Relation of Cancer-Related Fatigue with Depression and Functional Status among Elderly Patients Undergoing Radiotherapy

¹Shaimaa Samir Hegazy, ²Amira Ahmed Hassanein, ³Ibrahim Ali Awad, ⁴Eman Baleegh Meawad,

¹Demonstratorof Gerontological Nursing, Faculty of Nursing, Mansoura University ²Professor of Medical Surgical Nursing, Faculty of Nursing, Mansoura University ³Professor of Oncology and Nuclear Medicine, Faculty of Medicine, Mansoura University ⁴Lecturer of Gerontological Nursing, Faculty of Nursing, Mansoura University Corresponding Author: ¹Shaimaa Samir Hegazy

Abstract

Background: Cancer related fatigue, depression and functional dependence are among a confusing array of symptoms which commonly presented in the patients undergoing cancer treatment. These symptoms especially fatigue still largely ignored in older adults, hence, identifying these symptoms and analyzing the correlation which can be exist may have a special concern and are considering important cues for effective management of these symptoms.

Aim: Determine the relation of cancer related fatigue with depression and functional status among elderly patients undergoing radiotherapy.

Method: This is a descriptive correlational study designcarried on 120 elderly cancer patients that were attending the outpatient clinic of the Oncology and Nuclear medicine departmentat Main Mansoura University Hospital and were undergoing radiotherapy, patients were interviewed individually by the researcher to collect data using the study tools; Tool I : Interview questionnaire sheet, Tool II: Revised Piper Fatigue Scale, Tool III: Geriatric Depression Scale –short form, Tool IV:Katz and Akpom scale, and Tool V: Lawton and Brody scale. **Results:** Fatigue was positively correlated with depression and Katz scale for activity of daily livings; the higher fatigue was associated with higher depression and lower independency level. Also, there was a positive moderate correlation between depression and functional dependence in anactivity of daily livings.

Conclusion: Fatigue, depression, and functional dependence are commonly and correlated symptoms in elderly cancer patients undergoing radiotherapy. **Recommendations:** Counseling sessions and educational program should be offered to elderly patients to be aware of the core information about fatigue, additionally, supportive care interventions and treatment of the associated symptoms (depression) should be a part of a comprehensive management strategy of cancer related fatigue.

Key Words: Cancer, Cancer related Fatigue, Depression, Elderly Patients, Functional status, Radiotherapy.

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I. Introduction

Globally, the number of older adults with cancer is rapidly growing and it is expected to increase significantly ⁽¹⁾.In the USA, over 60 % of new cancer diagnoses and approximately 70 % of cancer mortality occur in patients aged 65 years and over ⁽²⁾. In Egypt; according to National Cancer Registry Program, the incidence of cancer is expected to increase from approximately 115,000 patients in 2013 to more than 331,000 in 2050, almost 3-fold increase. This increase reflected both population growth and demographic change mainly due to ageing of population ⁽³⁾. At the same time, the early diagnosis, improved treatment, and better supportive care have improved cancer survival rates in the United States ⁽⁴⁾, consequently, a greater number of elderly patients will become cancer survivors and these patients may have persistent side effects from cancer therapy and will need continued supportive care interventions ⁽⁵⁾. Elderly patients are more likely to have side effects of cancer therapy and often presents with age-related physiological changes in multiple organ systems andincreasing comorbidities, which predispose to fatigue ⁽⁶⁾.

Cancer-related fatigue (CRF) is the most prevalent and distressing side effect of cancer and its treatment affecting both cancer patients and survivors ⁽⁷⁾ Although it has been estimated that up to 70 % of elderly with cancer experience fatigue, this symptom is still largely ignored in ageing population ⁽⁶⁾ CRF is more severe,

persistent, and debilitating than normal fatigue which caused by lack of sleep or overexertion and it is not relieved by rest or sleep⁽⁸⁾, therefore, the National Comprehensive Cancer Network(NCCN) define cancer related fatigue as "distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" ^{(9).}

Cancer related fatigue is a multi-factorial, hence, the development of fatigue can be influenced by a variety of contributing factors which includes demographic, medical, psychological, behavioral, andbiological factors. Being unmarried and having low income are considered a demographic factor for developing fatigue in some reports ⁽¹⁰⁾. Additionally, especially in older adults, the other contributing factors as medical comorbidities, medications, nutritional issues, physical deconditioning, depression, and sleep disorder are also influence the development of fatigue ^(6,10).

