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Radiotherapy-induced fatigue in Palestinian breast cancer survivors

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ABSTRACT

Background: No study has investigated the cancer-related fatigue (CRF) among Palestinian breast cancer survivors. Our purpose is to assess, compare, and correlate CRF in breast cancer survivors undergoing radiotherapy (RT) with study variables.

Methods: CRF in breast cancer survivors was assessed using Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-F) (version 4). The sample consisted of 148 breast cancer survivors undergoing RT. Data was collected between 1 May 2021 and 1 September 2021. The means and standard deviations of the questionnaire using one-way ANOVA, and Pearson correlation coefficient were reported.

Results: Respondents ages ranged from 20 to >65 years old and was divided into four groups: (20–35, 36–50, 51–65, and >65 years, respectively). The total fatigue mean was 2.88 and the SD was 0.84, indicating an intermediate fatigue level among breast cancer survivors. Study survivors with higher education were more likely to be fatigued (F =7.68, P-value =0.001). Divorced survivors were more prone to fatigue compared to married survivors (F =5.83, P-value= 0.001). Finally, survivors who do not have children were more vulnerable to exhaustion compared to those with children (F =7.35, P-value =0.001). Also, younger survivors were more prone to fatigue, compared to older survivors (F =5.29, P-value = 0.002). Results also showed a positive relationship between each of the variables; the number of children (R =0.221, P-value =0.007), age (R =0.311, P-value =0.000), and duration of treatment (R =0.290, P-value =0.000), which means that the greater the number of children, the younger the age, or the longer the duration of treatment, the more fatigue is reported in breast cancer survivors.

Conclusions: Fatigue is frequently observed in breast cancer survivors undergoing RT. It can limit RT treatment continuity. Therefore, early detection of fatigue can help survivors adhere to RT treatment and achieve better clinical results.

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Introduction

Fatigue is a poorly defined feeling. It is often defined as the most painful complaint that affects quality of life (Bower & Ganz, 2015). Fatigue can be felt by healthy people as a normal after a busy day or exercise, which disappears soon after getting some rest or sound sleep. Fatigue is one of the most common symptoms that cancer survivors experience, findings which were also supported by additional independent research (Chow et al., 2019; Saligan et al., 2015b). Cancer is a life-threatening illnesses and cancer survivors need constant support and follow-up (Abu-Odah et al., 2020; Connor & Sepulveda Bermedo, 2014). However, breast cancer survivors perceive fatigue in a negative way as chronic, disabling and life- and activity-limiting experience (Kalkman, 2005; Prins et al., 2001; Servaes et al., 2002b; Vercoulen, 1996).

The interest in cancer-related fatigue research has increased significantly in the past few years. Exhaustion can result from prolonged stress caused by multiple factors, and it is widely known that fatigue is one of the most common and bothersome side effects of cancer and its treatment (Fisch et al., 2014; Wang et al., 2014). CRF is one of the most common, bothersome, and persistent side effects of cancer and its treatment (Bower, 2014; Lin et al., 2019) and has been defined as the painful, persistent and subjective feeling of physical, emotional and/or cognitive exhaustion or fatigue associated with cancer/cancer treatment that is out of proportion to recent activity and interferes with normal functioning, sexual dysfunction (Berry, 2018), negatively impacting a patient's overall quality of life (Wang et al., 2014). CRF is a constant feeling of fatigue that cannot be relieved by sleep or rest and leads to loss and shrinkage of Quality of life (Inglis et al., 2021). CRF has adverse emotional, social, occupational, and economic consequences for breast cancer survivors and their caregivers (Curt et al., 2000).

Most CRF studies have focused on fatigue that occurs during and after treatment (Curt et al., 2000; Servaes et al., 2002a). However, some breast cancer survivors experience significant fatigue even before treatment onset (Ancoli-Israel et al., 2014), which is usually not assessed, and gives less clue about the trajectory of cancer symptoms, and is considered a limitation since most studies assessed CRF during or after treatment. Fatigue may appear before the start of treatment and usually increases during cancer treatment, including radiation therapy, chemotherapy, hormone therapy, and/or biological therapy. The prevalence of fatigue during treatment ranges from 25% to 99% (Servaes et al., 2002a). About one-third of women experience moderate to severe fatigue up to 10 years after diagnosis (Bower et al., 2006).

