

Malnutrition Predictors among Breast Cancer Women Undergoing Chemotherapy

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Abstract: Malnutrition is a problem that greatly affects cancer patients throughout the course of the disease and it may be present from the moment of diagnosis until the end of treatment. Therefore, nutrition screening is an important step to identify cancer patients who are at risk for malnutrition to maximize the efficiency of treatment. The current study was performed to evaluate malnutrition predictors among breast cancer women undergoing chemotherapy. The following research question was formulated to fulfill the aim - What are the malnutrition predictors among breast cancer women undergoing chemotherapy? A descriptive research design was utilized in the current study. The research was conducted in the oncology department at a selected teaching university hospital in Cairo, Egypt. A convenience sample of 60 adult conscious patients with breast cancer undergoing chemotherapy was recruited. Structured interview questionnaire and nutritional screening related indices were used to collect data. Results showed that the most reported risk factors affecting nutrition especially at the end of treatment were stomach trouble, vomiting, stomatitis, taste alteration, decreased appetite and swallowing difficulty (96.7, 96.7, 86.7, 83.3, 78.3 and 78.3%) respectively. Based on nutritional risk index, all study subjects were at major risk for malnutrition. It can be concluded that the considerable breast cancer women were in poor nutritional status before, during and after chemotherapy. So, comprehensive nutritional assessment and appropriate nutritional intervention are necessary for the treatment of breast cancer women undergoing chemotherapy. The current study results contribute to the body of evidence that nutrition screening is important to identify those at nutrition risk to prevent nutritional problem among breast cancer woman and to help to remain active and healthy within the community. Therefore, nutritional assessment should become an integrated part of the total management of breast cancer woman. Hospital and healthcare organizations should have a written policy and a specific set of protocols for identifying patients at nutritional risk to provide information required for treatment protocol through the appropriate nursing care plan.

Key words: Breast Cancer • Malnutrition Predictors • Nutrition Screening • Risk Factors • Chemotherapy • Adverse Events • Nutrition Risk Index

INTRODUCTION

Breast cancer is the second most frequent invasive cancer affects women worldwide and the second-ranking leading cause of cancer death among the woman age 40-44 after lung cancer. It accounts for 23% of all new cancer cases and 14% of all cancer deaths [1, 2]. Among Egyptian women, breast cancer is the most prevalent type of cancer (38.8%); and constitutes (29%) of National Cancer Institute cases [3]. According to WHO (2006), the estimated number of new cancer cases will rise from 10 million diagnosed in 2000 to 15 million in 2020. Advanced

diagnostic methods and new treatment strategies have effectively contributed to the increase in life expectancy of cancer patients [4- 5].

Surgical management is the first mode of therapeutic intervention and fundamental treatment strategies in the majority of breast cancer cases. Surgery combined with radiotherapy has been the typical treatment to control loco-regional disease to avoid recurrence from micro-metastasis. Also, adjuvant chemotherapy is the cornerstone of breast cancer treatment modality to kill or inhibit clinically undetectable micro-metastasis after primary surgery and to improve survival.

Adjuvant chemotherapy may increase 10-year survival by 7–11% in premenopausal women with early-stage disease and by 2–3% in women aged over 50 in both node-negative and node-positive disease [6]. Cancer patients undergoing chemotherapy usually experience a variety of symptoms as a result of chemotherapy-induced toxicity [7]. However, Anti-cancer treatment can induce nausea, vomiting, anorexia, sore throat, dry mouth, taste alteration, stomach trouble as mucositis, diarrhea, constipation and fatigue which eventually lead to poor nutritional status or malnutrition [8-11].

It is widely known, that patients with cancer have limited ability of food intake, due to a variety of factors such as the side effects of chemotherapy and the type of cancer, which result to the impairment of their immune system and their general functional status, predisposing thus, the appearance of depression. Another explanation of this result is, that in a high level of depression patients are unwilling to consume food and consequently the treatment of cancer is temporarily delayed until the treatment of depression. Finally, Studies had shown that low serum albumin concentrations in malnourished patients with advanced cancer resulted in a low clearance of highly albumin-bound drugs which, in turn, caused increased free drug concentration and contributed to unexpected toxicity. Also, several of the common chemotherapeutic agents bind to red blood cells; anemia is associated with a greater concentration of free drug in the circulation and contributes to unexpected drug toxicity [7, 12]. So, the main goal before, during and after treatments is to maintain adequate calories for weight maintenance and adequate protein to optimize the immune system, strength and tolerance to treatments [13]. The American Cancer Society recommends that people going through chemotherapy pay extra attention to nutrition because a healthy diet can help speed recovery to improve health status outcomes [14].

The nutritional status plays a key on the anticancer treatment outcome. High risk of malnutrition among cancer patients is associated with negative outcomes including increased morbidity; poor response and tolerance to treatment; decreased the quality of life and thus, increased health-care costs. Early identification of malnutrition and appropriate nutrition support may lead to beneficial outcomes including improvements in nutritional status and quality of life. So, nutrition screening must be applied to all patients and hence, provide systematic identification as opposed to ad hoc referral of patients requiring further assessment and nutrition support if required. In the absence of nutrition screening, malnutrition may not be recognized or treated [15-18].

Breast care nurse is the first person who deals with the patient from admission until discharge from the hospital. The role of the breast care nurse is to provide ongoing counseling, information and support relating to all aspects of breast care for breast cancer women and clarify or reinforce information and provide continuity of care throughout the treatment process. One of the most important roles of nurses is nutritional status assessment related to risk factors affecting nutritional status as well as to the harmful effect of cancer treatment [19]. So, adequate nutrition should be considered a priority by nurses for developing strategies for the promotion, maintenance and/or recovery of the nutritional status. Therefore, the aim of this study was to evaluate malnutrition predictors among breast cancer women undergoing chemotherapy in the oncology department at Cairo University.

Significance of the Study: About 30 - 40 % of all patients in hospital are undernourished. A large part of these patients are undernourished when admitted to hospital but the majority of these patients develop further while in hospital [20-22]. Studies have demonstrated that anywhere from 30 to 87% of cancer patients are diagnosed with malnutrition, with 30 – 60% of cancer patients diagnosed with protein- calorie malnutrition [23, 24].

Cancer-associated malnutrition is major cause of morbidity and mortality in cancer. Approximately 50% of cancer patients are at risk of malnutrition. In Egypt, breast cancer is the most cancer among women, representing 18.9% of total cancer cases. A significant proportion of patients with breast cancer seem to experience malnutrition. A recent study carried out on patients with breast cancer found about 40% of cancer patients die of malnutrition before they would have died of their cancer [25]. The incidence of obesity is most commonly documented among women recently diagnosed with breast cancer ranges from 24-38% added to 40-70% of breast cancer women receiving adjuvant chemotherapy gain weight changes [26].

