV breast cancer had more severe psychiatric symptoms.

**Conclusions:** Psychiatric comorbidity and childhood trauma are common in patients with breast cancer. Patients with psychiatric comorbidity have more grades III and IV tumor grading. Patients with grade IV breast cancer have more severe psychiatric symptoms.

**Keywords:** Breast cancer, Childhood trauma, Psychiatric comorbidity

### INTRODUCTION

Breast cancer is the most common cancer in females in developed countries<sup>(1)</sup>. In Egypt, breast cancer is the most common malignancy in women, accounting for 38.8% of cancers in this population, with the estimated number of breast cancer cases nearly 22,700 in 2020 and forecasted to be approximately 46,000 in 2050. It is estimated that the breast cancer mortality rate is around 11%, being the second cause of cancer-related mortality after liver cancer<sup>(2)</sup>.

Most patients with breast cancer experience some psychosocial distress as problems in interpersonal relationships, financial strains and emotional distress<sup>(3)</sup>, as about one half of breast cancer patients experience significant distress levels<sup>(4)</sup>. These high levels of distress increase the risk of depression and anxiety with subsequent adverse effect on compliance to cancer treatment<sup>(5,6)</sup>.

The common psychosocial difficulties reported by patients with breast cancer include fear of recurrence, disturbed body image, physical symptoms, sexual dysfunction, illness and treatment related persistent anxiety, marital problems, and mortality related existential concerns<sup>(7)</sup>.

In patients with breast cancer, childhood trauma is associated with higher levels of fatigue, stress and psychological distress<sup>(8)</sup>, and has a significant impact on patients' reaction and adjustment to cancer diagnosis<sup>(9)</sup>, as exposure to childhood trauma together with environmental stress may lead to gene and gene expression alterations<sup>(10)</sup>. The patients with breast

cancer who were exposed to childhood trauma were found to suffer from cognitive dysfunction following chemotherapy<sup>(11)</sup>, and to be at increased risk of emotional distress related to cancer<sup>(12)</sup>.

During the first year following diagnosis of breast cancer, patients are particularly vulnerable to anxiety and depression<sup>(5)</sup>. Unrecognized and untreated depression increases functional impairment and physical symptoms and leads to poor adherence to treatment leading to reduced quality of life, more substance use, anxiety, sleep disorders, sexual dysfunction, immune system dysfunction, more fatigue and pain, rapid cancer progression and increased mortality<sup>(13-15)</sup>.

The rates of comorbid psychiatric disorders with breast cancer following diagnosis and recurrence range from 14% to 38% of patients<sup>(12,16)</sup>. Moreover, because of illness and treatment related variables as physical symptoms, the rates of developing serious levels of depression and anxiety increase<sup>(17)</sup>.

In Egypt, 48% of patients with breast cancer were found to have psychiatric problems; the rates were 38.8% for major depressive disorder, 29.6 % for generalized anxiety disorder and 9.2% for panic disorder<sup>(18)</sup>.

In comprehensive management of patients with breast cancer, it is necessary to enhance coping strategies, improve environmental and personal resources, and to implement counseling, psycho-education, individual as well as group psychotherapy,

psychopharmacological interventions, self-help groups and peer support <sup>(19)</sup>.

The aim of this study was to detect psychiatric comorbidity and impact of childhood trauma in patients with breast cancer and study their relations with tumor grading and histopathological characteristics.

## PATIENTS AND METHODS

This cross sectional study was conducted in Minia Health Insurance Hospital and Minia Oncology Center. Aim of the study was discussed and explained to oncology department team who helped us in recruiting patients diagnosed with breast cancer. We recruited 150 patients diagnosed with breast cancer who met our inclusion and exclusion.

**Inclusion Criteria:** Female patients diagnosed with breast cancer, and age above 18 years old.

**Exclusion criteria:** Refusal of the patient to participate in the study procedures, patient who had a previous diagnosis of another cancer in the past, patient who were undergoing investigations for cancer, and patient who were suffering from any other serious illness.

### Tools of the study:

#### *Symptom Checklist 90 Revised (SCL-90-R)*<sup>(20)</sup>:

The **Symptom Checklist-90-R (SCL-90-R)** is a self-report relatively brief psychometric assessment. It is designed to evaluate symptoms of psychopathology and psychological problems. It is also used in following the outcome and progress of psychological as well as psychiatric interventions for research purposes <sup>(20)</sup>.