Breast cancer is the most common type of cancer diagnosed among females and fatigue is one of the most common and weakening side effects of breast cancer survivors (Berger et al., 2012). Despite the prevalence and severity of CRF, it often goes without evaluation, undiagnosed and unmanaged (Borneman et al., 2010). These problems affect not only cancer survivors, but also their family members and their caregivers (Curt et al., 2000). Despite the heavy burden of persistent fatigue in breast cancer survivors, treatments remain limited and face challenges in implementation (Berger et al., 2015).

Anxiety, fatigue and pain were among the most severe symptoms breast cancer survivors undergoing RT reported negatively impacted their overall quality of life. It is also indicated that following RT, fatigue negatively affects bodily function and may lead to

decreased adherence to medical treatment (Xiao & Torres, 2019). Cancer survivors are often affected by these stressful symptoms in contrast to normal fatigue (Abrahams et al., 2016).

Women with breast cancer commonly experience multiple psychological symptoms throughout cancer diagnosis and treatment trajectory (Tsaras et al., 2018). These psychological symptoms have a detrimental impact on cognitive function and can compromise quality of life (Pitman et al., 2018).

There is significant individual variation in the longitudinal course of cancer-related fatigue that a focus on intermediate levels may obscure (Bower, 2014). For example, some breast cancer survivors experience very little fatigue throughout the course of treatment and stay alive, while others experience extreme fatigue that persists for years after completion of treatment. Understanding the factors that contribute to this variability has important implications for identifying and treating breast cancer survivors at risk, yet, it is unclear whether these are causes or consequences of fatigue (Fisch et al., 2014; Wang et al., 2014). Although there is a body of literature devoted to understanding and identifying evidence-based treatments for cancer-related fatigue, there are still gaps in the literature, especially for breast cancer survivors during initial treatment period (Ehlers et al., 2020).

Also, breast cancer survivors at late cancer stages have more needs compared to those who are at earlier stages (Au et al., 2013). A study showed that the assessment of symptoms, anxiety, depression, uncertainty, and observed stress had a direct effect on the stress of breast cancer survivors receiving RT, while social support had an indirect effect on the stress of breast cancer survivors (Park & Kim, 2020). Muszalik et al. indicated that breast cancer survivors undergoing RT rated their quality of life as average, and showed that older breast cancer survivors over the age of 71 years undergoing RT were more affected (Muszalik et al., 2016). Education and marital status also had an important effect on quality-of-life ratings with educated women in good financial standing status who had a reporting much higher rates of fatigue, compared to women with less education and lower socio-economic status. CRF prior to cancer treatment often has symptoms of whole-body tiredness, which is usually not relieved by rest or sleep (Piper, 1992). However, it was reported that both of the frequency and severity of CRF increased by around 30%, with the majority of the increase in frequency occurring by the 3rd week of treatment, in a group of breast cancer survivors undergoing 5 weeks of treatment period (Hickok et al., 2005). A group of researchers reported in their study (Xiao et al., 2016) that in women diagnosed early with breast cancer, fatigue did not change or decrease significantly during or after radiation therapy. CRF related to RT comes initially from the ionizing radiation effects on the human body. Additionally, the daily treatment visits to the RT facility involves a drastic change in every patient life routine. Furthermore, personal responsibilities make a small amount of fatigue add to the whole tiresome experience. Also, the psychologic impact of receiving fewer prognostic information may contribute to feelings of depression, anxiety, and fatigue (Hickok et al., 2005). It was also noted that breast cancer survivors who prolong their treatment may suffer more physical and mental disorders during radiation therapy (Xiao et al., 2016). Ruiz-Casado et al. showed that fatigue was consistently greater in younger women, obese women, and diabetics (Ruiz-Casado et al., 2021). Women often reported symptoms of fatigue such as pain, depression, insomnia, and cognitive impairment. The

results indicated that younger women with a lower education level are less likely to have breast cancer treatment (Li et al., 2020). Another study indicated that fatigue increases slightly during RT cycles, and at a younger age, primary sadness, anxiety, and psychological/pain-related comorbidities are strong predictors of fatigue (Kishan et al., 2016). Moreover, it was shown that for all female breast cancer survivors, fatigue increased with increasing duration of radiation therapy in breast cancer survivors (LaRiviere et al., 2020).

