FATIGUE IN METASTATIC BREAST CANCER PATIENTS: NURSING PERSPECTIVES

Dr. Ehsan A. Yahia,

Lecturer of Medical-Surgical Nursing

Faculty of Nursing, Kasr Al-Aini, Cairo University, Egypt

Corresponding author Mail: ehsanyahia@cu.edu.eg

ABSTRACT:

Fatigue is a commonly reported complaint worldwide among both healthy and unhealthy individuals. Cancer-related fatigue is a known symptom due to many factors, including the disease itself and management protocols. Metastatic breast cancer patients are one of the specific groups facing that problem. The causes beyond cancer-related fatigue may be cancer and the cancer treatments such as chemotherapy and or radiotherapy. This research aimed to explore the factors affecting fatigue among patients with metastatic breast cancer to plan nursing interventions to manage that issue. The study subjects consisted of 30 female patients diagnosed with metastatic breast cancer presented to the Oncology unit at Kasr Al-Aini university hospital. The results of this study indicated a significant relationship between fatigue and the stage of the disease. In addition, there is a positive relationship between levels of fatigue and inflammatory markers. The study also found that there is a strong relationship between oxidative stress indicators and level of fatigue. Therefore, nurses should assess all the factors affecting fatigue level to plan a quality nursing management protocol for this particular category of patients.

Keywords: Fatigue, Metastatic Breast Cancer, Cancer, Nursing, Fatigue Assessment Scale, FAS, Cancer Related Fatigue.

I. BACKGROUND:

Fatigue is the state of exhaustion, lack of energy, and motivation. It can be physical, emotional, or both. It differs from sleepiness or drowsiness, which results from the need for sleep. Symptoms of fatigue include having little or no energy, muscle aches, pains, weakness or slowness, trouble thinking clearly or concentrating, and lack of ability to do daily tasks. Fatigue could also be a response to excessive physical and mental activities. Usually, fatigue can be resolved with rest or decreasing activity. Fatigue is a frequent complaint related to a variety of health issues. Markedly, it is a symptom and not associated with disease or health

disorder. Various illnesses cause fatigue, and the symptoms can be physical, psychological, or a combination of both. (Potter, 2004); (Pederson, Munch, Groenvold, 2003)

Fatigue is one of the most complicated symptoms reported by cancer patients. It has an impact on the quality of life for both patients and their caregivers, which health professionals do not always recognize (Curt, 2000) ; (Jeffrey, 1993)

Cancer-related fatigue (sometimes simply referred to as "cancer fatigue" is one of the frequently reported side effects of cancer and cancer treatments. It is often labeled as "paralyzing." Usually, it is presented suddenly, not as a result of activity or exertion, and it does not subside by rest or sleep. It may not finish even after cancer treatment is complete. (Othayoth, Mathi, Bheemanapally, Kakarla, & Botlagunta, 2015)

1. **Definitions:** Fatigue is characterized by a decreased capacity for work and reduced efficiency to daily accomplishment, usually escorted by a feeling of weariness and\or tiredness. Fatigue could be acute and presents suddenly or chronic and persist (Shiel, 2019). Generally, cancer-related fatigue cannot be attributed to a single cause but has a multifactorial etiology. (Munch, Strömgren, Pedersen, et al., 2006).
2. **Incidences:** The European Association for palliative care defines fatigue as one of the most common symptoms in palliative care settings, reported in 80% of cancer patients and up to 99% of patients following radiotherapy or chemotherapy (Radbruch, Strasser, Elsner, et al., 2008).
3. **Levels of Cancer Fatigue:**
    - **Primary fatigue:** is known to be related to cancer itself. Cancer cells produce chemicals and hormones that make the patient feel tired, feel full, and cause other complex problems. **(**Brown, 2004)
    - **Secondary fatigue:** is caused by another medical condition and can last one month or more, but it usually lasts less than six months. Physiologic fatigue is an imbalance in the daily routines of exercise, sleep, diet, or other activity that is not due to other underlying medical conditions and is relieved with rest. Chronic fatigue lasts longer than six months and is not relieved with rest. Figure (1)

illustrates the different factors that lead to secondary fatigue. (Morris, Anderson, Galecki, Berk, Maes, 2013)