It is normed on individuals 13 years and older and consists of 90 items giving nine scores for primary symptom dimensions and three scores representing global distress indices. The primary symptom dimensions are somatization, obsessive-compulsive, depression, anxiety, interpersonal sensitivity, hostility, phobic anxiety, psychoticism, paranoid ideation, and a category of "additional items" <sup>(21)</sup>.

There are three SCL-90 global indices: 1) Global Severity Index (GSI): average score of the questionnaire's 90 items, 2) Positive Symptom Distress Index (PSDI): average score of the above zero scored items, and 3) Positive Symptoms Total (PST): number of the above zero scored items. The GSI is supposed to be the disorder's current level best single indicator, while PSDI is an intensity measure assessing patient's response style (attenuating or augmenting symptoms) <sup>(20)</sup>.

#### *Childhood Trauma Questionnaire (CTQ)*:

This is a 28-item inventory assessing five domains; three childhood abuse domains (sexual, physical, and emotional), and two childhood neglect

domains (physical and emotional). It has excellent specificity and sensitivity regarding scores of each domain in properly classifying cases of neglect and abuse in patients with psychiatric disorders <sup>(22)</sup>. It is concerned with early childhood trauma occurring at or before age 12 years. The current study employed 5 data points representing the CTQ subscales: sexual abuse, physical abuse, emotional abuse, emotional neglect and physical neglect. On each subscale, scores of 10 or higher were considered positive for abuse while scores of less than 10 were considered negative for abuse <sup>(22-24)</sup>.

### Ethical consideration:

**We explained the aim as well as the procedures of the study to all participants after reassuring them about confidentiality. All participants provided a written informed consent before enrollment in the study. The approval to conduct this study has been obtained from Minia University Academic and Ethical Committee. Data related to histopathological diagnosis such as grading and staging was collected from hospital records after taking authority permission. This study has been carried out in accordance with The Code of Ethics of the World Medical Association for studies involving humans (Declaration of Helsinki). The participants had the right to withdraw from the study at any stage without any negative consequences.**

### Statistical analysis:

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for the Social Sciences) 20<sup>th</sup> version. Descriptive statistics performed for numerical variables were mean, standard deviation (SD), median, interquartile range (IQR), minimum and maximum, while numbers and percentages were done for categorical variables. Chi square test was used for comparing groups regarding categorical variables while Independent sample t test was used for comparing groups regarding quantitative variables. P value < 0.05 was considered statistically significant.

## RESULTS

In this cross sectional study we recruited 150 patients diagnosed with breast cancer. The mean age of the sample was 51.67± 8.6 years, the majority (70%) were married and 60% were employed. Regarding contraception, 35.3% of patients had a history of oral hormonal contraception, while injectable contraception and IUD rates were 15.3% and 34.7% respectively. Forty patients (26.7%) reported positive family history of breast cancer (Table 1).

**Table (1): Sociodemographic and illness characteristics of the studied sample (N=150)**

Socio-demographic and illness related variables		Total sample (n=150)	
Age (years)	Mean± SD	51.67± 8.6	
	Median (IQR)	51 (45- 57.25)	
	Range	35- 72	
Marital status		<b>Number</b>	<b>Percent</b>
	Single	4	2.7 %
	Married	105	70.0 %
	Divorced	3	2.0 %
	Widow	38	25.3 %
Residence	Rural area	64	42.7 %
	Urban area	86	57.3 %
Employment	Employed	90	60.0 %
	Un Employed	60	40.0 %
Religion	Muslim	99	66.0 %
	Christian	51	34.0 %
Pregnant while diagnosed with Breast cancer	Yes	3	2.0 %
	No	147	98.0%
Lactation	Lactating	134	89.3 %
	Artificial Feeding	12	8.0 %
	Not lactating	4	2.7 %
Smoking	No	150	100 %
Contraception	Oral Hormonal contraception	53	35.3 %
	Injectable contraception	23	15.3 %
	Mechanical IUD	52	34.7 %
	No contraception	22	14.7 %
Family history of breast cancer	Positive	40	26.7%
	Negative	110	73.3%

SD= standard deviation, IQR: interquartile range

Psychiatric comorbidity as measured by the SCL-90-R revealed that 113 patients (75.3%) had psychiatric comorbidity; somatization was the most common psychiatric comorbidity. Among those patients with psychiatric comorbidity, there were 69 patients with Positive Symptom Distress Index (PSDI) indicating intensity of the positive symptoms, 32 patients with Positive Symptom Total (PST) and 27 with Global Severity Index (GSI) indicating that those patients were in need to start medications (Table 2).