In Palestine, cancer is considered a major cause of mortality after heart disease and cerebrovascular disease (Abu-Odah et al., 2021) and is the third leading cause of death in Palestine (at 14%), which is expected to elevate the burden and create challenges in cancer care delivery to late-stage breast cancer survivors (Halahleh & Gale, 2018). The present study is concerned with the Palestinian situation, where the healthcare services and access to these services mostly varies from other countries around the world. In 2003, the Augusta Victoria Hospital (AVH) identified the urgent need for establishing RT facility in Palestine, which is not available in other local hospitals. Therefore, AVH established the first RT Department in the Palestinian Territories and East Jerusalem (Augusta Victoria Hospital, 2023). Currently, the AVH is the only Palestinian specialized cancer hospital, which receives breast cancer survivors from both the West Bank and Gaza Strip for oncology and RT (Sabateen et al., 2022). It is difficult for Palestinian people to reach the RT facility in AVH, which is located in Jerusalem. In order to reach Jerusalem, Palestinian citizens/breast cancer survivors from the West Bank or Gaza strip need to apply for and obtain an Israeli permit to enter and reach any facility within Jerusalem, which is not easy to apply for and not always guaranteed to obtain (ALMasri & Rimawi, 2020).

The number of long-term breast cancer survivors is increasing (Bray et al., 2004; Maass et al., 2021). Previous research showed that many breast cancer survivors suffer from fatigue during and after treatment (Minton & Stone, 2008; Saligan et al., 2015a). CRF in breast cancer survivors is still generally under-investigated and needs more focus and investigation within Palestine. The main aim of the present study is to assess, compare, and correlate CRF experienced by Palestinian breast cancer survivors undergoing RT with study variables. To the best of our knowledge, this is the first study to report CRF in Palestinian breast cancer survivors undergoing RT. First, we assessed CRF experienced by Palestinian breast cancer survivors. Second, we explored sociodemographic and clinical factors including radiation treatment period (1 to over 3 months), which gives a clue on the trajectory of CRF among breast cancer survivors. Since there is a lack of support for breast cancer survivors to alleviate CRF, our results will help in providing counselling and support, and reducing CRF for breast cancer survivors.

Methods

Study design and sample/survivors

The present study is a descriptive-analytical study in which all adult female breast cancer survivors attending the RT department at AVH Hospital, Jerusalem, were approached during the study period. The AVH, located in Jerusalem, is the only Palestinian

specialized cancer hospital, which receives breast cancer survivors from both the West Bank and Gaza Strip for oncology and radiotherapy. The inclusion criteria are (a) woman aged 18 and above, (b) diagnosed with breast cancer, (c) no history of psychiatric condition, mental disorder or dementia, which is assessed according to hospital physician and gathered from AVH patient information system, (d) adequate knowledge of Arabic/English languages and satisfactory level of communication, and (e) consent to participate in the study. The targeted total number of breast cancer survivors was 200 during the study period. The sample of respondents consisted of 148 breast cancer survivors, who provided their consent by completing the survey, as explained in the survey cover. The remaining 52 survivors who attended at the RT facility did not provide their consent, and therefore were excluded. The sample size was calculated using (Raosoft, Inc., Seattle, USA), with 95% confidence interval and 0.05 error. The survivors' demographic characteristics were: academic education, number of children, age, and the duration of treatment. Survivors were categorized into four age groups: 20–35, 36–50, 51–65, and over 65 years old, respectively. The treatment duration was categorized into three categories: <1 month, 1–3 months, and >3 months, respectively. All survivors were asked to answer the FACIT-F Scale (version 4) in breast cancer (Kosinski et al., 2013), as shown in Table 1. The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) subscale developed in 1997 (Vogelzang et al., 1997), is a 13-item questionnaire that asks survivors to rate mental and physical fatigue aspects and how they impact their daily life (Cella et al., 2005; Yellen et al., 1997). Previously, the FACIT-F was used to assess fatigue in oncology breast cancer survivors with anaemia (Yellen et al., 1997). Afterwards, it has been validated in a number of populations including rheumatic disease (Chandran et al., 2007; Hewlett et al., 2011), inflammatory bowel disease (Tinsley et al., 2011), iron deficiency anaemia (Acaster et al., 2015), and in Chronic Obstructive Pulmonary Disease (COPD) (Stridsman et al., 2013; Stridsman et al., 2015), which resulted in worldwide reliable fatigue questionnaires (Egerton et al., 2015). Each item in the FACIT-F scale has responses ranging from 0 ('not at all') to 4 ('very much'). Negative phrased item score is reversed, meaning that a higher score is better (i.e. less fatigue). The total score of FACIT-F ranges between 0 and 52. In our study, the FACIT-F scale was only used to assess the impact domain (Fatigue Subscale). The FACIT-F questionnaire was translated into Arabic for ease of use since it is the first