The exactly mechanism responsible for CRF are not yet completely understood but there are a variety of biological mechanisms have been proposed and investigated over the past two decades. These include cytokine dysregulation, hypothalamic pituitary-adrenal (HPA) axis dysregulation, five hydroxy tryptophan (5-HT) neurotransmitter dysfunction, alterations in adenosine triphosphate(ATP) and circadian rhythm disruption ⁽¹¹⁾. The cytokinesdysregulation especially the pro-inflammatory cytokines is the most approved mechanism and has an empirical attention ⁽¹⁰⁾. Cancer therapy and the tumor itself can contribute to elevated level of cytokine in plasmawhich results in increased level of fatiguevia cytokine signaling in the central nervoussystem. Before a cancer therapy, thepro-inflammatory cytokines (PICS) as interlukin-1 (IL-1), IL-6, and tumor necrosis factor (TNF- α) are found in the micro environment of tumors, an increased level of these cytokines will lead to development of anemia, cachexia, anorexia and depressionwhich having a role in developing CRF⁽¹²⁾. During a cancer treatment, the activation of these cytokinesis usually related totissue damage from radiation or chemotherapy⁽¹⁰⁾, these cytokines serves as a mediator for inflammatory response or sickness behavior through stimulating the brain to induce sickness feeling. Fatigue is one component of 'sickness behavior' which defined as a coordinated set of adaptive behavioral changes that occur in patient with active infection or inflammation to promote survival. Patients with cancer usually complain of symptoms that may be similar to physiologic components of sickness behavior syndrome (SBS) that precipitated by infection or inflammation. Behavior symptoms of sickness may include pyrexia, general fatigue, decreased appetite, disturbance in sleep, diminished interest of activity, and cognitive impairment. These changes are caused by the release of inflammatory cytokines, therefor, the pro-inflammatory cytokines have an important role in developing fatigue (13,14)

Also, it has been found that inflammation play a role in the development of depression ⁽¹⁵⁾, this is evidenced byMeszaros et al., (2012)and Iacovides& Andreoulakis, (2011), who demonstrated that patients with inflammatory disorders have elevated rates of depression comorbidity. Therefore, fatigue and depression have some similarity in its mechanism by which inflammation playing a role in developing both symptoms in cancer patients ⁽¹⁵⁾. Fatigue and depression have been found to be highly correlated both in cancer patients and in cancer survivors ⁽¹⁶⁾; depression is often a part of a cluster of interrelated symptoms, including fatigue and insomnia ⁽¹⁷⁾. The high prevalence of depression in cancer patients make it a particular concern especially in elderly ⁽¹⁸⁾, which ranged from 16%-26% in oncology elderly patients. The identification of depression in elderly is challenging and it usually unrecognized and untreated. This under recognition may be related to certain factors, it may be due to an older adult tend to hide their affective symptoms like sadness and instead presenting with fatigue and decreased initiation. Another factor is that the health care professionals considers the depression is normal part of aging ^{(19,20).} Although fatigue and depression are heterogeneous symptoms and can be measured independently, both symptoms can be overlapped; lack of energy and feeling weakness is one of a diagnostic criterion that confirming depression. Understanding the factors that can independently cause fatigue and/or depression, and the nature of relationship between two these symptoms have a particular concern ^{(21).}

Cancer-related fatigue adversely affects psychological, social, and physical well-being, it impairs usual functioning andinterferes with patient's ability to perform their daily activities. Additionally, fatigue and depression may act synergistically among cancer patients resulted in deterioration in the qualityof life and impaired functional status ⁽¹⁵⁾. The older adults with cancer have a profound negative impact on their functional status; it was attributed to physiological changes that affects musculoskeletal system ⁽²²⁾, moreover, comorbidity and chronic musculoskeletal diseases that more prevalent in elderly are common causes of disability, which complicating the optimal functioning ⁽²³⁾. Functional status is the ability of persons to ambulate and perform daily living activities to meet their basic needs, fulfill usual roles, and maintain their independency ⁽²⁴⁾. Level of physical activity can be influenced by fatigue in which patients presenting with sever fatigue are usually less active and more dependent. Thus, assessment of functional status and CRF is an important aspect to plan an intervention program in order to improving physical activity that can help in preserving functional status and minimizing cancer fatigue ⁽²⁵⁾.

II. Aim of the study:

Determine the relation of cancer related fatigue with depression and functional status among elderly patients undergoing radiotherapy

Research question:

What is the relation of fatigue with depression and functional status of elderly patients undergoing radiotherapy?

III. Materials and method:

Materials:

Study design:

A descriptive, correlational research design was used in this study.

Setting:

This study was conducted in the outpatient clinic of the Oncology and Nuclear medicine department at Main

Mansoura University Hospital.

Subjects:

A Purposive sample of one hundred and twenty (120) elderly cancer patients collected within a period of three months (from the 1st of May to the 1st of August, 2016), aged 60 years and above, attending the above mentioned setting, scheduled to receiving radiotherapy, and able to communicate. Those who diagnosed with a psychiatric or neurological disorder, or having sever organ failure were excluded from the study sample.

Tools:

Five tools were used to collect data for this study

Tool I: Interviewquestionnairesheet: -

This tool was designed by the researcherand included three parts.

-Part one: the demographic characteristics of the older adults such as age, sex, marital status, level of education living condition and place of residence.

- Part two: includes clinical data as medical history of chronic diseases.

- Part three: Disease related characteristics which include cancer type, treatment type, number of radiation sessions, and side effects of radiotherapy.