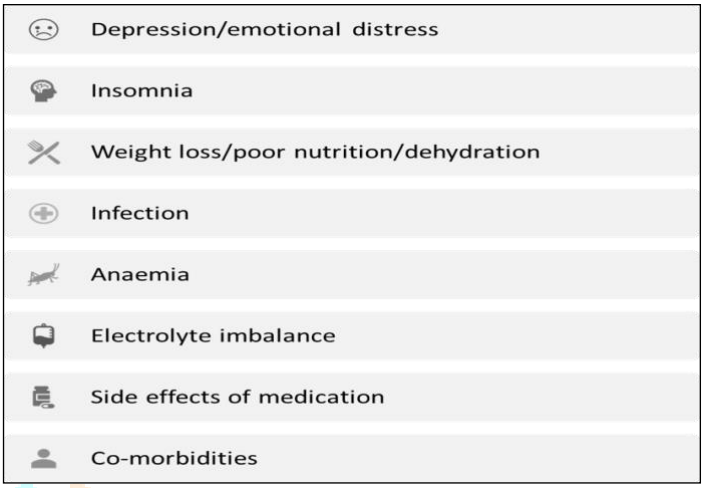

Figure (1): different factors lead to secondary fatigue.

4. Factors underlying fatigue:

- ***Nutritional factors:***

(Inglis, Lin, Kerns, et al.; 2019) Addressed the physiological process underlying several nutritional factors leading to cancer-related fatigue, as shown in figure (2).

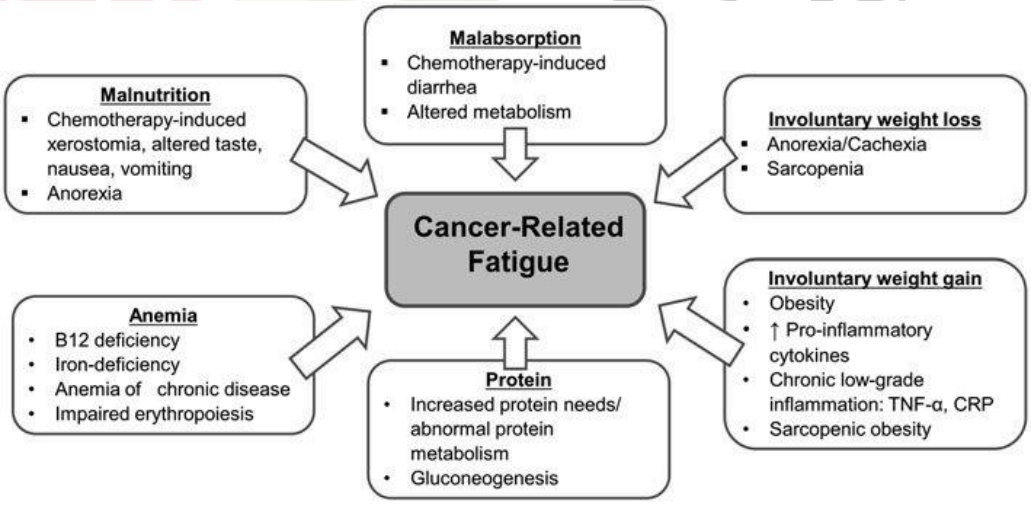

Figure (2): Nutritional factors that contribute to cancer-related fatigue. TNF-a, tumor necrosis factor-alpha; CRP, C-reactive protein.

- ***Oxidative stress:***

is known as an imbalance between the producing free radicals and reactive metabolites, so-called oxidants or reactive oxygen species (ROS), and their elimination by protective

mechanisms, referred to as antioxidants. This imbalance leads to damage of essential biomolecules and cells, potentially impacting the whole organism. (Repka & Hayward, 2018).

- ***Inflammatory markers:***

One of the frequently used test tools in clinical practice is inflammatory marker tests. The three most commonly used are erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and plasma viscosity (PV). These biological parameters are usually assessed as a 'rule-out test by clinicians trying to exclude serious underlying disease (Watson, de Salis, Hamilton, et al., 2016).

Interestingly, other conditions that also present fatigue are related strongly to inflammation (e.g., tumor-related fatigue, organ failure, chronic infectious diseases, endocrine diseases, autoimmune diseases, etc. (Scheibenbogen et al., 2014). there is some evidence that the physiological mechanisms causing fatigue in cancer are also linked to fatigue in other chronic diseases, more research is needed to explore inflammation, and the autonomic nervous system, and other mechanisms related to fatigue in a variety of chronic illnesses (Matura et al., 2018).