Table 1. Questionnaires answers of survivors ($n = 148$).

No.	Item	Mean	SD
1	I feel fatigue	3.16	1.14
2	I feel weak all over	2.94	1.12
3	I feel listless (washed out)	2.71	1.12
4	I feel tired	2.82	1.21
5	I have trouble starting things because I am tired	2.70	1.19
6	I have trouble finishing things because I am tired	2.59	1.19
7	I have energy	2.48	1.37
8	I am able to do my usual activities	3.07	1.11
9	I need to sleep during the day	3.13	1.27
10	I am too tired to eat	3.47	1.16
11	I need help doing my usual activities	2.56	1.30
12	I am frustrated by being too tired to do the things I want to do	2.84	1.17
13	I have to limit my social activity because I am tired	2.94	1.27
Total fatigue		2.88	0.84

language of participants. The translation was performed according to the recommended translation procedure by European Organization for Research and Treatment of Cancer EORTC (Kuliś et al., 2017).

Data collection

After obtaining the hospital administration permission, all survivors were approached during their appointment visits to the RT facility of the hospital. All survivors were informed about the study on the day of questionnaire filling after giving a written informed consent to comply with ethical considerations, and approve their agreement to participate in the study. Survivors were given the questionnaires to be filled in the presence of researchers, to assist them in clarifying any ambiguous parts and/or to answer their inquiries. Data collection was performed personally by the researchers between 1 May 2021 and 1 September 2021. The demographics and distribution of survivors in the study sample are shown in Table 1. The total number of collected and analysed questionnaires was 148.

Ethical considerations

According to the 2000 Declaration of Helsinki for ethical standards, this study was approved by Al-Quds University Research Ethics Committee (Ref No: 187/REC/2021) on 27 April 2021. Informed consent was obtained from each participant prior to her participation. The survey was anonymous, and all data confidentiality was assured.

Measurement of fatigue

The FACIT-F (version 4) in breast cancer questionnaire items were rated on a 0–4 Likert scale (0 = strongly disagree to 4 = strongly agree) (Table 1). The higher the scores, the less the fatigue level in breast cancer survivors undergoing RT. Descriptive statistics measured the level of fatigue in breast cancer survivors among the sampled population using the following key: 2.33 and less indicated a low level, 2.34–3.67 indicated an average level, and 3.68 and above indicated a high level of fatigue in breast cancer survivors. The Data was checked for normality using Kolmogorov–Smirnov test and Shapiro–Wilk test with p-value < 0.05. Normality test indicates that the data was normally distributed (Kolmogorov– Smirnov test (P-value = 0.200) and Shapiro–Wilk test (P-value = 0.164)).