Tool II: The Revised Piper fatigue scale (PFS-R): -

It is a multidimensional self-report instrument that is widely used for assessing cancer related fatigue in cancer patients, and developed by Piper et al., 1998⁽²⁶⁾. The scale consists of 22 numerical items using a 0-10 numeric scale while 0 represent no fatigue and 10 represent a maximum fatigue, and five additional open ended questions related to the temporal dimension of fatigue, its perceived cause, effect, relief, and additional symptoms but not included in the scoring. These 22 items divided into four subscales which measure four dimensions of fatigue: behavioral/severity (6 items), affective meaning (5 items), sensory (5 items), and cognitive/mental (6 items). The severity codes are: none (0), mild (1-3), moderate (4-6) and severe (7-10).

Tool III: Geriatric Depression Scale (GDS-SF) short form: -

It is an effective tool used for screening and assessment of depression in older adults and developed bySheikh and Yesavage, $1986^{(27)}$. The scale consists of 15 questions with "yes" or "no" answers which focused on mood rather than physical symptoms. It was modified from the long form scale (30-item) to focus on items with the highest correlation to depressive symptoms in validation studies. Of the 15 items, assign one point (1) for questions number (1, 5, 7, 11, 13) when answered negatively and assign one point (1) for the rest of questions when answered positively. The scores are added and categorized as the following: No depression: 0-4; mild: 5-8; moderate: 9-11; and severe: 12-15.

Tool IV: Katz and Akpom scale:

Katz scale is frequently used in clinical practice as a part of a comprehensive geriatric assessment (CGA) to measure patient's ability to perform the basic activity of daily living (ADL) independently. It was developed by Katz and Akpom,1976⁽²⁸⁾, and consists of six items including bathing, dressing, toileting, transferring, continence, and feeding. These six different items were measured and scored according to the patient's actual performance of thesefunctions. Each itemwas scored from 1 to 3; where 1 indicates full independence, 2 indicates that thepatient need assistance, and3indicates total dependence. The score of each item was added to obtain the total score and patients were categorized as the following: totally dependent: patient who scored 13 to 18 points, partially dependent: patient who scored 7 to 12 points, and independent: patients who scored 6 points.

Tool V: Lawton and Brody Scale:

The Lawton Instrumental Activities of Daily Living Scale (IADL) is an appropriate instrument to assess independent living skills especially in older adults. It was developed by Lawton and Brody,1969⁽²⁹⁾ and consists of eight items which considered more complex than ADLs. It includes ability to use telephone, shopping, food preparation, housekeeping, laundry, transportation, responsibility for own medication and handling finances. The areas of food preparation, housekeeping, laundering are excluded for men. Each item was scored from one to three; score 3 indicate that the patient can perform the task without any assistance, score 2 indicate that the patient need some help to perform the task and score 1 indicate that the patient unable to perform the task at all. The total score of the scale range from 8-24 point and patients can be categorized as thefollowing; independent: patients who scored 21-24, partially dependent: patients who scored 13-20, and totally dependent: patients who scored 8-12.

Method:

- 1. An official letter was issued from the Faculty of Nursing, Mansoura University to the director of the Oncology and Nuclear Medicine Department at Main Mansoura University Hospitals.
- 2. The head of the radiotherapy unit of the Oncology and Nuclear Medicine Department was informed about the purpose of the study, the schedule of data collection in order to obtain their approval to interview the elderly patients.
- 3. Tool I (interview structured sheet) was developed by the researcher after review of the relevant literature.
- 4. The Arabic versions of the study tools were used and revised by 7 experts in the fields of gerontological nursing, medical surgical nursing, and community health medicine, as a jury to test its content validity and feasibility. The necessary modifications were done accordingly.
- 5. The reliability of tool IIwas assured by means of Cronbach's coefficient alpha. It indicated that toolII has a reliability of 0.94.
- 6. Necessary approval was obtained from the ethical committee of the faculty of nursing, Mansoura University.
- 7. Patient's privacy was assured and confidentiality of the collected data was maintained.
- 8. A pilot study was conducted on fifteen (15) elderly patients from the radiotherapy unit of the Oncology and Nuclear Medicine Department before starting the data collection to check and ensure the feasibility of the tools in providing the required data and to make the necessary modifications, these patients were excluded from the study sample. From this pilot study, the researcher found that the best time to the patients for data collection was before receiving their sessions.
- 9. Based on the schedule of the radiotherapy unit the researcher visited the clinics 5 days per week from Saturday to Wednesday, a face to face interview was conducted with each patient who fulfilled the inclusion criteria of the study.
- 10. The necessary data were collected using the study tools and reviewing patient's records, the time for each interview ranged from 20 to 30 minutes and the data collection covered a period of three months from the first of May 2016 till the first of August 2016.