Surgery, radiotherapy and chemotherapy offered to breast cancer woman are often aggressive, resulting in side effects that can seriously affect the ability to take sufficient nutrition. Nausea and vomiting can be severe that patients are unable to take anything orally. This has a similar effect to the onset of chemotherapy-induced mucositis; while diarrhea can cause total malabsorption of nutrients, if only for a few days. Many women will encounter all three treatment modalities, thereby increasing the risk of serious malnutrition, which can compromise response to treatment [15]. Cancer patients

can face a harrowing journey from diagnosis and treatment to recovery. This can be prevented if special attention is paid to the nutritional care. However, the lack of a widely accepted nutrition screening system in hospital that detects patients who might benefit clinically from nutritional support is commonly seen as a major limiting factor to improvement [22].

Thus, nutrition screening is an important step to identify cancer patients who are at risk for malnutrition and to provide information required for treatment protocol preparation. It is important to start appropriate nutrition assessment and support as soon as possible. Nurses keen to provide sound nutritional screening assessment and guidance that come armed with knowledge of modalities best suited to enhance survival. Therefore, it is important to determine nutritional status of cancer patients before starting chemotherapy to maximize the efficiency of treatment. Hence, the researcher has decided to evaluate malnutrition predictors among breast cancer women undergoing chemotherapy. The researcher aspires that these research findings will contribute some useful knowledge in the area of nutritional assessment and its related interventions of cancer patients undergoing chemotherapy, as well as encourages others to investigate and propose protocol of care for such patients. Breast cancer nurses are ideally placed to deliver these initial messages and to refer breast cancer women to dieticians or nutritionists for further health post-recovery.

MATERIALS AND METHODS

Aim: The current study was conducted to evaluate malnutrition predictors among breast cancer women undergoing chemotherapy in the oncology department at Cairo University.

Research Question: the following research question was formulated to fulfill the aim of the current study: What are the malnutrition predictors among breast cancer women undergoing chemotherapy?

Design: An exploratory descriptive research design was used to achieve the aim of the current study [27]. This design helped researcher to observe, describe and document aspects to provide rich descriptive details about malnutrition predictors among breast cancer women undergoing chemotherapy.

Setting: The study was conducted in oncology department at Al-Kaser Al-Aini (Manial University) hospital, in Cairo-Egypt.

Subjects: A convenience sampling of 60 woman aged 20 and above, diagnosed with breast cancer at any stage who were taking only chemotherapy treatment. Other inclusion criteria, they must able to understand the procedure of the study, what was required from them and give consent for the study. Also, they were willing to undergo anthropometric measures. The exclusion criteria were those with other malignancies; any type of illness that may affect nutritional status as psychiatric illness affecting nutrition as anorexia nervosa, patients with zenker diverticulum, malabsorption syndrome or metabolic syndrome affecting digestion; kidney and liver diseases were excluded, also, the women who were receiving enteral and/or parenteral nutrition.

Tools: Data pertinent to the study variables were collected through two main tools:

Structured Interview Questionnaire: It was designed by the researcher and covered patient characteristics which include: (a) Demographic characteristics such as age, marital status, education and occupation. (b) Clinical parameters variables related to current medical diagnosis and its stage, type of surgery, length of hospital stay, time of chemotherapy administration, number of chemotherapy sessions and course of treatment duration.

Nutritional Screening-Related Indices: It was carried out using 2 main tools: (1) Nutritional Assessment tool and (2) Nutritional risk index (NRI).

Nutritional Assessment Tool: Adopted from Jarvis [28] this tool was modified and translated into Arabic version and then tested for validity and reliability by El Feky [29]. The needed modifications were done by experts in the field of medical-surgical nursing specialty, faculty of nursing Cairo University and Oncology department. The tool includes four main parts: (i) Anthropometric measurement; (ii) Risk factors affecting nutritional status; (iii) Biochemical markers; (iv) Screening summary.

Anthropometric Measurements: Help to evaluate the patient's nutritional status through the 4 measurement components:

Body Mass Index (BMI): Provides a simple, yet accurate method of assessing whether a patient is at risk from either over-or-underweight. It was calculated as weight (In kilograms) divided by height (In meters) squared. BMI was categorized according to the international standards into 5 groups: (i) Underweight if BMI was

Table 1: Standard Reference for Woman: Weber and Kelley [32]

Categories	TSF	MUAC	MAMA
Standard reference.	16.5	28.5	23.2
Mild malnutrition: 90 – 99 % of standard reference.	14.9	25.7	20.9
Moderately malnutrition: 60 -90 % of standard reference.	9.9	17.1	13.9
Severely malnutrition: < 60% of standard reference.	< 9.9	< 17.1	< 13.9

under 18.5 kg/m², (ii) Normal weight if BMI was 18.5 - 24.9kg/m², (iii) Overweight if BMI was 25 - 29.9kg/m², (iv) Obesity if BMI was 30-39.9 kg/m² and (v) Extreme obesity ≥ 40kg/m². A healthy BMI is a level of 19 or greater to less than 25 kg/m² [30, 31].

Triceps Skin Fold Thickness (TSF): indirectly measures subcutaneous fat stores and is therefore an index of total body fat because approximately half of total body fat is directly under the skin [30, 32].

Mid Upper Arm Circumference (MUAC): It was recorded using a plastic measuring tape. The adult’s right upper arm was flexed to 90 degrees at elbow. The midway between the tip of the acromium and the tip of the olecranon process was identified to measure skeletal muscle mass. Although it is not a useful measurement when used alone, it is used as a part of the procedure of calculating mid- arm muscle area [32, 33].

Mid-Arm Muscle Area (MAMA): Is considered to be a more sensitive measure of long –standing malnourishment to measure protein store in skeletal muscle mass by subtracting subcutaneous fat from arm circumference. $MAMA = MUAC (cm) [3.142 \times TSF] (cm)$ [32, 34] (Table 1).

Biochemical Markers: An objective evaluation of organ function can be determined using Complete Blood Count such as Hemoglobin (12.1 to 15.1 gm/dl), RBCs (4.2 to 5.4 million cells / mcl), WBCs (4.5000 to 10.000 cells / mcl) and albumin (3.8 to 5.1 gm /dl) [35].

Risk Factors Affecting Nutritional Status: It covers 13 items answered by yes or no such as suffer from decreased appetite, taste alteration, chewing difficulty, difficulty swallowing, vomiting, gum thickening, stomatitis, diarrhea, constipation, stomach trouble (Gastritis, heart burn, abdominal pain and fullness) food allergy / tolerance, unable self –feeding and mobility alteration.

Screening Summary: Include five questions, answered by yes or no, related to marked underweight; overweight;

unintentionally weight loss, at least 3 risk factors affecting nutrition and serum albumin is less than or equal 3.5 gm/dl. Scoring system: If the patient has at least one question of them marked by yes, she was considered at high risk for developing nutritional problems.