- ***Stage of cancer:***

Fatigue is linked to the advancement of the cancer stage; it is a frequently reported symptom in palliative care patients who have cancer metastasis or other severe and life-threatening illnesses. Unfortunately, it is also usually underestimated and undertreated symptoms in this category of patients and other palliative care patients, including those with end-stage heart failure. Fatigue has substantial negative physical, psychosocial, and economic drawbacks for patients and their caregivers. However, as it is a primarily subjective experience with multidimensional causes, the assessment and management of fatigue in palliative care settings can be complex. (Robinson, Kissane, Brooker, et. Al., 2015)

- ***Comorbidities:***

Cancer comorbidities are associated with fatigue, while cancer metastasis is associated with an increased risk of worsening fatigue. Comorbidities cause symptoms

of fatigue independent of cancer. The presence of cancer and cancer metastasis worsen the symptom of fatigue. Unexplained chronic fatigue (UCF) is best viewed from a biopsychosocial perspective as a multidisciplinary issue. A monodisciplinary view may lead to a false diagnosis of chronic fatigue syndrome (CFS) as psychiatric or sleep disorders that could be managed may go unnoticed. (Mariman, Liesbeth Delesie, Els Tobback, et. al., 2013)

5. Impact of fatigue on the quality of life:

Fatigue poses a robust negative effect on the patient's daily life. Patients report that fatigue is the most problematic side effect of cancer. Some patients may appear well while they are still experiencing severe fatigue. Fatigue causes an inability to carry out daily tasks efficiently. It creates feelings of frustration and isolation. Persistent feelings of sadness or frustration need prompt attention and seeking medical help. (Pederson et al., 2016). Many types of research found that fatigue affects different domains of life for patients with advanced cancer, including mood, relationships, ability to walk, and feelings of satisfaction and self-esteem. (Coakley et al., 2002).

6. Management of fatigue:

The initial step to managing fatigue is to outline its effects on the patient. Primary care physicians, nurses, or oncologists should assess patient feelings, including the duration of fatigue. The health care provider should ask the patient to write a diary of his\her feelings from day to day. It can help caregivers learn when the patient has the most and least energy and the factors causing the fatigue. Conditions like pain or anemia that might be contributing to fatigue should be managed. (Nice, 2004). Fatigue symptoms related to modifiable factors (e.g., workload, stress, coping strategies, depression, overcommitment) are much more likely to recover than fatigue symptoms related to external factors, such as a viral infection. (Brown, 2004). The following Figure illustrates the management of fatigue.

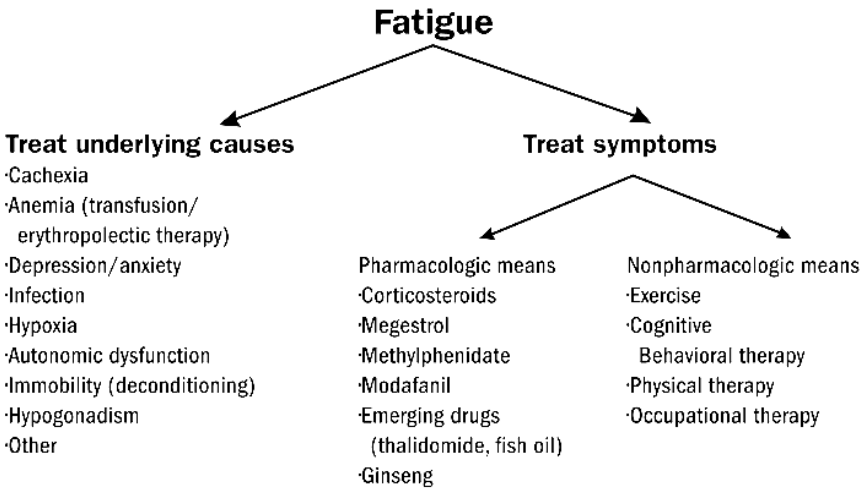

Figure (3): Illustrates management of fatigue. (Thomas et al., 2008)

7. Nursing Perspectives:

Fatigue represents a complex and frequent symptom in cancer patients and influences their quality of life. Nurses deal with cancer-related fatigue through all steps of the nursing process, starting from fatigue assessment and accurate detection of fatigue symptoms, types, and underlying causes, moving to state accurate nursing diagnosis to plan nursing intervention to reduce fatigue to the minimum level. As shown in the Appendix, sample nursing intervention to manage fatigue. (Cassiani & Lira, 2018); The role of breast cancer nurse begins with risk assessment as the first level moving to follow up care of survivors and palliative care. The nursing role includes research, education, and clinical practice (Yahia, Atteya & Elmorsy, 2016).