Statistical Analysis

Data entry and statistical analysis were done using SPSS version 20.0. Data were presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, means and standard deviations for quantitative normally distributed variables, while medians and ranges were used for quantitative not normally distributed variables. Spearman rank correlation was used for assessment of the inter-relationships among quantitative variables. Statistical significance was considered at p-value ≤ 0.05 .

IV. Results

Part I: Demographic characteristics of the study subjects:

Table (1) shows the socio-demographic characteristics of the studied subjects, the age of studied elders ranged from 60 to 87 with a mean age of 64.1 ± 4.7 years. Females constituted 55.0% of the study subjects while males constituted 45.0%. Regarding the marital status, the majority of patients (83.3%) were married and 16.7% of them were widows or divorced. Concerning the residence of the studied elders, the majority of them (85%) were living in rural areas and 15% in urban areas. Regarding the level of education, about half of the studied sample (51.7%) were illiterate and 29.2% of them were able to read and write

As regards to patient's occupation before retirement, 45% of studied elders were housewives, while workers and farmers constituted 44.2% of study sample The rest of the patient (10.8%) were employee. In relation to living condition, about three quarter of studied elders (74.2%) living with spouse and kids while 18.3% of them living with one of sibling.

Part II: Medical history and disease related characteristics of the study subjects:

Table (2) shows the distribution of elderly cancer patients according to their medical history and disease related characteristics, the table shows that more than half of the studied sample (62.5%) suffered from other chronic disease and the hypertension was most frequently disease reported by the studied sample which represent 24.2% of the studied elders, while diabetes mellitus was found in 20%. Concerning the cancer type, breast cancer was more prevailing among the studied elders which constituted 35% followed by lung and gastrointestinal cancer which constituted the same percentage (9. 2%). As for the duration of cancer, more than half of study sample (53.3%) diagnosed with cancer for more than six months, while 46.7% of them diagnosed within less than six months. Regarding the site of radiation, 38.3% of the study sample received radiation at pelvic/abdominal site, 30% at breast site and 19.2% at head and neck site. In relation to number of radiation sessions, slightly more than tow third (69.2%) of study sample received more than ten sessions, while the rest of them (30.8%) received less than ten sessions. Concerning the radiation side effects, the majority of studied elders (98.3%) were suffering from gastrointestinal side effects, while more than half (63.3%) were suffering from skin side effects. Regarding the other side effects, fatigue and insomnia were more reported which constituted 91.6% and 71.7% respectively. Figure (1) show the distribution of the elderly cancer patients according to the treatment types. The figure shows that the majority of studied elders (85%)were undergoing to adjuvant radiotherapy. Figure (2) show the distribution of the elderly cancer patients according to start of radiotherapy from weeks. The figure shows that patients who were in 1st -2nd week of radiation sessions constituted 27.5% of studied elders, while slightly more than half (51.7%) were in 3^{rd} - 4^{th} week and 20.8% of them were in 5^{th} - 6^{th} week.

Part III: Fatigue, depression, and functional status of the study subjects:

Table (3) shows symptoms severity and level of independence in elderly cancer patients, concerning the fatigue level, the majority of studied elders (88.3%) were moderately fatigued, 8.3% were mild and 3.3% were severe. In relation to depression severity, more than half of studied elders (64.2%) were suffering from mild depression, while the rest of them (35.8%) were suffering from moderate depression. Regarding the level of independence, slightly more than half (50.8%) of the study sample were independent, while the rest of them (49.2%) were partially dependent in their activity of daily living (ADLs), while more than two third (73.3%) of the study sample were independent in their instrumental activity of daily living (IADLs).

Part IV: Correlation matrix of fatigue, depression, and functional status of the study subjects:

Table (4) shows the correlation matrix of elderly cancer patients' fatigue, depression and functional status, this table show moderate positive and significant correlation between fatigue and depression ($r = .45^{**}$), and between fatigue and activity of daily livings according to Katz scale ($r = .334^{**}$). It was observed that there was moderate positive and significant correlation between depression and activity of daily livings according to Katz scale ($r = .503^{**}$); this positive correlation means that higher depression significantly correlated with more dependency level, and a moderate negative correlation between Katz and Lawton scale ($r = .-.362^{**}$); the higher score in Katz means more dependency, while in Lawton means more independency and this explained the negative correlation.

V. Discussion

Neoplastic diseases will soon be the leading cause of death in North America and Western Europe. The incidence of cancer increases exponentially with age; therefore, cancer is considered the disease of the elderly ⁽³⁰⁾, and the elderly cancer patients may face greater treatment related toxicities due to the aging ⁽³¹⁾. One of the most prevalent and distressing symptoms associated with cancer and its treatment is cancer related fatigue(CRF). ⁽³²⁾. During a cancer therapy, fatigue can affect the patient's ability to tolerate treatment and may result in treatment discontinuation, as well as, it can interfere with activity of daily livings, interfere with usual functioning and diminishes the quality of life ⁽³³⁾