Nutritional Risk Index (NRI): It is considered to be one of the important biochemical parameters to assess the nutrition status of patients. NRI has been used as a nutrition status tool for the surgical and cancer patients and it was found to be a sensitive and positive predictor of malnutrition in these patients. The formulae based calculation of NRI provides some objectivity in the assessment of nutrition status. It was originally derived from the serum albumin concentration and the ratio of present to usual weight. $NRI = 1.519 \times \text{Serum Albumin (G/L)} + 0.417 \times (\text{Current Weight/ideal body weight}) \times 100$. Body Weight (BW) change was calculated as: $(\text{Current BW in kilograms} - \text{ideal BW in kilograms}) / \text{ideal BW} \times 100$. Ideal BW was calculated according to the Lorentz formula that takes into account patient’s height as follows: $IBW [kg] = \text{Height (cm)} - 100 - [\text{Height (cm)} - 150] / 4$. Scoring system: four grades of nutrition-related risk: a) Severe nutrition risk: NRI (<83.5); (b) Mild nutrition risk (NRI 83.5-97.5); (c) Borderline nutrition risk (NRI: 97.5-100); (d) No nutrition risk: (NRI >100) [36].

Validity and Reliability: Study tools were designed and adopted by the researcher after extensive literature review and submitted to a panel of five reviewers and experts in medical surgical nursing and oncology department. Modifications of tools were done according to panel judgment. Reliability of the tools was tested using Cronbach’s Alpha.

Pilot Study: Once permission was granted to proceed with the proposed study. A pilot study was conducted on 10% of the sample in the same selected study setting to estimate the needed time for data collection to judge the feasibility, objectivity, test the ability of the tool to elicit the desired information and also, to test appropriateness, content, wording and order. The needed modification was done and the subjects of the pilot study were excluded from the actual research subject.

Procedure: The study was conducted through the following 3 phases: The first assessment was carried out on admission “During hospitalization and before chemotherapy”. During the first assessment, the subjects who were scheduled for chemotherapeutic administration and meet the criteria for possible inclusion were identified from admission records with the help of doctors and nurses of oncology department. Each woman who had been scheduled to receive her subsequent chemotherapy treatment was invited to participate in this study. The researcher started by introducing herself and explaining the purpose of the study briefly to the patients. Every subject was met individually and written informed consent for participation was obtained. Data were collected from study subjects via a structured interview and nutritional screening – related indices under the supervision of the researcher.

The Second Assessment: Was carried out at the middle of treatment (6 weeks- 12 weeks) using nutritional screening – related indices. *The third assessment* was carried out after the end of treatment using nutritional screening – related indices. The questionnaire sheets consumed about 30-45 minutes to be fulfilled by the researcher. Every phase lasted about 5 months (The beginning of March 2014 and ended at May 2015).

Ethical Considerations: Primary approval to conduct the study was obtained from research ethics committee of faculty of nursing - Cairo University. For ethical reasons, an official permission was taken from hospital administrators and the concerned authorities’ personnel in the study setting. Also, each eligible patient who met the inclusion criteria was informed about the purpose of the study and its importance. The researcher emphasized that participation in the study is entirely voluntary; anonymity and confidentiality are assured through coding the data. Informed written consent was obtained from each subject for their participation and the right to withdraw from the study at any time was also communicated to all of them. The subjects were assured that the data will not be reused in another research without his acceptance.

Statistical Analysis: Upon completion of data collection, data were analyzed using SPSS program version 20, then tabulated. Relevant statistical analysis was used to test the obtained data. Descriptive and inferential statistics were done such as mean and standard deviations; frequency; percentage and independent t-test. The level of significance was considered at the 5% level ($p = 0.05$).

RESULTS

Statistical findings of the current study were presented in the following order: the first section is devoted to description of the demographic characteristics and clinical parameters variables. The second section presents the result that answered the research question in relation to variables of nutrition screening-related indices.

Section I:

Demographic Characteristics: The study subjects consisted of 60 adult female patients who are married (88.3%); housewives (91.7%); with the age ranged from 20 to ≤ 50 years, with mean of (40.06 ± 6.33) years. In relation to literacy level, almost half of the study subjects (53.3%) can read and write and only (10%) have higher education.

Clinical Parameters Variables: All study subjects’ current medical diagnosis was invasive ductal carcinoma in the second stage of cancer. In relation to types of surgery, (43.3%) of them had radical mastectomy and (35%) had lumpectomy. Also, (98.3 %) of study subjects were hospitalized for less than one week. Regarding to time of chemotherapy administration, the highest percentage of the study subjects (78.3%) received chemotherapy post-surgery and (66.7%) have started chemotherapy less than one month after surgery. There were (93.3%) of the study subjects received eight chemotherapy sessions and continued for 24 weeks as a course of treatment.

Section II: Nutrition Screening-Related Indices

Nutritional Assessment Tool: The tool includes 4 main parts: (1.1) Anthropometric measurement; (1.2) Biochemical markers; (1.3) Risk factors affecting nutritional status; (1.4) Screening summary.

Anthropometric Measurements: As regarding to BMI, on admission (51.7%) of study subjects were obese which was decreased in the middle and end of treatment to (38.3 and 31.7%) respectively. On admission, middle and end of treatment had above normal results in relation to TSF (98.3, 96.7 and 96.7%) respectively; Also, MUAC (91.7, 88.3 and 76.7%) respectively and finally MAMA (100, 98.3 and 98.3%) respectively. All mean scores of all anthropometric measurements in the end of treatment had decreased compared to on admission among all study subjects (Table 2).

Table 2: Frequency and percentage distribution of anthropometric measurements among the study subjects (N=60)

Parameters	On admission		Middle of treatment		End of treatment	
	No	%	No	%	No	%
BMI (kg/m²):						
Normal 18.5- 24.9	02	03.3	07	11.7	17	28.3
Overweight 25- 29.9	27	45.0	30	50.0	24	40.0
Obese 30-34.9	31	51.7	23	38.3	19	31.7
X±SD	30.15±3.17		29.06±3.46		28.01±4.76	
TSF (mm):						
Normal	01	01.7	02	03.3	02	03.3
Above Normal	59	98.3	58	96.7	58	96.7
X±SD	4.23±0.5		4.08±0.59		3.97±0.68	
MUAC (cm):						
Below normal	02	03.3	03	05.0	07	11.7
Normal	03	05.0	04	06.7	07	11.7
Above normal	55	91.7	53	88.3	46	76.7
X±SD	35.27±3.97		33.72±5.05			
MAMA (cm):						
Normal	00	00.0	01	01.7	01	01.7
Above Normal	60	100	59	98.3	59	98.3
X±SD	36.31±4.02		34.61±5.04			

Table 3: Frequency and percentage distribution of biochemical markers among study subjects (N= 60).