Instrument validity and reliability

To check the reliability of the study tool, the questionnaire was distributed among nine experts in the field to get a comprehensive evaluation of the content domain of the questionnaire. The stability of the study tool was determined using Cronbach Alpha, since it is a measure of the internal consistency reliability and summarizes the correlations across the study instrument items. Additionally, Pearson correlation coefficient was used to measure the association/ correlation between questionnaire questions and study variables. Correlation Coefficient values may range between −1 and +1, where −1 indicates

a perfect negative correlation, a 0 indicates no correlation, and +1 indicates a perfect positive correlation. When a Correlation Coefficient lies between ±0.50 and ±1, then there is a strong correlation. If a Correlation Coefficient lies between ±0.30 and ±0.49, then there is a medium correlation, whereas small correlation has values below +0.29. Results of study tool internal consistency test shows strong consistency (Cronbach alpha = 0.91), indicating that the study tool was suitable for the study population. Generally, Cronbach's alpha values above 0.7 are generally considered acceptable.

Statistical analysis

Data statistical analysis was carried out using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA). The association between participant demographics, number of children of participants, duration of the radiation treatment period, and fatigue were analysed through the means and standard deviations for every part of the questionnaire using Cronbach's Alpha, one-way ANOVA, and Pearson correlation coefficient. A *P*-value of less than 0.05 was considered statistically significant.

Results

Characteristics of the sample

In total, 148 questionnaires were completed by breast cancer survivors. The response rate was 74%. Table 2 shows the study population and their demographic information, including educational level, number of children, age, and duration of treatment, in addition to their frequency distribution, percentages and one-way ANOVA statistical analysis. The ages of the respondents ranged from 20 to over 65 years old. According to educational level, there were 51 (34.5%) of survivors who received less than secondary

Table 2. Qualitative variables frequency distribution, percentages, and one-way ANOVA statistical analysis for fatigue in breast cancer survivors.

Participant demographic characteristics			Statistical analysis One-way ANOVA	
Patient characteristic	Variable	Frequency (*n*%)	Mean (SD)	*F* (*P*-value)
Education	Less than secondary school	51 (34.5)	2.94 (0.75)	7.68 (0.001**)
	Secondary school – BSc	80 (54.1)	2.70 (0.76)	
	Higher than BSc	17 (11.5)	3.52 (1.09)	
Marital Status	Single	12 (8.1)	2.47 (0.66)	5.83 (0.001**)
	Married	111 (75.0)	2.86 (0.84)	
	Divorced	16 (10.8)	3.57 (0.71)	
	Widowed	9 (6.1)	2.46 (0.47)	
Number of children	None	22 (14.9)	3.07 (0.83)	7.35 (0.001**)
	1–2	33 (22.3)	2.50 (0.69)	
	Three or more	93 (62.8)	2.63 (0.84)	
Age	20–35	10 (6.8)	3.16 (0.98)	5.29 (0.002*)
	36–50	53 (35.8)	3.00 (0.65)	
	51–65	35 (23.6)	2.62 (0.72)	
	Over 65	50 (33.8)	2.40 (0.69)	
Duration of treatment	less than a month	38 (25.7)	2.47 (0.81)	7.22 (0.001**)
	One to three months	57 (38.5)	2.93 (0.66)	
	More than three months	53 (35.8)	3.11 (0.93)	

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.

school education, while 80 (54.1%) of them received a BA degree, and 17 (11.5%) received further higher education beyond BA. About (63%) 93 survivors have more than three children.

Level of fatigue

Table 1 shows the 13-item FACIT-F scale used in the study to assess fatigue and its impact. Each item means and standard deviations for all study survivors are shown in Table 1. The total fatigue mean was 2.88 and the SD was 0.84, which indicates an intermediate fatigue level among breast cancer survivors. Answers to questionnaire items indicate that the highest mean was for: I am too fatigued to eat (3.47), followed by: I feel fatigued (3.16), whereas the lowest mean was for: I have energy (2.48).