Recent research evidence of nursing role during fatigue suggests that physical exercise and management of underlying causes, such as anemia or clinical depression, are effective nursing interventions in decreasing cancer-related fatigue. However, a wide range of other practical interventions and complementary medicine can be helpful such as acupressure and acupuncture, stress reduction technique, relaxation, energy conservation practices, anticipatory guidance, and preparatory information, as well as attention-restoring activities (Kirshbaum, 2010).

II. METHODOLOGY

- **Aim and research question:** This current research aims to assess the factors contributing to fatigue in metastatic breast cancer patients.

  Research questions:

  Q1: What are the factors contributing to fatigue in metastatic breast cancer patients?

  Q2: What are the physiological correlates of fatigue in metastatic breast cancer patients?

- **Research design:** Exploratory, descriptive research design: Exploratory-descriptive design, usually field studies in natural settings, provide minimal control over variables. Instead, the collected data contribute to the development of theory or explain phenomena from the perspective of the subjects being studied (Brink & Wood, 1998).

- **Setting:** This study was conducted in oncology outpatient clinics at Kasr Al-Aini university hospital in Cairo – Egypt.

- **Study subjects:** The study subjects 30 Egyptian adult females with metastatic breast cancer patients undergoing follow-up treatment at Kasr Al-Aini Oncology department.

- **Instrumentation:** Modified Arabic fatigue severity scale (translated and modified by the researcher) was used to determine fatigue levels among the study sample. Pearson Byars Fatigue Feeling Checklist was utilized to measure clinical fatigue. Biological indicators such as inflammatory markers were also documented.

- **Validity and Reliability of the study tools:** The face and content validity of the current study tool was tested by a panel of three experts' faculty members of Oncology and Medical-Surgical Nursing at Cairo University. Study tools were tested for Reliability using test-retest = (0.8).

- **Ethical consideration:** Official permission was obtained from the hospital's administrators to conduct the study. The aim and nature of the research and the value were explained to the study subjects who met the inclusion criteria. The subjects signed informed consent to participate in the current study. Anonymity and confidentiality were assured by coding the acquired data. Study subjects were assured that participation in the current study was voluntary, and they can withdraw from the research study any time without effect on the provided care.

- **Procedure:** The study was conducted over four steps; assessment, planning, implementation, and evaluation. The assessment step involves collecting data through an extensive review of related literature using the available scientific database. In the planning step, based on the assessment outcome, the final format of the study instruments was developed. In addition, the final frame about time, frequency of patients' interviews was developed. The implementation phase was done over one year from November 2017 to October 2018; the researcher conducted an explorative, descriptive study of 30 patients with metastatic breast cancer where the following items were the assessed level of fatigue, symptoms of fatigue, stage of disease, as well as related biological parameters. Finally, the evaluation step involved statistical analysis of the collected data to answer the study questions.

- **Data analysis:** The acquired data were tabulated and analyzed by using SPSS version 20. In addition, descriptive statistics, including percentage, means, frequency distribution, standard deviations, and correlational tests, were also used.

III. RESULTS & DISCUSSION:

Table (1) present the age and activity level of the studied subjects; regarding studied patients' age, 43.3 % of them were within the period ranged between 45– less than 55 years with a mean of 46 ± 3.6

Item	No.	%	SD ± X
Age			48 ± 3.6
35 < 45 years	8	26.7%	
45 < 55 years	13	43.3%	
55 < 65 years	9	30.0%	
Activity level			
Bed rest restriction	6	20.0%	
light activity	17	56.7%	
Moderate activity	4	13.3%	
Active	3	10.0%	

Figure (4) represents the frequency distribution of Breast Cancer Treatment among the studied subjects; most subjects (76%) underwent surgical removal of cancer, noting that some patients used more than one treatment. In addition, (100%) managed by chemotherapy, (56%) received radiotherapy, while half of the studied subjects (50%) used hormonal therapy.