In the present study, the major characteristics of the studied elders were young old, female, married, illiterate, and house wives. Regarding the age, it is considered the major risk factor for many cancers and older adults make up the largest segment of the cancer population ⁽³⁴⁾. In this study, the majority of elders were young old with a mean age of 64.1 ± 4.7 . This can be attributed to the treatment type in which the majority of studied elders were received radiation as an adjuvant treatment especially after a surgery, a surgery options usually omitted in very old or frail elderly due to the higher complication that may occur. These findingare in line with the finding of studies conductedinCanada and Jordan by**Koo et al., (2012)**, and**Ahmed and al Gamal, (2014)**, who revealed that the average age of elderly patients was 65 ± 12 years, and 63.4 years old respectively ^(35,36). This is in contrast with the finding of a study conducted in France by **Corre et al (2016)**who found that the median age was 77 years old in the elderly with Advanced Non–Small Cell Lung Cancer ⁽³⁷⁾.

As for sex, females constituted more than one half of the studysubjects. This may be attributed to the fact that certain types of cancers are associated with gender like breast cancer, which more common in females and constituted more than one third of study sample. This is in line with the finding of a study conducted in USA by **Hurria etal.**, (2011), and a study conducted in Mexico by **Zepeda et al.**, (2016), which reveals that females were constituted more than one half of the study sample ^(38,39). These finding are in contrast with a studies in Portugal and California by **Silveira et al.**,(2011), and **Miaskowski et al.**, (2011), who reported that male was more prevailing in their studies ^(40,41).

In relation to presence of other chronic disease, hypertension was reported by almost one quarter of the studied elders followed by diabetes mellitus. This result may be attributed to the fact that advancing age is usually associated with presence of numbers of chronic disease and comorbidities. These findings are in line with a study conducted in a china by **Yong et al (2012)**, and a study conducted in Thailand by **Chindaprasirt et al ., (2014)**, which reported that the hypertension was the most common chronic disease in cancer patients ^(42,43).

As for cancer type, the probability of developing breast cancer increases with ageing which more than 50% of breast cancer cases diagnosed in women older than 65 years old ⁽⁴⁴⁾. In the current study, breast cancer was the commonest type of cancer which reported by more than one third of the study subjects, this may be explained by the fact that radiation therapy is standardly offered after breast-conserving surgery (BCS) or when regional lymph nodes are involved. After lumpectomy, adjuvant radiotherapy considers a standard of care ⁽⁴⁵⁾. This result is in line with a study by **Magdy**, (2015), and a study by **Tag elmelok**, (2015), in Egypt, el Mansoura which found that breast cancer was more prevalent in their studies ^(46,47).

Radiotherapy-induced fatigue is a common early and long-lasting side effect of radiation therapy which usually underestimated ⁽⁴⁸⁾. In the current study, more than three quarter of the study subjects had a moderate fatigue level according to the revised piper fatigue scale with a total mean score 5.5 ± 1.0 . This may be attributed to the majority of patients in this study were in a third and fourth week of radiation therapy and fatigue tend to increase after the second week of treatment. This finding agrees with **Borneman et al., (2011)**, and **withIwase et al., (2015)**, who reported that moderate fatigue was more prevailing among their study subjects ^(49,50). This finding is in contrast with **Kim et al., (2013)**, who reported that majority of women undergoing radiation therapy for breast cancer had a mild fatigue score on PFS ⁽⁵¹⁾.

Fatigue and depression are usually associated symptoms ⁽¹⁰⁾, in elderly cancer patients, depression may be related to specific health risks as longer hospital stay and increase mortality rates ⁽¹⁵⁾. In this study, nearly two third of the study subjects had a mild depression according to geriatric depression scale-short form (GDS-SF). This finding agrees with **Frazzetto et al.**, (2012), who reported that nearly half of elderly breast cancer patients and survivors were mild depressed ⁽⁵²⁾. In contrast, a study done in India by **Kroenke et al.**, (2010), who found that the mean score of depression was 1.64 on a 0-4 scale of Hopkins Symptom Checklist (SCL) depression scale, which represent moderate depression ⁽⁵³⁾.

CRF has a considerable negative impact on normal functioning, it interferes with patient's ability to perform normal daily activities and overall quality of life ⁽⁵⁴⁾. In the current study, according to Katz scale, slightly more than half of the study subjects were independent while the rest were partially dependent in their activity of daily living (ADLs). According to Lawton scale for instrumental activity of daily living (IADLs), nearly three quarter of patients were partially dependent while the rest were independent. The more limitation in IADLs may be attributed to the fact that these activities are more complex than ADLs, another explanation is that females were more prevailing in this study, which hada responsibility of food preparation, laundry and housekeepingtasks. These finding supported by **Gironés et al.**, (2010), who reported that the majority of breast cancer survivors were independent in ADL while found more limitation in IADLs as the majority were partially dependent in their ADLs and IADLs ^(55,56).