Table 2 shows the frequency distribution and percentages for qualitative variables along with the results of one-way ANOVA statistical analysis. Results show statistically significant differences in the level of fatigue within the variable of academic education (F =7.68, P-value =0.001) for education higher than a bachelor's degree (M= 3.52, SD =1.09), compared to the remaining education levels. Furthermore, by considering the martial status of survivors, there was a significant difference in the level of fatigue experience (F =5.83, P value =0.001), as divorced survivors had higher fatigue average (M = 3.57, SD =0.71) when compared to the other marital status groups. Moreover, when considering the association between fatigue and participant children number, there was a significant difference in the level of fatigue experienced with the number of children of the patient (F =7.35, P-value =0.001), while the survivors without children had greater fatigue level with mean (M =3.07), compared to those having 1–2 children (M =2.50), and to those having 3 or more children (M =2.63).

Moreover, there was a significant difference in the level of fatigue with the patient's age at the time of treatment (F =5.29, P-value =0.002). Survivors between 20 and 35 years of age had higher levels (M =3.16, SD =0.98), compared to older survivors (36–50 yrs, M =3), (51–65yrs, M =2.62), and (over 65 yrs, M =2.40). Also, there was a significant difference in the level of fatigue according to treatment duration (F =7.22, P-value =0.001), especially for treatments greater than three months (M =3.11, SD =0.93), compared to shorter treatment periods (<1 month, M =2.47) and (1–3 months, M =2.93).

Table 3 shows a Pearson correlation coefficient between fatigue and study variables. Table 4 shows the number and percentage of study survivors according to fatigue level. It can be seen that the fatigue experience is different among participant with 29 (19.6%) breast cancer survivors suffering from high fatigue level compared to 35 (23.6%) survivors expressing low fatigue level.

Table 3. Pearson correlation coefficient between study variables and fatigue.

	Pearson correlation coefficient	
Variable	*R*	*P*
Number of children	0.221	0.007**
Age	0.311	0.000**
Duration of treatment	0.290	0.000**

**Correlation is significant at the 0.01 level (two-tailed).
R: Correlation coefficient.
P: *P*-value.

Table 4. Frequency and percentage of women experiencing different levels of fatigue.

Fatigue level	Number of breast cancer survivors	Percent (%)
Low (1–2.33)	35	23.6
Medium (2.34–3.67)	84	56.8
High (3.68–5)	29	19.6
Total	148	100

Discussion

This study aimed to understand the factors influencing fatigue levels in breast cancer survivors undergoing radiation therapy. We found that educational level, marital status, number of children, age, and duration of treatment are significant predictors. Obviously, any patient diagnosed with cancer goes through several levels of stress and emotional fluctuations. The radical changes in lifestyle, fear of death, changes in the physical shape, the change in self-perception, as well as the financial and functional considerations, all of which are very important issues for anyone who develops cancer.

The current study showed that breast cancer survivors who have higher education are more likely to become fatigued. For instance, when comparted with less educated workers, it was reported that highly educated workers reported higher levels of stress when considering less work advancement or facing the threat of losing a job (Schoger, 2023). This fact, along with being treated for cancer, adds extra fatigue in individuals being treated for breast cancer who think too much on losing their jobs as a result of being ill. Similar results were reported in other studies (Bower et al., 2019; Muszalik et al., 2016; Xiao et al., 2016). Highly educated survivors usually read more about cancer and subsequent effects and therefore would be more anxious about their physical and mental health status. Also, breast cancer survivors may suffer from sleep difficulties, loss of appetite, acute phobias and anxiety, and obsessing anxiously about the future, especially as it affects the ability to continue in the job or work.

It was also found that divorced women are more prone to exhaustion than others, since divorced women face the burden of divorce and fear that they will not receive attention from parents and lack of social support, which agrees with results found in another study (Park & Kim, 2020). It has been shown that women who do not have children are more likely to be exhausted than those who have children. This fatigue among women without children is linked to the fear of death and their fear that they may be unable to conceive as childbearing in our middle eastern society is the insurance for the continuation of marriage life.