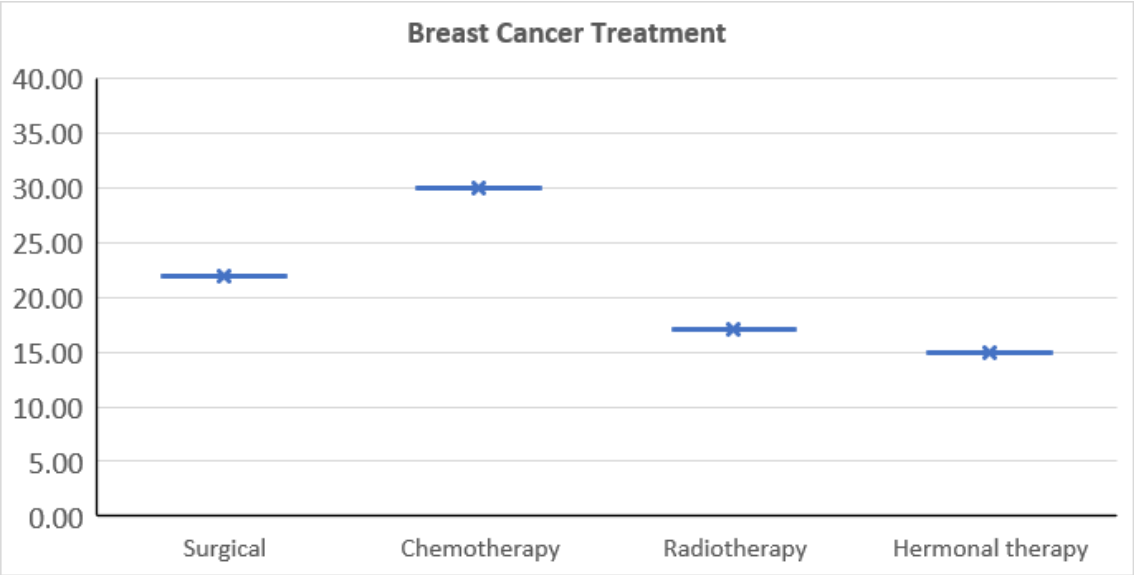

Figure (4): frequency distribution of Breast Cancer Treatment.

Table (2): represents the number and percentage of fatigue indicators; (100%) of the subjects bothered by fatigue. The majority of them identified themselves as nervous persons and getting tired quickly. On the other hand, a minority of the studied subjects identified themselves as happy persons or having enough energy for everyday life.

No	**Items**	NO.	%
1	I am bothered by fatigue	30	100.0%
2	I get tired very quickly	23	76.7%
3	I do not do much during the day	20	66.7%
4	I have enough energy for everyday life	10	33.3%
5	Physically, I feel exhausted	17	56.7%
6	I have problems starting things	13	43.3%
7	I have problems thinking clearly	15	50.0%
8	I feel no desire to do anything	18	60.0%
9	Mentally, I feel exhausted	16	53.3%
10	When I am doing something, I can concentrate reasonably well	17	56.7%
11	Have you been a very nervous person?	23	76.7%
12	Have you felt so down in the dumps that nothing could cheer you up?	20	66.7%
13	Have you felt calm and peaceful?	12	40.0%
14	Have you felt downhearted and low?	14	46.7%
15	Have you been a happy person?	10	33.3%

Figure (6): illustrates the relationship between stage of disease and level of fatigue score among studied subjects, which shows an increase of fatigue level with advancement of the stage of the disease.