Parameters	On admission		Middle of treatment		End of treatment	
	No	%	No	%	No	%
Hemoglobin (Hb):						
Normal:	26	43.3	00	00.0	02	03.3
Abnormal:	34	56.7	60	100	58	96.7
X±SD	11.84 ± 0.6		10.96 ± 0.49		12.02 ± 11.97	
RBCs:						
Normal:	57	95.0	44	73.3	05	08.3
Abnormal:	03	05.0	16	26.7	55	91.7
X±SD	4626500 ± 418770.70		4139666.67 ± 333395.31		3772333.33 ± 320478.28	
WBCs (x 10⁹):						
Normal:	60	100	48	80.0	10	16.7
Abnormal:	00	00.0	12	20.0	50	83.3
X±SD	5642.17 ± 887.71		4369.83 ± 661.43		3772.33 ± 706.54	
Albumin (g/L):						
< 3.5 g/L:	59	98.3	42	70.0	16	26.7
> 3.5g /L:	01	01.7	18	30.0	44	73.3
X±SD	4.2 ± 0.27		3.81 ± 0.34		3.53 ± 0.38	

Biochemical Markers: On admission, biochemical markers revealed that (56.7%) of study subjects had abnormal hemoglobin (Hb) level, which increased in the middle and end of treatment to be (100 and 96.7%) respectively. Only (5%) of study subjects had abnormal levels of RBCs on admission, increased in the middle and end of treatment to be (26.7 and 91.7%) respectively. Regarding WBCs, (100%) of study subjects had normal level on admission; deterioration appeared in the middle and end of treatment to be (20 and 83.3%) respectively. On admission (98.3%) of study subjects had normal

albumin levels, while abnormal levels of albumin appeared in the middle and end of treatment to be (30 and 73.3%) respectively (Table 3).

Risk Factors Affecting Nutritional Status: On admission, all patients reported no symptoms except regarding some symptoms such as swallowing difficulties, constipation, stomach troubles and food allergy/ tolerance (1.7, 3.3, 21.7 and 6.7%) respectively. In the middle of treatment course; the majority of patient suffer from stomach trouble, vomiting, taste alteration, decreased appetite, difficulty

Table 4: Frequency and percentage distribution of perceived risk factors affecting nutritional status among study subjects (N=60)

	On admission		Middle of treatment		End of treatment	
	No	%	No	%	No	%
Decreased appetite	00	00.0	47	78.3	47	78.3
Taste alteration	00	00.0	50	83.3	50	83.3
Chewing difficulty	00	00.0	06	10.0	08	13.3
Difficulty swallowing.	01	01.7	42	70.0	47	78.3
Vomiting	00	00.0	57	95.0	58	96.7
Gum thickening	00	00.0	00	00.0	00	00.0
Stomatitis	00	00.0	39	65.0	52	86.7
Diarrhea	00	00.0	29	48.3	25	41.7
Constipation	02	03.3	16	26.7	22	36.7
Stomach trouble	13	21.7	58	96.7	58	96.7
Food allergy / tolerance	4	6.7	7	11.7	7	11.7
Unable self –feeding	00	00	6	10	6	10
Mobility alteration	00	00	6	10	8	13.3

Table 5: Frequency and percentage distribution of screening summary among study subjects (N=60)

Variables	On admission		Middle of treatment		End of treatment	
	No	%	No	%	No	%
Markedly underweight:						
Yes:	00	00.0	00	00.0	00	00.0
No:	60	100	60	100	60	100
Markedly overweight:						
Yes:	58	96.7	53	88.3	43	71.7
No:	02	03.3	07	11.7	17	28.3
Unintentionally loss 10% of usual body weight:						
Yes:	00	00.0	03	05.0	43	71.7
No:	60	100	57	95.0	17	28.3
At least 3 risk factors affecting nutrition:						
Yes:	01	01.7	56	93.3	56	93.3
No:	59	98.3	04	06.7	04	06.7
Serum albumin = 3.5mg/dl:						
Yes:	01	01.7	18	30.0	44	73.3
No:	59	98.3	42	70.0	16	26.7

Table 6: Prevalence of malnutrition based on Nutrition risk index score (N = 60)

Grades	On admission	Middle of treatment	End of treatment
Major risk < 83.5 - N (%)	60 (100%)	60 (100%)	60 (100%)
Minimum	46.25	42.83	40.39
Maximum	78.37	74.84	82.36
Mean ± SD	62.25 ± 5.95	59.58 ± 6.59	57.22 ± 9.18
t (p value)	On admission and middle of treatment: .848 (.000)*		
	On admission and end of treatment: .547 (.000)*		
	Middle of treatment and end of treatment: .889 (.000)*		

* Significant at the p < 0.05 probability level / NS= Not Significance

swallowing and stomatitis (96.7, 95, 83.3, 78.3, 70 and 65%) respectively. In the end of treatment, the majority of patient still suffer from stomach trouble, vomiting, stomatitis, taste alteration, decreased appetite and swallowing difficulty (96.7, 96.7, 86.7, 83.3, 78.3 and 78.3%) respectively (Table 4).

Screening Summary: None of study subjects had marked underweight in the three intervals. Regarding markedly over weight, on admission (96.7%) were overweight; this percentage was decreased in the middle and end of treatment (88.3 and 71.7%) respectively. All study subjects had no weight loss on admission. Only (5%) of study

subjects in middle of treatment and (71.7%) in the end of treatment had lost unintentionally 10% of usual body weight. On admission only, (1.7%) have at least three risk factors affecting nutrition, this percentage was increased to be (93.3%) in the middle as well as end of treatment. Regarding albumin level, only (1.7%) had serum albumin ≤ 3.5 mg/dl. In the middle and end of treatment, this percentage was increased to be (30 and 73.3%) respectively (Table 5).

Nutritional Risk Index (NRI): Based on nutritional risk index; all study group was at major risk for malnutrition with mean score (62.25 ± 5.95 ; 59.58 ± 6.59 ; 57.22 ± 9.18) respectively. There is a significant statistical differences among study subjects on admission and middle of treatment; on admission and end of treatment; and finally at middle of treatment and end of treatment with (.848 and .547 and .889) respectively at $p = .000$ (Table 6).

DISCUSSION

Breast cancer is the most common human malignancy in women and major public health issues in the world, especially in developing countries. Most studies deal with the effects of chemotherapy on mounting the survival. A few studies have looked at the effects of chemotherapy on nutritional status. Facts about changes in nutritional status because of cancer or its treatment will not only help in the improved management of nutritional alterations but will also facilitate the better clinical outcome. The nutritional status of breast cancer women receiving chemotherapy in Egypt is unknown accurately as there is no accurate statistical documentation either for the number of breast cancer patients or the nutritional status of them. Therefore, the aim of this study was to evaluate malnutrition predictors among breast cancer women undergoing chemotherapy in the oncology department at Cairo University.

According to Demographic Characteristics: More than half of study subjects were aged between $40 \leq 50$ years old and can read and write. More than three-quarters of the current study subjects were married and housewives.

Regarding clinical parameters; all study subjects were diagnosed with invasive ductal carcinoma in the second stage. This finding might reflect the fact that the majority of the female population in developing countries / low-income countries don't seek medical advice except in the late stage and could be related to lack of information which can help them to take informed decisions. This is

contradicted with the study carried out by some researchers who stated that about only one fifth of study subjects were diagnosed with invasive ductal carcinoma in the second stage [37].

In relation to surgery, more than two third of study subjects had radical mastectomy and lumpectomy, approximately all study subjects hospitalized for less than one week, from the researcher point of view this period of hospital stay is matched with the character of closed wound of the surgery without any complications and the early discharge as the result of stabilized patients' condition post-surgery. Also, the current trend in all fields of surgery is toward shorter hospital stays.