Among demographic variables, age was associated with an increase in fatigue scores, with greater fatigue seen among younger breast cancer survivors (Table 2). It was also found that younger people are more prone to stress compared to those who are older, according to various studies (Bower et al., 2019; Kishan et al., 2016; Mao et al., 2018; Muszalik et al., 2016; Ruiz-Casado et al., 2021). Younger breast cancer survivors are more likely to fear cancer diagnosis and death (Avis et al., 2012; Wells & Fedric, 2001), because they are in the prime of life. The socio-political intricacies and complexities that Palestinian breast cancer survivors face are several. Initially, getting from the West Bank or Gaza to Jerusalem is difficult and not always guaranteed because of the Israeli occupation. Additionally, some societal norms among breast cancer survivors

such as lack of support from family and friends may negatively affect them and could result in increased CRF. Moreover, younger breast cancer survivors are less able to reach the only available radiation therapy facility in the city of Jerusalem, which initially requires them to get a permit to get into Jerusalem through various checkpoints around Jerusalem. Also, sometimes, a young patient needs older companion for travelling and escorting to the AVH, which adds more stress-related fatigue. In addition to the aforementioned travel obstacles, getting to the hospital requires changing more than one mode of transportation, which can be daunting for young breast cancer survivors.

According to table 3, the level of correlation between outcome variables and fatigue can be classified between low to medium (0.221, 0.311, and 0.290, for number of children, age, and treatment duration, respectively). As the number of children of breast cancer participant increases, the physical stress and fatigue is raised due to high parent responsibility and care given and spread among more children ($R = 0.221$). Additionally, as participant gets older, fatigue is more pronounced and felt ($R = 0.311$). Moreover, it has been shown that survivors who stay in hospital for longer periods are more prone to fatigue, and survivors who are treated for long periods are more susceptible to fatigue ($R = 0.290$), which is a result of physical and financial burden, as shown in other studies (Kishan et al., 2016; LaRiviere et al., 2020).

It is well known that radiation destroys both cancer cells and normal tissues in the irradiated area, which results in adverse treatment-related effects such as fatigue, gastrointestinal symptoms, and dermatologic effects (Damber & Aus, 2008). According to the National Comprehensive Cancer Network (NCCN), radiotherapy-induced fatigue (RIF) was categorized as a clinical subtype of cancer-related fatigue (CRF) (Piper & Cella, 2010). RIF is characterized by a pervasive, subjective tiredness feeling, which is persistent over time. RIF usually results in sleep disturbance, depression, decreased physical activity, and lower health related quality of life (Berger & Mitchell, 2008; Holliday et al., 2016; Pinto et al., 2013). It was reported that RIF may influence mitochondrial markers and cause them to dysfunction, which may worsen fatigue symptoms during RT (Hsiao et al., 2013; Hsiao et al., 2014). Also, it is suggested that RIF could be generated from a lower mitochondria capability in utilizing oxygen and synthesizing adenosine triphosphate (ATP), thus resulting in lower physiological and cellular energy (Eghbal et al., 2004). The RIF slightly increases by the beginning of the 3rd week of treatment, then it significantly gets worse by the 6th week, and then remains at elevated levels after the

Table 5. Multivariate analysis (two-way ANOVA) for fatigue among breast cancer survivors treated with RT in Palestine.

Variable	Sum of squares	Degree of freedom (df)	Mean square	*F*	Significance (*P*-value)
Number of Children	1.387	2	0.693	1.239	0.293
Age	4.383	3	1.461	2.510	0.061
Duration of treatment	9.478	2	4.739	8.141	0.000**
Age vs. duration of treatment	6.876	5	1.375	2.362	0.043*
Error (among groups)	79.751	137	0.582		
Total	1333.107	149			

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.

completion of RT, as reported by Danjoux et al. (2007), Dhruva et al. (2010), Holliday et al. (2016) and Hsiao et al. (2013).

Table 5 shows multivariate analysis for fatigue among breast cancer survivors treated with RT in Palestine. It is noted that *F* for the total age vs. duration of treatment (2.362) with $\alpha = 0.043$ which is < 0.05, hence there is a significant difference in fatigue between breast cancer survivors according to age vs length of treatment. The differences were in favour of age (older than 51 yrs) and length of treatment (> 3 months).