**Table (2): Prevalence of psychiatric comorbidity in the whole sample as measured by SCL-90-R (N=150)**

SCL- 90-R	Number	Percent
Depression	61	40.7%
Somatization	88	58.7%
Obsessive Compulsive	35	23.3%
Anxiety	37	24.7%
Hostility	38	25.3%
Paranoid Ideation	11	7.3%
Phobic Anxiety	20	13.3%
Interpersonal Sensitivity	28	18.7%
Psychotic	24	16%
GSI (Global Severity Index)	27	18%
PST (Positive Symptom Total)	32	21.3%
PSDI (Positive Symptom Distress Index)	69	46%
Total number of patients with psychiatric comorbidity	113	75.3%
Total number of Patients without psychiatric comorbidity	37	24.7%

Patients reported severe to extreme childhood trauma were in domains of physical neglect (28%), physical abuse (22.7%), emotional neglect (7.3%), emotional abuse (18%) and sexual abuse (2%) (Table 3).

**Table (3): Childhood trauma as measured by Childhood Trauma Questionnaire (CTQ) in the whole sample (N=150)**

Childhood Trauma	Number	Percent
<b>Physical Neglect</b>		
Non/ Minimal	45	30.0 %
Low to Moderate	41	27.3 %
Moderate To Severe	22	14.7 %
Severe to Extreme	42	28.0 %
<b>Physical Abuse</b>		
Non/ Minimal	90	60.0 %
Low to Moderate	17	11.3 %
Moderate To Severe	9	6.0 %
Severe to Extreme	34	22.7 %
<b>Emotional Neglect</b>		
Non/ Minimal	95	63.3 %
Low to Moderate	35	23.3 %
Moderate To Severe	9	6.0 %
Severe to Extreme	11	7.3 %
<b>Emotional Abuse</b>		
Non/ Minimal	70	46.7 %
Low to Moderate	38	25.3 %
Moderate To Severe	15	10.0 %
Severe to Extreme	27	18.0 %
<b>Sexual abuse</b>		
Non/ Minimal	130	86.7 %
Low to Moderate	14	9.3 %
Moderate To Severe	3	2.0 %
Severe to Extreme	3	2.0 %
<b>Total CTQ</b>		
Non/ Minimal	50	33.3 %
Low to Moderate	64	42.7 %
Moderate To Severe	17	11.3 %
Severe to Extreme	19	12.7 %

Breast cancer patients with psychiatric comorbidity had more grade III and IV in tumor grading compared to patients without psychiatric comorbidity (all were grade II). Regarding histopathological diagnosis, psychiatric comorbidity group showed more invasive duct and squamous cell carcinomas while group without psychiatric comorbidity showed more lobular as well as metastatic carcinomas. Furthermore, the non-psychiatric comorbidity group showed more patients who were receiving hormonal as well as chemotherapy than psychiatric comorbidity patients who were found to be receiving more radiotherapy and that difference was statistically significant (Table 4).

**Table (4): Comparison between patients with and patients without psychiatric comorbidity regarding grading, histopathology and current treatment of breast cancer**

		Without psychiatric comorbidity (n=37)		With psychiatric comorbidity (n=113)		P Value
		Number	Percent	Number	Percent	
<b>Grading</b>	<b>II</b>	37	100%	103	91.2%	0.06
	<b>III</b>	0	0%	6	5.3%	0.15
	<b>IV</b>	0	0.0%	4	3.5%	0.25
<b>Histopathological Diagnosis</b>	<b>Invasive Duct Carcinoma</b>	28	75.7%	100	88.5%	0.06
	<b>Lobular Carcinoma</b>	6	16.2%	7	6.1%	0.06
	<b>Metastatic Carcinoma</b>	3	8.1%	3	2.7%	0.14
	<b>Squamous cell carcinoma</b>	0	0.0%	3	2.7%	0.32
<b>Type of current treatment</b>	<b>Hormonal</b>	6	16.2%	10	8.8%	0.21
	<b>Chemotherapy</b>	23	62.2%	67	59.3%	0.78
	<b>Radiotherapy</b>	4	10.8%	36	31.9%	<b>0.01*</b>
	<b>No treatment</b>	4	10.8%	0	0.00%	<b>&lt;0.001</b>

Regarding the relation between histopathological diagnosis of breast cancer and childhood psychological trauma as measured by CTQ, patients with squamous cell carcinoma had the highest scores on physical abuse and total CTQ scores while patients with invasive duct carcinoma had highest score in emotional neglect when compared to other histopathological diagnoses and these differences among groups were statistically significant (Table 5).