Fatigue and depression are strongly correlated in cancer populations. The association between two these variables is complex; fatigue is a symptom of depression, but may also precipitate depressed mood due to interference with social, occupational, and leisure activities ⁽¹⁰⁾. The finding of this study approved that a moderate positive and significant correlation between fatigue and depression; the higher fatigue was associated with higher depression. Fatigue can lead to functional limitation making the patients less active and more dependent on caregiver, this absolutely had a negative impact on psychological status of the patients and precipitate depression. This finding is in line with other studies in Iran and United States, **Vahdaninia et al.**, (2010) and Brown et al., (2013), who demonstrated that there was a strong positive and significant correlation between fatigue and depression^(57,58).

Functional status is also another important concern which usually affected by fatigue and aging process ⁽⁵⁹⁾. The present study tests the association between fatigue and functional ability in terms of activity of daily living (ADL) and instrumental activity of daily living (IADL), the results revealed that a statistically significant and a moderate positivecorrelation between fatigue and Katz score for ADL; the higher score in Katz scale means more dependency, hence, higher fatigue was significantly correlated with more dependency in ADLs. This finding agrees with **Cheng and Lee**, (2010), who assess effect of fatigue on functional status in older adults with cancer using Karnofsky performance scale (KPS) for functional status and symptoms distress scale (SDS-C) for fatigue and other symptoms, they found a negative moderate correlation between KPS and fatigue. Lower score in KPS means lower functional status, so that, the correlation was negative which means that the patients scored higher fatigue experience lower functional status ⁽¹⁷⁾. Also, **Rotonda et al.**, (2013), who studied the factors associated with fatigue after surgery in breast cancer women and concluded that an increase in fatigue score was significantly correlated with decreased physical and role functioning ⁽⁶⁰⁾.

In aging population, depressive symptoms can interfere with the elder's ability to perform the basic activity of daily living⁽⁶¹⁾. Therefore, the current study analyzed the associations between depression and functional status, it has been found that a significant and amoderate positive correlation between depression and Katz scale for ADLs. This means the higher depression score is significantly correlated with more dependency. Patients who are dependent in their basic activity usually need assistance and those patients appeared to perceive their dependency as a source of burden for their caregivers, this cause additional stress to the patient and become depressed. Another explanation of why depression and functional status were associated is that dependency on other usually related to loss of power over decision making and those patients were relying on other to decide on them behave on what and when to do most of things of their daily livings.

The finding of this study is in line with **Yagli et al.**, (2015), who suggested that depressive symptoms were worse among more sedentary patients with breast cancer and also found a negative correlation between physical activity level and psychological status in which women who were less active experience higher depression ⁽⁶²⁾. In the same context, **Magyari et al.**, (2017), conducted a study to evaluate psychological distress and its risk factors among Hodgkin lymphoma survivors, their results revealed that psychological distress was significantly lower in active patients ⁽⁶³⁾. Moreover, **Tejada et al.**, (2017), also concluded that colorectal cancer patients who are functionally independent may have better results in anxiety and depression at 1 year after surgery ⁽⁶⁴⁾.

VI. Conclusion and Recommendations

Conclusion

Based on findings of the present study, it can be concluded that majority of the studied elders reported a moderate fatigue, which significantly correlated with depression and basic activity of daily livings.

Recommendations

Based on the finding of this study the following recommendations are suggested: -

- Counseling sessions should be offered to elderly patients, families and caregivers to encourage them to ask questions and provide the assistance in a form that they can understand. The individual counseling is recommended to each patient in order to identify the potential risk factors of fatigue which can be important keys for its management.
- Development and application of educational program for elderly cancer patients involving an educational sessions and through use of brochures and written materials regarding the core information about cancer related fatigue and effective coping strategies, to improve patient's understanding to their fatigue level, to manage it early as possible, and to prevent it to get worse
- Supportive care interventions (exercise and psychosocial interventions) and treatment for other symptoms (depression) should be a part of a comprehensive management strategy for fatigue, the elderly cancer patients should be informed about such interventions through use of brochures and/or booklet distributed to each patients in the outpatient's clinics, this will help patients to participates in their care plan, making them controlled over their daily activity, and improves their sense of autonomy.

Further research

Fatigue is a subjective and a fluctuating symptoms which can be changed over the time, further research is needed to identify the daily and intraday variation of fatigue during a cancer treatment, its relationship with the identified correlated factors, and whether other variable that may contribute to it.