Various ways to deal with fatigue have been reported in the literature. For instance, by changing lifestyle and eating habits, participants could easily deal with the stress-related fatigue (Bantema-Joppe et al., 2015; Swann, 2008). By changing the contents of food diets, eating small meal amounts at many fractions, and having light and less fried meals, would increase nutritional intake and alleviate the fatigue (Tsai et al., 2010). Additionally, adequate nutrition and hydration are helpful for managing fatigue (Ahlberg et al., 2003). Fatigue can be also managed by reducing down the work time, increasing rest times, and engaging in energy-saving and sleep-improving activities help in coping with CRF (Ahlberg et al., 2003).

There is evidence that exercise intervention in breast cancer survivors has been effective in improving CRF (Barsevick et al., 2002; Barsevick et al., 2004). Older breast cancer survivors with better lower extremity muscle strength and higher physical activity reported less fatigue (Rao, 2004). Galantino et al. (2003) also reported that Tai-Chi (a traditional Chinese exercise) and walking effectively reduced fatigue in women with breast cancer. Moreover, the application of exercise programme in early breast cancer survivors reduced the extent of fatigue and enhanced physical functions (Carlson & Garland, 2005).

This study will be used to advance clinical care and provide support for breast cancer survivors, either through radiation oncology team or breast cancer survivor family, which would reduce the distress from the fatigue. If fatigue was noticed and diagnosed in the initial appointments by the radiation therapy team, it can be properly treated. It is of utmost importance to diagnose and recognize fatigue at the first appointments of RT. The radiation oncology team should be fully aware, well-educated, and well-noting the physical condition/fatigue status of breast cancer survivors attending the RT. This study would therefore recommend that the AVH-RT facility carries out a CRF survey for all breast cancer survivors attending RT, to help in assessing CRF before, during, and after RT sessions.

A very important and actionable recommendation to alleviate fatigue among Palestinian breast cancer survivors and other cancer survivors is through establishing more RT centres at various cities across Palestine, which will certainly relieve the suffering of breast cancer survivors travelling from the West Bank/Gaza, to the only current RT-AVH, in Jerusalem. It is also necessary to provide education, counselling, and support for breast cancer survivors either face to face, or via online educational programmes that offer psychological treatments remotely, such as the cognitive behaviour therapy (CBT), specifically the Internet CBT. The aforementioned ways of dealing with fatigue can be advised to breast cancer survivors to reduce their CRF. Additionally, breast cancer survivors who receive their families support during transportation and through various treatment sessions, can adjust and overcome CRF. Results and recommendations of this study will be shared with the Palestinian Ministry of Health and AVH to show the

importance of providing an educational programme that alleviates CRF (maybe in the form of Internet CBT), for breast cancer survivors, which will greatly help current and future cancer patient in Palestine.

Limitations

In this study, we did our best to consider all breast cancer survivors undergoing RT. However, some breast cancer survivors declined to participate. Also, the results of the study were confined to the survivors of a single radiation oncology facility in Palestine, which is a potential for selection bias. It is recommended that interested researchers conduct further studies to make continuous assessment of factors influencing the experiences of CRF in breast cancer survivors.

Conclusion

Fatigue is frequently observed in breast cancer survivors undergoing RT. During RT, the severity of fatigue increased significantly for survivors who have higher education, the youngest women (20–35 years), the divorced women, and those without children. The duration of treatment directly correlated to an increase in the severity of fatigue symptoms experienced with longer courses of treatment resulting in higher levels of fatigue. The results contribute to and expand upon already present research related to fatigue and its impact on the health status of breast cancer survivors. Fatigue may limit RT treatment continuity. Therefore, early detection and mitigation of fatigue would help breast cancer survivors to adhere to RT treatment and achieve better clinical results in breast cancer treatment regimens. It also provides insights into evaluating effective nursing, patient education, and symptom management.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Hussein ALMasri and Omar Rimawi. The first draft of the manuscript was written by Hussein ALMasri and Omar Rimawi and all authors commented on previous versions of the manuscript. Both authors read and approved the final manuscript.

Consent to participate

Informed consent was obtained from all individual survivors included in the study. Before data collection, all respondents were given information about the nature of the study. The data collected were reported in general terms and did not involve any identifying data. All the data were kept confidential and securely held for the required time. The data were entered into a computerized database, and the use of a code protected the identity of the survivors.

Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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