Multimodality treatment method, including surgery, preoperative and postoperative adjuvant therapy, has been employed to achieve the better clinical outcome. So, all study subjects had chemotherapy, more than three quarters of them received chemotherapy post-surgery and more than two thirds started chemotherapy less than one month after surgery. From the researcher point of view; this could reflect the protocol of treatment at this study setting as this time depends on the duration of wound healing and the rest period post-surgery. The majority of the study subjects received eight chemotherapy sessions and continued for 24 weeks as a treatment course; this could be elaborate on the protocol of treatment that conducted in the current study setting. Many authors concluded that compared with postoperative radiotherapy or chemotherapy alone, neoadjuvant therapy has the potential to reduce the incidence of distant failure in high-risk patients, increase preservation rates and improve pathological complete response [38].

In relation to nutrition screening-related indices; consists of 2 parts: (1) Nutritional assessment which include anthropometric measurement; biochemical markers, risk factors affecting nutritional status and screening summary, (2) Nutritional risk index (NRI). It was conducted at three intervals, the first assessment was done on admission before starting chemotherapy, the second assessment was done at the middle of chemotherapy treatment (After 6 to 12 weeks) and the third assessment was done at the end of chemotherapy treatment.

Anthropometric measurements can be easily performed as a non-invasive approach to evaluate patients' nutritional status. Anthropometric measurements such as BMI, TSF, MUAC and MAMA are important for comparison with future measurements in order to judge the significance of any changes (Progress or regress) over the time. None of study

subjects had marked underweight in the three intervals. The current study revealed that BMI on admission, more than half of the study subjects were obese. Half of study subjects in the middle of treatment and more than one third at the end of treatment were overweight.

The majority of study subjects in three intervals had above normal results of TSF, MUAC and MAMA. These results could be related to the majority of the study subjects were either obese or overweight before starting chemotherapy. There was a significant decrease in the mean of all anthropometric measurements at the end of treatment. This deterioration could be explained as the result of the decrease in the oral intake leading to decreased body weight because of the side effects of chemotherapy treatment such as decreased appetite, swallowing difficulties, stomatitis and vomiting. Therefore, it is of utmost importance that the nutritional status of breast cancer women is routinely assessed and easy anthropometric measures such as BMI should be performed as part of the treatment of these patients.

However, some authors reported that for a critically ill patient, muscle loss is very early and rapidly, 17% of muscle mass could be lost in 10 days in the acute stage. So, Malnutrition is a structural and functional alteration of the body composition, which encompasses both nutrient loss and nutrient gain "Undernourishment and over-nourishment". Malnutrition is often used to specifically refer to undernourishment where an individual is not getting enough calories, protein, or micronutrients [20, 21 & 24]. Also, another authors concluded that patients with a BMI of 30 kg/m² or more exhibited a significant increase in the risk of developing distant metastases after 10 years (Increased by 46%) and in the risk of dying as a result of breast cancer after 30 years (Increased by 38%) [1].

Bone marrow suppression is the most common and most serious side effect of chemotherapy in which one or more of the main types of blood cells are decreased. Blood cell counts often reach the lowest level about 7- 14 days after chemotherapy [39]. So, biochemical markers were monitored in the current study such as Hb, RBCs, WBCs and albumin. All laboratory tests of the current study revealed that the majority of study subject have normal value on the admission except Hb level and then deterioration appeared in the middle of treatment and end of treatment. This could reflect the side effect of chemotherapeutic agents on the blood cells. These results are compatible with many researchers who stated that the majority of study subjects had anemia, leukopenia, erythrocytopenia and albuminaemia with chemotherapy

[40-46]. Other researchers found that anemia and hypoalbuminemia contributes to unexpected drug toxicity which result to impairment of nutritional status [7, 12].

In relation to risk factors affecting nutritional status; high risk of malnutrition among cancer patients was shown to delay the rate of recovery and increase cancer deaths. Chemotherapy treatment induces anorexia, sore throat, dry mouth, taste alteration, nausea, diarrhea, constipation and fatigue which eventually lead to weight loss and malnutrition. Malnutrition in cancer patients reduces responses to the treatment and increases treatment-associated side effects often lowering the intensity of treatment protocol and sometimes treatment withdrawal [15].

On admission, all patients reported no symptoms except regarding some symptoms such as difficulty swallowing, constipation, stomach troubles and food allergy / tolerance. In the middle of treatment course and end of treatment; the majority of study subjects suffer from stomach trouble, vomiting, taste alteration, decreased appetite, difficulty swallowing and stomatitis. From the researcher's point of view that the patients experienced poor appetite related to taste changes secondary to chemotherapy side effects; which made the food not tasty and this cause the patient decrease the oral intake to avoid this annoying feeling which leads the patient to change the type of food and decreases the amounts of food intake and that affects the nutrition of the patients. Also, the swallowing difficulties could be related to dryness of mouth and stomatitis. Stomatitis causes painful sensation in mouth with any oral intake, therefore the patients tended to decrease oral intake to avoid that painful sensation.

This congruent with many studies were done by many researchers who reported that more than three-quarters of patients receiving chemotherapy experienced decreased appetite, metallic taste, dysphagia, vomiting and stomatitis [47-50]. Other authors concluded that not only chemotherapy drugs cause upper GIT problems; but also buildup of waste products as a result of destruction of cancer cells which can cause loss of appetite, taste alteration and smell, which can make foods seem less appetizing. This can lead to weight loss and malnutrition [51-54].

As regarding to lower gastrointestinal risk factors such as constipation and diarrhea are common problems for oncology patients. The growth and spread of cancer as well as its treatments contribute to these conditions [55-57]. All the study subjects haven't diarrhea on admission. Diarrhea started among study subjects in the

middle of treatment and continued to the end of treatment. Diarrhea can occur throughout the continuum of cancer care and effects can be physically and emotionally devastating. It is more prevalent than constipation among study subjects. So, diarrhea remains a significant symptoms burden for people with cancer. Diarrhea can alter dietary patterns, trigger dehydration, create electrolyte imbalance, which affect nutritional status [58]. This is in agreement with many studies who mentioned that more than one third of study subjects complained of diarrhea [48, 59-61].

More than one quarter and more than one third of study subjects in middle of treatment and end of treatment respectively had constipation. This could be as a result of decreased activity, depression and anxiety as the result of the disease process as well as inadequate fluid and food intake which could affect negatively on patient's nutrition. This study result is in agreement with a study done by many authors mentioned that about one fifth of study subjects complained of constipation [47, 48, 62].

It can be summarized that risk factors affecting nutritional status are those symptoms that impede oral intakes, such as stomach trouble, vomiting, taste alterations, decreased appetite, difficulty swallowing and stomatitis which may induce pain, depression and anxiety. Early recognition and detection of risk factors for malnutrition are increasingly recognized as imperative in the development of standards of quality of care in oncology practice, especially among nurses. So, assessment of nutritional status for the patient receiving chemotherapy is one of the crucial nurses' roles in order to detect and manage any nutritional problems which can affect patients' health status and the prognosis of the disease.