**Table (5): Comparison between histopathological diagnoses of breast cancer regarding childhood trauma as measured by CTQ**

Childhood Trauma	Invasive Duct Carcinoma	Lobular Carcinoma	Metastatic Carcinoma	Squamous cell carcinoma	Test	p- value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD		
Physical Neglect	10.91±4.86	8.85±3.13	7.50±1.64	14.00±.00	6.500	0.089
Physical Abuse	9.59±6.58	5.69±1.32	7.00±2.19	16.00±.00	9.300	<b>0.026</b>
Emotional Neglect	9.57±4.41	7.77±1.48	5.50±.55	7.00±.00	9.100	<b>0.029</b>
Emotional Abuse	10.77±5.83	9.15±2.30	6.50±.55	9.00±.00	3.030	0.387
Sexual abuse	5.64±2.10	5.46±.88	5.00±.00	5.00±.00	2.100	0.543
<b>Total CTQ</b>	<b>46.18±17.81</b>	<b>35.31±5.59</b>	<b>31.50±1.64</b>	<b>51.00±.00</b>	<b>12.600</b>	<b>0.006</b>

SD= standard deviation

As regard the relation between tumor grading and severity of comorbid psychiatric symptoms; patients with grade IV tumors had the highest scores (more severe) in depression, psychotic, anxiety, somatization, obsessive compulsive, impulsivity and GT, GSI and PSDI domains of SCL-90-R than patients with grade II and III and these differences between groups were statistically significant (Table 6).

**Table (6): Comparison between different grades of breast cancer regarding psychiatric symptomatology as measured by SCL-90-R**

Psychiatric Comorbidity	Grade II	Grade III	Grade IV	Kruskal-Wallis Test	p- value
	Mean±SD	Mean±SD	Mean±SD		
Depression	1.80±.73	2.23±.25	3.00±.00	11.332	<b>0.003</b>
Psychotic	0.57±0.68	.35±.38	1.60±.00	9.489	<b>0.009</b>
Paranoid ideation	0.78±0.86	0.67±.73	.00±.00	4.484	0.106
Anxiety	1.31±0.96	1.55±0.06	2.60±.00	6.789	<b>0.034</b>
Somatization	1.75±0.90	1.84±0.09	2.83±.00	6.367	<b>0.041</b>
Obsessive compulsive	1.25±0.86	0.80±0.06	2.50±.00	9.568	<b>0.008</b>
Impulsivity	1.01±0.88	0.83±.00	2.00±.00	6.182	<b>0.045</b>
Phobias	0.93±1.03	0.72±0.01	0.00±0.00	5.528	0.063
Extra	13.13±5.55	13.5±3.83	17.00±.00	3.791	0.150
Sensitivity	1.37±.90	1.06±.06	2.11±.00	3.792	0.150
<b>Grand Total</b>	<b>117.62±49.25</b>	<b>115.0±28.48</b>	<b>188.00±.00</b>	<b>8.802</b>	<b>0.012</b>
GSI	1.31±.55	1.28±.32	2.09±.00	8.694	<b>0.013</b>
PST	52.58±25.06	50.50±6.02	62.00±.00	2.130	0.345
Intensity	25.46±17.95	22.52±.23	20.46±.00	1.723	0.423
PSDI	2.32±.49	2.24±.28	3.03±.00	10.698	<b>0.005</b>

SD= standard deviation; GSI: Global Severity Index; PST: Positive Symptom Total; PSDI: Positive Symptom Distress Index; Extra (sleep pattern, disturbance of appetite, guilt feeling and thinking about death)

## DISCUSSION

Our objectives were to study the prevalence and contributing factors of psychiatric comorbidity in patients with breast cancer. Our participants' mean age was 51.67 years that was similar to the findings of previous studies where mean age of patients with breast cancer was 50.8 years <sup>(25)</sup>.