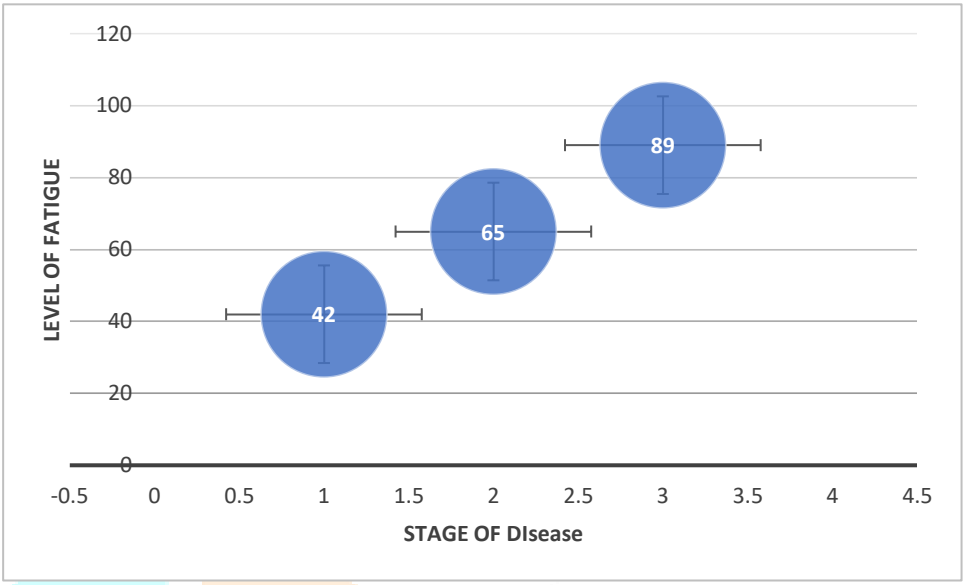

Figure (6): Relationship between stage of disease and level of fatigue score

Table (3): represents the relationship between fatigue and its underlying factors, which indicates a significant relationship between fatigue with inflammatory markers and oxidative stress indicator score.

Item	r.	Sign.
- oxidative stress indicator score & level of fatigue	6.097	.002
- Inflammatory Markers (serum ESR) & level of fatigue	8.342	.004
Significance level ≤ 0.5		

IV. CONCLUSION

Severe, devastating fatigue is common in cancer patients. For many, it is the symptom that interferes most with regular routines. Determining the factors underlying fatigue among metastatic breast cancer patients is crucial for this category of patients who

continue to experience fatigue as a chronic health issue. Implications for nursing practice are essential through all the steps of the nursing process.

Clinically observed, every modality used to manage cancer may cause fatigue, as can complications of the disease such as sleep disruptions, infections, malnutrition, hypothyroidism, and anemia. In addition, there is a significant overlap between depression and fatigue in many patients. Therefore, the evaluation should include an attempt to identify reversible causes of exhaustion and screening for depression.

Given the heterogeneity of patients, individualized approaches are needed, aiming to provide patient-centered nursing care.

V. LIMITATIONS

1. Lack of patients' commitment to follow-up made the study took a long time (one year) to collect valid data from 30 subjects

2. Group number is a limited generalization not possible.

VI. RECOMMENDATIONS

According to the results of the findings of the current study, recommendations offered for future research are:

1. A similar research can be conducted in large sample size and with different target populations.
2. We are developing and testing various nursing interventions for fatigue management.

VII. ACKNOWLEDGMENT

Dedicated to the hero of my life; my Mom, "Soad Mohammed Mahgoub," a Metastatic breast cancer survivor. Also, I present all gratitude to all metastatic breast cancer survivors who keep inspiring me all the time by their faith, hope and love.

REFERENCES

1. Brink, P. J., & Wood, M. J. (1998). Exploratory-descriptive designs. In *Advanced design in nursing research* (pp. 283-286). SAGE Publications, Inc., https://www.doi.org/

2. Brown H (2004). The management of fatigue in advanced cancer related fatigue. *European Journal of Palliative Care* 11 (1): 16 -18

3. Cassiani, S. H. D. B., & Lira, J. C. G. (2018). Nursing perspectives and the "Nursing Now" campaign.

4. Coakley A, Huthcinson T, Saltmarsh P, Kelly A, Ellershaw J E. Marshall E, Brunston H (2002) *International Journal Of Palliative Nursing* 8 (8) 381- 388

5. Curt, G. A. (2000). The impact of fatigue on patients with cancer: overview of FATIGUE 1 and 2. *The Oncologist*, *5*, 9-12.

6. Inglis JE, Lin PJ, Kerns SL, Kleckner IR, Kleckner AS, Castillo DA, Mustian KM, Peppone LJ. Nutritional Interventions for Treating Cancer-Related Fatigue: A Qualitative Review. Nutr Cancer. 2019;71(1):21-40. DOI: 10.1080/01635581.2018.1513046. Epub 2019 Jan 26. PMID: 30688088; PMCID: PMC6456409.