Nutrition screening summary is the process of identifying patients with characteristics commonly associated with nutrition problems that may require comprehensive nutrition assessment [15]. Screening summary includes questions related to underweight, overweight, unintentional weight loss, risk factors affecting nutrition and serum albumin. Approximately the majority of study subjects were overweight from admission until the end of treatment. The majority of study subjects in the middle as well as end of treatment had at least three risk factors affecting nutrition such as stomach trouble, vomiting, taste alteration, decreased appetite, difficult swallowing and stomatitis. Also, regarding albumin level, one third and about three quarter of study subjects had low hypoalbuminemia in the middle and end of treatment. The screening summary addressed that if any subject had at least one question marked by

yes, this means that she is high risk for nutritional problems. All study subjects in the current study had at least one question of the screening summary marked by yes after starting chemotherapy; it meant that all study subjects had nutritional problems during the period of chemotherapy treatment. Many authors defined malnutrition by a weight loss $\geq 5\%$ within 1 month or $\geq 10\%$ within 6 months, a body mass index ≤ 18.5 kg/m² in patients aged < 70 years or ≤ 21 kg/m² in patients aged ≥ 70 years and/or albuminemia < 35 g/L [63]

Regarding nutritional risk index (NRI); there is no universally accepted gold standard for defining malnutrition. Many researchers consider measurement of serum proteins such as albumin to be an adequate assessment of nutritional status. The NRI was originally derived from the serum albumin concentration and the ratio of present to usual weight [36]. Based on nutritional risk index; all study subjects was at major risk for malnutrition. There is a significant statistical differences among study subjects on admission and middle of treatment; on admission and end of treatment; and finally at middle and end of treatment. Some authors concluded that the NRI is a simple and accurate tool; it requires only routine measurement of albumin and weight at admission. The systematic use of NRI would allow clinicians to identify suitable patients for nutritional support [64].

Based on the current study, nutritional parameters such as anthropometric measurement, biochemical markers, risk factors affecting nutrition status, screening summary and finally NRI concluded that all breast cancer woman undergoing chemotherapy were at major risk for malnutrition as result of chemotherapy side effect. So, every patient should be oriented with these nutritional problems and learn how to cope with it. Patients should report any problems or complains that may affect nutrition as early as possible for early management and prevention of any affection on the general health.

CONCLUSIONS

Based on findings of the current study, malnutrition is associated with the development of chemotherapy-induced toxicity in patients with breast cancer, which adversely affect the prognosis of patients. Therefore, early nutritional assessment and detection of risk factors might allow identification of patients at higher risk of developing chemotherapy toxicity and the implementation of an adequate nutritional support might be accompanied by beneficial effects when treating patients with chemotherapeutic agent; in turn, this may permit completion of maximum oncologic therapy and

improve treatment results with a more favorable toxicity profile. Nutritional intervention in patients at risk of malnutrition leads to a better prognosis, reducing the morbidity and mortality, improving quality of life. So, identifying predictors of malnutrition is crucial for the allocation of nutritional interventions during the critical window among breast cancer women undergoing chemotherapy. The identification of malnutrition risk in patients based on objective nutrition screening –related indices is the first step to attain proper nutritional care, in order to reduce the frequency of malnutrition and its consequences.

RECOMMENDATIONS

In the light of the current findings, the following were recommended:

Recommendations for further researchers: (i) Replication of the study on a larger probability sample selected from different geographical areas in Egypt is recommended to obtain more generalizable data. (ii) Developing oncology rehabilitation program that may contribute in reducing nutritional problems of chemotherapy-induced toxicity in breast cancer women.

Recommendations related to patients: (i) Nutritional programs for all patients with cancer should be provided continuously to ensure providing good, adequate and healthy diet all times of treatment either in hospital or at home. (ii) Teaching the patient with cancer by qualified nurses about appropriate management to cope with physical problems related to treatment. (iii) Providing psychological support for patient and their family by encouraging them to participate in their management approaches.

Recommendations for Medical Team and Hospital Administrators: (i) Nutritional assessment should become an integrated part of the total management of breast cancer patient. (ii) Nursing curricula should include a separate section on patient education related healthy nutrition for cancer patient. (iii) All health care providers should be exposed to training programs that address the nutritional problems of breast cancer women undergoing chemotherapy that takes in consideration the proper discharge preparation in order to prevent and minimize as possible nutritional problems. (iv) Involving the nursing staff in educational courses to improve their knowledge about chemotherapy side effect and appropriate interventions to reduce these effects. (v) The presence of dietitian is very important all the time interacting with the patient, assessing, counseling, nutritional teaching for patients and their families.

REFERENCES

1. Bering, T., S.F. Maurício, J.B. Da Silva and M.I.T. Correia, 2015. Nutritional and metabolic status of breast cancer women. *Nutr. Hosp.*, 13(2): 751-758.
2. Brennan, S.F., M.M. Cantwell, C.R. Cardwell, L.S. Velentzis and J.V. Woodside, 2010. Dietary patterns and breast cancer risk: a systematic review and meta-analysis. *American Society for Nutrition*, 91: 1294-302.
3. Cho, C., L. Buglar, E. Jacobson, M. Crew, J. Marsh, M. Murdoch and M. Strong, 2014. What is breast cancer. *Understanding Breast Cancer A guide for people with cancer, their families and friends*. Cancer Council Australia, pp: 8.
4. World Health Organization (WHO), 2006. *Guidelines for Management of Breast Cancer*.
5. Ibrahim, A.S., H.M. Khaled, N.N. Mikhail, H. Baraka and H. Kamel, 2014. Cancer Incidence in Egypt: Results of the National Population-Based Cancer Registry Program. *Journal of Cancer Epidemiology*, pp: 1-18.
6. Salem, A.A.S., M.A.E. Salem and H. Abbass, 2010. *Breast Cancer: Surgery at the South Egypt Cancer Institute Cancer*, pp: 1771-1778.
7. Polikandrioti, M., E. Evaggelou, S. Zerva, M. Zerdila, D. Koukoularis and E. Kyritsi, 2008. Evaluation of Depression in Patients Undergoing Chemotherapy. *Health Science Journal*, 2(3): 162-172.
8. Lee, V., A. Goyal, C. Hsu, J. Jacobson, R. Rodriguez, and A. Siegel, 2015. Dietary Supplement Use among Patients with Hepatocellular Carcinoma. *Integ Cancer Ther.*, 14(1): 35-41.
9. American Society of Clinical Oncology, 2014. *Understanding Chemotherapy*. *Cancer.Net*. Retrieved from: http://www.cancer.net/sites/cancer.net/files/asco_answers_chemotherapy.pdf.
10. The Royal Marsden NHS Foundation Trust, 2014. *Chemotherapy: Your questions answered*. London. Retrieved from : <http://www.royalmarsden.nhs.uk/cancer-information/patient-information/booklets/chemotherapy.pdf>.
11. Breast Cancer Campaign, 2013. *Treating Breast Cancer*. England and Wales. Retrieved from: <http://www.breakthrough.org.uk/about-breast-cancer/treatment>.
12. Boussiosa, S., G. Pentheroudakisa, K. Katsanosb and N. Pavlidisa, 2012. Systemic treatment-induced gastrointestinal toxicity: incidence, clinical presentation and management. *Annals of Gastroenterology*, 25: 106-118.