We found higher rates of psychiatric comorbidity (73% of patients) than previously reported figures as **Fallowfield et al.** <sup>(26)</sup> reported psychiatric comorbidity in 36.4% in their sample while **Shandilya et al.** <sup>(25)</sup> reported comorbid psychiatric disorders in 45% of their sample. These differences in rates of psychiatric comorbidity may be explained by the fact that at time of

psychiatric screening in our study, 25% had stage IIIA, 16% had stage IIIB and 26% had stage IV of breast cancer indicating advanced stages of breast cancer. Moreover, more than half of our patients were living in urban areas experiencing stressful life events in a more sensitive way than those living in rural areas due to differences in medical and psychological knowledge as well as in social network and support <sup>(25)</sup>.

As regards frequency of psychiatric comorbidity in patients with breast cancer and in agreement with previous studies that reported high rates of somatic symptoms (e.g. pain, fatigue, reduced energy and sense of weakness) <sup>(27)</sup>, major depressive disorder (38.8%), generalized anxiety disorder (29.6%) and

panic disorder (9.2%)<sup>(18)</sup>, our patients were found to suffer from somatization (58.7%), depression (40.7%), hostility (25.3%), anxiety (24.7%), obsessive compulsive (23.3%), interpersonal sensitivity (18%), psychosis (16%), phobic anxiety (13.3%) and paranoid ideation (7.3%). Moreover, **Grabsch et al.**<sup>(28)</sup> reported depression and/or anxiety in 35.7% of breast cancer patients.

#### **Probable contributing factors in psychiatric comorbidity:**

We tried to analyze each variable separately to find its impact on psychiatric condition of our participants but in fact these variables are interrelated and potential overlap cannot be completely avoided.

#### **History of childhood trauma:**

About two thirds of our participants reported different types of childhood trauma in different severity degrees where physical neglect was the most common (70%) while sexual abuse (13.3%) was least common type of childhood trauma experience. That was in line with a recent study that reported childhood trauma experience in about half of breast cancer patients<sup>(29)</sup>.

In exploring the relation between childhood trauma and breast cancer symptoms and progression, childhood emotional abuse was found to be associated with more intrusive breast cancer symptoms<sup>(30)</sup>. Furthermore, childhood neglect and abuse were associated with elevated inflammatory markers (C reactive protein and interleukin-6) in patients with breast cancer with associated increased risk of recurrence and poor response to treatment<sup>(31)</sup>. Interestingly, we found that patients with squamous cell carcinoma had the highest scores on childhood physical abuse; patients with invasive duct carcinoma had the highest scores on childhood emotional neglect. Although, we believe that there is no direct causal relationship between type of childhood trauma and type of breast cancer and that this area needs more extensive longitudinal research, previous studies reported that patients themselves believe in that as when asked to specify a cause of breast cancer, 58% reported stress as a cause of cancer development<sup>(32)</sup>.

#### **Factors related to breast cancer characteristics and treatment:**

Although, the comparison between patients with breast cancer having psychiatric comorbidity and those without psychiatric comorbidity regarding tumor grading, different histopathological characteristics, hormonal receptor characteristics, and type of current treatment revealed no statistically significant differences except for radiotherapy treatment and that these findings were in agreement with previous studies that reported the prevalence of psychiatric illness to be the same in early and advanced cases with breast cancer<sup>(33)</sup>. But when we studied the relation between tumor grading and each psychiatric symptom individually as measured by SCL-90-R we found that patients with grade IV tumors had the highest scores (more severe) in

depression, psychotic, anxiety, somatization, obsessive compulsive, impulsivity and GT, GSI and PSDI domains than patients with grade II and III and these differences between groups were statistically significant.

Logistic regression analysis was conducted to reveal factors predicting psychiatric comorbidity as the dependent variable among different variables including the five domains of childhood trauma questionnaire as independent variables and revealed that history of physical abuse was one of the predictors of psychiatric comorbidity in patients with breast cancer. That was in contrast to reports of previous studies that found emotional abuse to be the only predictor of psychiatric comorbidity in patients with breast cancer<sup>(34)</sup>. This difference may be attributed to the differential perception of psychological trauma in Arab individuals as well as the effects of socioeconomic status and methodological differences.

We believe that this area needs more extensive longitudinal multicenter research on larger samples in different countries and cultures to reveal the complex relationship between breast cancer, traumatic psychological experiences and psychiatric comorbidity.

#### **CONCLUSIONS**

Psychiatric comorbidity and childhood trauma are common in patients with breast cancer. Patients with psychiatric comorbidity have more grades III and IV in breast cancer grading. Patients with grade IV breast cancer have more severe psychiatric symptoms.

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