7. Jeffrey D (1993)" There is nothing more I can do" – *An Introduction to the Ethics of Palliative Care*. The Lisa Foundation Sainsbury Foundation, Penzance

8. Kirshbaum M. Cancer-related fatigue: a review of nursing interventions. Br J Community Nurs. 2010 May;15(5):214-6, 218-9. doi: 10.12968/bjcn.2010.15.5.47945. PMID: 20453821.

9. Mariman, Liesbeth Delesie, Els Tobback, Ignace Hanoulle, Erica Sermijn, Peter Vermeir, Dirk Pevernagie, Dirk Vogelaers. Undiagnosed and comorbid disorders in patients with presumed chronic fatigue syndrome. *Journal of Psychosomatic Research*. Volume 75, Issue 5, 2013, Pages 491-496, available @https://www.sciencedirect.com/science/article/pii/S0022399913002766)

10. Matura, L. A., Malone, S., Jaime-Lara, R. & Riegel, B. A Systematic Review of Biological Mechanisms of Fatigue in Chronic Illness. Biol. Res. Nurs. 20, 410–421 (2018).

11. Morris G, Anderson G, Galecki P, Berk M, Maes M. A narrative review on the similarities and dissimilarities between myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and sickness behavior. BMC Med. 2013;11:64.

12. Munch, T. N., Strömgren, A. S., Pedersen, L., Petersen, M. A., Hoermann, L., & Groenvold, M. (2006). Multidimensional measurement of fatigue in advanced cancer

patients in palliative care: an application of the multidimensional fatigue inventory. *Journal of pain and symptom management*, *31*(6), 533-541.

13. Nice (2004) *Guidance on Cancer Services. Improving Supportive and Palliative Care Adults with Cancer. The Manual.* London, NICE

14. Othayoth, R., Mathi, P., Bheemanapally, K., Kakarla, L., & Botlagunta, M. (2015). Characterization of vitamin–cisplatin-loaded chitosan nano-particles for chemoprevention and cancer fatigue. *Journal of microencapsulation*, *32*(6), 578-588.

15. Pederson L, Munch T N, Groenvold M (2003) The treatment of fatigue in palliative care patients. *European Journal of Palliative Care* 10 (6): 225-229

16. Potter J (2004) Fatigue experience in advanced cancer: a phenomenological approach. *International Journal of Palliative Medicine* 10 (1): 15-23

17. Radbruch l et al. (2008) Fatigue in Palliative Care Patients – An EAPC approach. *Palliative Medicine* 2008; 22(1) : 13-32

18. Repka, C. P., & Hayward, R. (2018). Effects of an exercise intervention on cancer-related fatigue and its relationship to markers of oxidative stress. *Integrative cancer therapies*, *17*(2), 503-510.

19. Robinson S, Kissane DW, Brooker J, Burney S. A systematic review of the demoralization syndrome in individuals with progressive disease and cancer: a decade of research. J Pain Symptom Manage 2015; 49:595

20. Scheibenbogen, C. et al. Chronisches Fatigue-Syndrom. Heutige Vorstellung zur Pathogenese, Diagnostik und Therapie. Tagliche Prax. (2014)

21. Thomas C. Rosenthal, Md; Barbara A. Majeroni, Md; Richard Pretorius, Md, Mph; And Khalid Malik, MD, MBA, Fatigue: An overview *Am Fam Physician.* 2008 Nov 15;78(10):1173-1179.

22. EA Yahia, S Atteya, N Elmorsy. Impact of designed nursing protocol on breast cancer screening practice: pilot study. International Journal of Research in Applied, Natural and Social Sciences. Vol (4), issue 8. Pages 41-48

23.Watson, J., de Salis, I., Hamilton, W. & Salisbury, C. 'I'm fishing really' - inflammatory marker testing in primary care: a qualitative study. Br. J. Gen. Pr. 66, e200–e206 (2016)

Appendix: ABBREVIATION

ACA	American Cancer Association
ACS	American Cancer Society
ADA	American Diabetic Association
BMI	Body Mass Index
CDC	Centers of Disease Control
CFS	Chronic Fatigue syndrome
CRF	Cancer Related Fatigue
DM	Diabetes Mellitus
FAS	Fatigue Assessment Scale
HTN	Hypertension
IL6	Interleukin 6
NCI	National Cancer Institute
ROS	Reactive oxygen species
RR	Relative Risk
TNF	Tumor necrosis factor.
UCF	Unexplained chronic fatigue
WHO	World Health Organization