13. Chemocare, 2015. What Might Affect Nutrition During Chemotherapy and How Should You Adjust Your Diet?. Retrieved from: <http://www.chemocare.com/chemoth-erapy/health-wellness/what-might-affect-nutrition-during-chemotherapy.aspx>.
14. Davis, S., 2013. Chemotherapy and Nutrition. The LIVESTRONG Foundation. Retrieved from: <http://www.livestrong.com/article/88553-chemotherapy-nutrition/>.
15. Seo, S.H., S.E. Kim, Y.K. Kang, B.Y. Ryoo, M.H. Ryu, J.H. Jeong, S.S. Kang, M. Yang, J.E. Lee and M.K. Sung, 2016. Association of nutritional status-related indices and chemotherapy-induced adverse events in gastric cancer patients. *BMC Cancer*, 16: 1-9.
16. Lua, P.L., N.Z. Salihah and N. Mazlan, 2012. Nutritional Status and Health-Related Quality of Life of Breast Cancer Patients on Chemotherapy. *Mal J. Nutr.*, 18(2): 173-184.
17. Vandebroek, A.J.V. and D. Schrijvers, 2008. Nutritional issues in anti-cancer treatment. *Annals of Oncology*, 5: 52-55.
18. Isenring, E., G. Cross, L. Daniels, E. Kellett and B. Koczwara, 2006. Validity of the malnutrition screening tool as an effective predictor of nutritional risk in oncology outpatients receiving chemotherapy, *Support Care Cancer*, 14: 1152-1156.
19. Bloomfield, J. and A. Pegram, 2012. Improving nutrition and hydration in hospital: the nurse's responsibility. *Nursing Standard*. 26(34): 52-56. Retrieved from: <http://journals.rcni.com/doi/abs/10.7748/ns2012.04.26.34.52.c9065>.
20. World Health Organization (WHO), 2016. What is malnutrition? Online Q & A.
21. Young, E.M., 2012. *Jump up to: Food and development*. Abingdon, Oxon: Routledge, 36-38. ISBN 9781135999414.
22. Kondrup, J., S.P. Allison, M. Elia, B. Vellas and M. Plauth, 2003. ESPEN Guidelines for Nutrition Screening 2002. *Clinical Nutrition*, 22(4): 415-421.
23. Kumar, N.B., 2012. Assessment of Malnutrition and Nutritional Therapy Approaches in Cancer Patients. *Nutritional Management of Cancer Treatment Effects*, pp: 7.
24. Facts for life, 2010. New York: United Nations Children's Fund. (4th ed.); pp: 61, 75. ISBN 978-92-806-4466-1.
25. Kehr, W., 2015. Introduction to Alternative Cancer Treatments - Chapter 8 - Judging Orthodox Medicine. *Cancer Tutor*. Retrieved from: <http://www.cancertutor.com/nocancer8/>.
26. Yarbro, C.H., D. Wujcik and H.B. Gobel, 2010. *Cancer Nursing: Principles and Practice*. 7th ed. Jones and Bartlett Publishers. United States of America, pp: 722-725.
27. Nieswiadomy, R.M., 2012. *Foundations of Nursing Research*, (6th ed.). Pearson Education, pp: 113.
28. Jarvis, C., 1996. *Physical Examination and Health Assessment*. (2nd ed). Saunders, Canada, pp: 134-138.
29. El-Feky, H., 2001. Relationship of Nutritional Status: Wound Healing and Hospital Stay among General Surgical Patients at El-Manial University Hospital. Unpublished Master Thesis, Faculty of Nursing, Cairo University.
30. Jarvis, C., 2012. *Physical Examination and Health Assessment*. (6th ed). Saunders, Canada, 130-131, 186-189.
31. WHO expert consultation, 2004. Appropriate Body-Mass Index for Asian Populations and its Implications for Policy and Intervention Strategies. *The Lancet*, pp: 157-163.
32. Weber, J. and J.H. Kelley, 2010. *Health Assessment in Nursing*. 4th ed. Wolters Kluwer, Lippincott Williams and Wilkins, pp: 165-167.
33. Indira, A., K. Kantha, G. Subramanyam and P.R. Mohan, 2016. Can Body Mass Index can be Replaced by Mid Upper Arm Circumference. *International Journal of Applied Research*, 2(6): 1025-1027
34. Abrhame, T. and J. Haidar, 2014. The Sensitivity and Specificity of Mid-Upper Arm Circumference Compared to Body Mass Index in Screening Malnutrition of Adult HIV Patients Taking ART: Evidence from Selected Facilities of Addis Ababa, Ethiopia. *Science Journal of Public Health*, 3(1): 19-24.
35. Vajpayee, N., S.S. Graham and S. Bem, 2011. Basic Examination of Blood and Bone Marrow. McPherson RA, Pincus MR, eds. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. 22nd ed. Philadelphia, PA: Saunders, an imprint of Elsevier Inc; pp: 509-535.
36. Aziz, E.F., F. Javed, B. Pratap, D. Musat, A. Nader, S. Pulimi, C.L. Alivar, E. Herzog and M.L. Kukin, 2011. Malnutrition As Assessed by Nutritional Risk Index is associated with Worse Outcome in Patients Admitted with Acute Decompensated Heart Failure: An ACAP-HF Data Analysis. *Heart International*, 6(1): e2:3-8.