Table (1):	Distribution	of the elderl	v cancer	natients	according to	their d	emographic	characteristics.	_
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Items	No= (120)	%		
Age (In years)				
• 60-64 yrs	77	64.2		
• 65+	43	35.8		
Mean±SD (Min-Max)	64.1±4.7 (60	64.1±4.7 (60.0-87.0)		
Gender:				
Male	54	45.0		
Female	66	55.0		
Residence:				

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Rural	102	85.0
Urban	18	15.0
Marital status:		
Unmarried (divorced/widow)	20	16.7
Married	100	83.3
Education:		
Illiterate	62	51.7
Read/write	35	29.2
Basic/intermediate	18	15.0
University	5	4.2
Occupation before retirement:		
Employee	13	10.8
Worker/farmers	53	44.2
Unemployed/housewife	54	45.0
Living condition:		
With spouse	9	7.5
With spouse and kids	89	74.2
With one of sibling	22	18.3

Table (2): - Distribution of elderly patients according to their medical history and disease related characteristics

Having other chronic disease 75 62.5 No 45 37.5 Diseases: ® 29 24.2 • Hypertension 29 24.2 • Diabetes 24 20.0 • Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagoods (cancer): ® - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Lung 11 9.2 • Lung 11 9.2 • Lung (Guecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions 37 <t< th=""><th></th><th>Items</th><th>No= (120)</th><th>%</th></t<>		Items	No= (120)	%
• Yes 75 62.5 • No 45 37.5 Diseases: 9 24.2 • Hypertension 29 24.2 • Diabetes 24 20.0 • Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Lung 11 9.2 • Lymphoma / Gynecological 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 • Others (Bone, Sarcomas, Skin) 10 8.3 • Others (Bone, Sarcomas, Skin) 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.4 • Chest 9 7.5 • Thi	Having oth	ner chronic disease		
• No 45 37.5 Diseases: [∞] - - • Hypertension 29 24.2 • Diabetes 24 20.0 • Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): [®] - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine / Oropharyngeal 10 8.3 • Others (Bone, Sarcomas, Skin) 10 8.3 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Pelvi-abdominal 46 33.3 • Breast 36 30.0 • Pelvi-abdominal 46 33.3 • Breast 36 69.2 • Chest	•	Yes	75	62.5
Diseases: ** 29 24.2 • Hypertension 29 24.2 • Diabetes 24 20.0 • Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): * - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.3 • Others (Bone, Sarcomas, Skin) 10 8.3 • Delvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 • No 2 1.7 Have gastrointest	•	No	45	37.5
• Hypertension 29 24.2 • Diabetes 24 20.0 • Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): ** - - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 16.6 • Endocrine / Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9	Diseases	:		
• Diabetes 24 20.0 • Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): [@] - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Jymphoma / Gynecological 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy: - - • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects - - • Yes 76 63.3	•	Hypertension	29	24.2
• Musculoskeletal disease 24 20.0 • Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): • • • • • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Cymphoma / Gynecological 18 16.6 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.3 • Others (Bone, Sarcomas, Skin) 10 8.3 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 • No. 37 30.8 <td>•</td> <td>Diabetes</td> <td>24</td> <td>20.0</td>	•	Diabetes	24	20.0
• Cardiac disease 19 15.8 • Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): [@] - - • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Castrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy: - - • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 • No. of sessions: - - • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects - - <td>•</td> <td>Musculoskeletal disease</td> <td>24</td> <td>20.0</td>	•	Musculoskeletal disease	24	20.0
• Other (renal, GIT, Respiratory) 27 22.5 Diagnosis (cancer): [@] . • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 • Breast 36 30.0 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 • More than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (G) side effects - - • Yes 76 63.3 • No 2 1.7 Have gaster side effects [@] - - • Yes	•	Cardiac disease	19	15.8
Diagnosis (cancer): * · • Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 • Breast 36 30.0 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 • No. of sessions: 83 69.2 • Yes 118 98.3 • Yes 76	•	Other (renal, GIT, Respiratory)	27	22.5
Breast 42 35.0 • Lung 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy:	Diagnos	is (cancer): [@]		
Lung 11 9.2 • Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy:	•	Breast	42	35.0
• Gastrointestinal 11 9.2 • Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy:	•	Lung	11	9.2
Lymphoma / Gynecological 18 15 • Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy: - - • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions: - - • Less than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects - - • Yes 118 98.3 • No 2 1.7 Have skin side effects - - • Yes 76 63.3 • No 2 1.7 Have skin side effects: [@] - - • Yes 76 63.3 • No 44 36.7 Other side effects: [@] - </td <td>•</td> <td>Gastrointestinal</td> <td>11</td> <td>9.2</td>	•	Gastrointestinal	11	9.2
• Prostate / Urinary bladder 18 16.6 • Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy:	•	Lymphoma / Gynecological	18	15
• Endocrine/ Oropharyngeal 10 8.4 • Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy: - - • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions: - - • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects - - • Yes 118 98.3 • No 2 1.7 Have skin side effects - - • Yes 76 63.3 • No 2 1.7 Have skin side effects: [@] - - • Yes 76 63.3 • No 44 36.7 Other side effects: [@] - - • Fatigue 110 91.6	•	Prostate / Urinary bladder	18	16.6