37. Timpe, L., S. Berkemeyer, M. Puesken, J. Tio, W. Heindel and S. Weigel, 2015. Rates of presurgical under estimation of breast cancer after standerized assessment of breast classifications. *George Thieme Velag KG Stuttgant. New York*, 187(6): 445-449.
38. Ful, K. and H. Pan, 2017. Nutritional status and risk factors for malnutrition in CRC patients undergoing neoadjuvant therapy. *Biomedical Research*, 28(10): 4406-4412.
39. Thomas, H., 2013. *The Best Treatment your Guide to Breast Cancer Treatment in England and Wales. (3rd ed). Breakthrough Breast Cancer. England*, pp: 16-47.
40. Naito, A., T. Mizushima, H. Takeyama, D. Sakai, M. Vemura, T. Kudo and M. Mori, 2014. Feasibility of Chemotherapy in Patients with Inflammatory Bowel Disease- Related Gastrointestinal Cancer. *Hepatogastroenterology*, 61(132): 942-950.
41. Wang, X., J. Ren, J. Zhang, Y. Yan, N. Jiang, J. Yu and H. Lyrly, 2016. Prospective Study of Cyclophosphamide, Thiotepa, Carboplatin Combined with Adaptive DC-CIK Followed by Metronomic Cyclophosphamide Therapy as Salvage Treatment for Triple Negative Metastatic Breast Cancer Patients (aged< 45). *Clin Transl Oncol*, 18(1): 82-87.
42. Migita, K., A. Nashimoto, H. Yabusaki, A. Matsuki and M. Aizawa, 2015. Efficacy of Neo-adjuvant Chemotherapy with Docetaxel, Cisplatin and S-1 for Resectable Locally Advanced Gastric Cancer. *Int Journal Clin Oncol*, 21(1): 102-109.
43. Asao, T., H. Nokihara, K. Yoh, S. Niho, K. Goto, H. Ohmatsu and Y. Ohe, 2015. Phase II Study of Amrubicin at a Dose of 45 mg/m² in Patients with Previously Treated Small- Cell Lung Cancer. *Jpn J. Clin Oncol.*, 45(10): 941-6.
44. Kainuma, O., F. Miura, O. Furukawa, H. Yamamoto, A. Cho, K. Sano and T. Asano, 2015. Feasibility and Efficacy of Gemcitabine Plus Cisplatin Combination Therapy After Curative Resection for Biliary Tract Cancer. *Journal of Hepatobiliary Pancreat Sci.*, 22(11): 789-794.
45. Yamashita, Y., K. Sirabe, K. Kawabe, N. Fujimori, T. Hisano, Y. Okabe and A. Funakosi, 2015. Gemcitabine in Combination with Cisplatin in Patients with Unresectable Advanced or Recurrent Biliary Tract Cancer- A Multicenter Prospective Observational Study in Fukuoka. *GanTo Kagaku Ryoho*, 42(10): 1185- 1194.
46. Yao, Z., G. Tian, S. Yang, Y. Wan, Y. Kang, Q. Liu and D. Lin, 2014. Serum Albumin as a Significant Prognostic Factor in Patients with Malignant Pleural Mesothelioma. *Tumor Biol.*, 35(7): 6839-6884.
47. Lu, J., L. Ma, X. Wang, Z. Liu, J. Wang and K. Li, 2014. Screening for prodromes of chemotherapy-induced vomiting and correlation between prodromes and chemotherapy-induced vomiting in lung cancer patients. *ZhonghuaZhong Liu ZaZhi.*, 36(7): 511-515.
48. Selle, F., E. Sevin, I. Ray-Conquard, V. Mari, D. Berton-Riquard, L. Favier and E. Pujade-Lauraine, 2014. A phase II study of lenalidomide in platinum-sensitive recurrent ovarian carcinoma. *Ann Oncol*, 25(11): 2191-2196.
49. Wilberg, P., M.J. Hjermstad, S. Ottesen and B.B. Herlofson, 2014. Chemotherapy associated oral sequelae in patients with cancers outside the head and neck region. *J Pain Symptom Manage*, 48(6): 1060-1069.
50. Ijpm, I., R.J. Renken, G.J. Ter Horst and A.K. Reyners, 2015. Metallic Taste in cancer patients treated with chemotherapy. *Cancer Treat Rev.*, 41(2): 179-86.
51. Coleman, E.A., J.Y. Lee, S.W. Erikson, J.A. Goodwin, N. Sanathkumar, V.R. Raj and E.J. Anaissie, 2015. GWAS of 972 antologous stem cell receipients with multiple myeloma identifies 11 genetic varients associated chemotherapy-induced oral mucositis. *Support Care Cancer*, 23(3): 841-850.
52. Chan, H.K. and S. Ismail, 2014. Side effects of chemotherapy among cancer patients in a Malaysian General Hospital: experiences, perceptions and informational needs from clinical pharmacists. *Asian Pac J. Cancer Prev*, 15(13): 5305-5309.
53. Michishita, C., E. Ikeda, M. Lida, Y. Suzawa, Y. Murayama and M. Yamamoto, 2015. The effect of routine Professional oral care on oral mucositis in hematologic chemotherapy patients. *GanTo Kagaku Ryoho*, 42(4): 463-366.
54. Yokoto, T., T. Onoe, H. Ogawa, S. Hamauchi, Y. Lida, T. Kamijo and T. Onisuka, 2015. Distinctive mucositis and feeding-tube depending in cetuximab plus radiotherapy for head and neck cancer. *JPN J. Clin Oncol.*, 45(2): 183-188.
55. Mazzeo, E., P. Antogni, M. Parmiggiani, C. D'Ambrosio, G. De Marco, L. Marra and F. Bertoni, 2014. IMRT-SIB with concurrent and neo-adjuvant platinum- based chemotherapy for Locally advanced head and neck squamous cell cancer: analysis of clinical outcomes in a retrospective series of a single institution. *Timori*, 100(6): 7.
56. Tahara, M., N. Kiyota, J. Mizusawa, K. Nakamura, R. Hayashi, T. Akimoto and M. Fujii, 2015. Phase II trial of chemoradiotherapy with S.1 plus cisplatin for unresectable locally advanced head and cancer (JCOG0706). *Cancer Sci.*, 106(6): 726-33.

57. Schuchter, L., 2014. Side Effects of Chemotherapy. Cancer.Net (Navigating Cancer Care). Retrieved from: <http://www.cancer.net/navigating-cancer-care/howcancer-treated/chemotherapy/side-effects-chemotherapy>.
58. Kapoor, V., S. Basur and A. Pandey, 2015. Chemotherapy and Oral Complications: The Most Neglected Side of Cancer. *Journal Adv Med Dent Scie Res.*, 3(1): 71-80.
59. Park, Y., J. Ji, J. Zalcborg, M. El-Serafi, A. Buzaid and M. Ghosn, 2015. Oxaliplatin /5-Fluorouracil- Based Adjuvant Chemotherapy as a standard of Care for Colon Cancer in Clinical Practice: Outcomes of the ACCELOX Registry. *Asia Pac Journal Clin Oncol.*, 11(4): 334-342.
60. Shigekawa, T., A. Osaki, H. Sekine, N. Sato, C. Kanbayashi, H. Sano and T. Saeki, 2015. Safety and Feasibility of Adjuvant Chemotherapy with S.1 in Japanese Breast Cancer after Primary Systemic Chemotherapy: A Feasibility Study. *BMC Cancer*, 15: 253.
61. LV, H., M. Yan, M. Zhang, L. Niu, H. Zeng and S. Cui, 2014. Efficacy Capecitabine Based Combination Therapy and Single-Agent Capecitabine Maintenance Therapy in Patients with Metastatic Breast Cancer. *Chin Journal Cancer Res.*, 26(6), 692-697.
62. Zhang, J., L. Wang, Z. Wang, X. Hu, B. Wang, J. Cao and Z. Shao, 2015. A Phase II Trial of Biweekly Vinorelbine and Oxaliplatin in Second- or Third – Line Metastatic Triple- Negative Breast Cancer. *Cancer Biol. Therapy*, 16(2): 225-232.
63. Klek, S., Z. Krznaric, R. H. Gundogdu, M. Chourdakis, G. Kekstas, T. Jakobson, P. Paluszkiewicz, D.V. Bender, M. Uyar, K. Demirag, K.A. Poulia, A. Klimasauskas, J. Starkopf and A. Galas, 2013. Prevalence of Malnutrition in Various Political, Economic and Geographic Settings. *Journal of Parenteral and Enteral Nutrition*, 39(2): 200-210.
64. Bouillanne, O., G. Morineau, C. Dupont, I. Coulombel, J.P. Vincent, I. Nicolis, S. Benazeth, L. Cynober and Aussel, 2005. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *the American Journal of Clinical Nutrition*, 82: 777-783.