• Others (Bone, Sarcomas, Skin) 10 8.3 Site of radiotherapy:	•	Endocrine/ Oropharyngeal	10	8.4
Site of radiotherapy: 46 38.3 • Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions: 37 30.8 • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects 98.3 69.2 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 69.2 • Yes 76 63.3 • No 2 1.7 Have skin side effects: $^{@}$ $ -$ • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ $ -$ • Fatigue 110 91.6 • Insomnia 86 71.7 <td>•</td> <td>Others (Bone, Sarcomas, Skin)</td> <td>10</td> <td>8.3</td>	•	Others (Bone, Sarcomas, Skin)	10	8.3
• Pelvi-abdominal 46 38.3 • Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions: $ -$ • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects $ -$ • Yes 118 98.3 • No 2 1.7 Have skin side effects $ -$ • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ $ -$ • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	Site of r	adiotherapy:		
Breast 36 30.0 • Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions: 37 30.8 • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects 98.3 69.2 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 69.2 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 67.2 • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ $ -$ • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7	•	Pelvi-abdominal	46	38.3
• Head and neck 25 20.9 • Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions: 37 30.8 • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects 98.3 69.2 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 67.2 • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ $ -$ • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Breast	36	30.0
• Chest 9 7.5 • Thigh / Lower back 4 3.3 No. of sessions:	•	Head and neck	25	20.9
• Thigh / Lower back 4 3.3 No. of sessions: 37 30.8 • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects 98.3 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 67.2 • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ 91.6 67.2 • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Chest	9	7.5
No. of sessions: 37 30.8 • Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects 83 69.2 • Yes 118 98.3 • No 2 1.7 Have skin side effects 2 1.7 • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ $-$ • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8 <td>•</td> <td>Thigh / Lower back</td> <td>4</td> <td>3.3</td>	•	Thigh / Lower back	4	3.3
• Less than 10 sessions 37 30.8 • More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects 83 69.2 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ $-$ • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	No. of se	essions:		
• More than 10 sessions 83 69.2 Have gastrointestinal (GI) side effects • Yes 118 98.3 • No 2 1.7 Have skin side effects • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Less than 10 sessions	37	30.8
Have gastrointestinal (GI) side effects 118 98.3 • Yes 118 98.3 • No 2 1.7 Have skin side effects 63.3 • Yes 76 63.3 • No 44 36.7 Other side effects: $^{@}$ 91.6 • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	More than 10 sessions	83	69.2
\cdot Yes 118 98.3 \cdot No 2 1.7 Have skin side effects \cdot \cdot \cdot Yes 76 63.3 \cdot No 44 36.7 Other side effects: $^{@}$ \cdot \cdot \cdot Fatigue 110 91.6 \cdot Insomnia 86 71.7 \cdot Weight loss 54 45.0 \cdot Chest pain 32 26.7 \cdot Dysuria 31 25.8 \cdot Pyrexia 1 0.8	Have gasti	ointestinal (GI) side effects		
• No 2 1.7 Have skin side effects - - • Yes 76 63.3 • No 44 36.7 Other side effects: [@] - - • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Yes	118	98.3
Have skin side effects 63.3 • Yes 76 63.3 • No 44 36.7 Other side effects: [@] 76 63.3 • Fatigue 110 91.6 • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	No	2	1.7
Yes 76 63.3 • No 44 36.7 Other side effects: [@] • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	Have skin	side effects		
• No 44 36.7 Other side effects: [@]	•	Yes	76	63.3
Other side effects: [@] 110 91.6 • Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	No	44	36.7
• Fatigue 110 91.6 • Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	Other si	de effects: [@]		
Insomnia 86 71.7 • Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Fatigue	110	91.6
• Weight loss 54 45.0 • Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Insomnia	86	71.7
• Chest pain 32 26.7 • Dysuria 31 25.8 • Pyrexia 1 0.8	•	Weight loss	54	45.0
• Dysuria 31 25.8 • Pyrexia 1 0.8	•	Chest pain	32	26.7
• Pyrexia 1 0.8	•	Dysuria	31	25.8
	•	Pyrexia	1	0.8

(@) Not mutually exclusive

Table (3): Symptoms	severity (fatigue.	depression) and	level of independence	v among the elderly	v cancer patients
()	~~····································			J	/

Items	N=120	%
Fatigue:		
Mild	10	8.3
Moderate	106	88.3
• Severe	4	3.3
Depression:		
Mild	77	64.2
Moderate	43	35.8
Total Katz:		
 Independent 	61	50.8
Partially dependent	59	49.2
Total Lawton:		
• Dependent	88	73.3
 Independent 	32	26.7

Table (4): -The correlation matrix of elderly cancer patients' fatigue, depression and functional status

Items	Spearman's rank correlation coefficient				
	Fatigue	Depression	Katz(ADLs)		
Fatigue					
Depression	.45**				
Katz	.334**	.503**			
Lawton	0.04	-0.11	-362**		

(**) Statistically significant at p<0.01





Figure (2): - Distribution of the elderly cancer patients according to start of radiotherapy from weeks

Start of radiotherapy from (weeks) 51.7% 60 50 1st-2nd week 40 7.5% 30 20.8% 🗖 3rd -4th week 20 🗖 5th -6th week 10 ο 1st-2nd week 3rd -4th week 5th -6th week

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