

Effect of Immune Enhancement Intervention on Clinical Outcomes of Patients with Breast Cancer Undergoing Chemotherapy

*Reda Dardier Hussein,**Kamelia Fouad Abdallah,*** Mostafa Mostafa Rezk,****Sabah Said Mohamed

* Medical Surgical Nursing Department– Faculty of Nursing- Beni Suef University, ** Medical Surgical Nursing- Faculty of Nursing- Ain Shams University *** General Surgery - Faculty of Medicine - Benha University, ****Lecturer of Medical Surgical Nursing- Faculty of Nursing-Benha University

Abstract

Breast cancer (BC) is a major public health problem worldwide. It is the second leading cause of death after lung cancer. More than half of patients with BC receive systemic chemotherapy as a form of treatment. They are good at killing cancer cells, but they can temporarily weaken immunity. The damaged to normal cells cause common unpleasant side effects including, nausea, vomiting , fatigue, infection...etc. The body's immune system is designed to fight off and recognize these abnormal cancer cells and kill them. For this reason if BC has been diagnosed, it is of great importance to re-build and keep the immune system in a good fighting condition. **The aim** of the present study is to evaluate the effect of immune enhancement intervention on clinical outcomes of patients with BC undergoing chemotherapy. **The research design** was quasi-experimental design. **Setting:** It was conducted at the clinical oncology department at Nasser Institute hospital(Cairo).**Sample:** A purposive sample included 100 patients divided into control and study groups. **Tools of data collection:** Data were collected using structured interview questionnaire, Australia-modified Karn of sky performance status scale, quality of life assessment scale & nutritional assessment sheet including laboratory investigation &tumor markers. **The results:** Showed that; (60% and 52%) of the study group and (68% and 48%) of control group were married and aged (50 - 70 years old) respectively and there was a highly significant difference existed between the two groups regarding their knowledge, quality of life, performance status for usual activities and nutritional status post intervention which in turn lead to highly significant decrease the tumor biomarkers among study group versus control group $P<0.001$. **Conclusion:** Immune enhancement intervention program had statistical significant positive effect on clinical outcomes of patients with BC undergoing chemotherapy. **Recommendations:** Further study is recommended to conduct the training and teaching of nurses about the immune enhancement intervention program and evaluate its impact on their performance and consequently on patients outcomes on the long run.

Key words: Breast Cancer, Chemotherapy, Immune System Enhancement.

Introduction

Breast cancer (BC) is the most common malignancy and the second leading cause of cancer deaths among

women. And it is the most common invasive cancer as it affects about 12% of women worldwide. The BC comprises 22.9% of invasive cancers in women and 16% of all female cancers. Over a quarter of a million women have the diagnosis of

BC every year and it kill about forty thousand women each year (**Eraky, 2016**).In 2008, BC caused 458, 503 deaths worldwide (13.7% of cancer deaths in women and 6.0% of all cancer deaths for men). It is more common 100 times in women than in men.In 2012, it comprised 25.2% of cancers diagnosed in women, making it the most common female cancer (**Nordqvist, 2016**).

The incidence of BC varies greatly around the world: It is lowest in less-developed countries and greatest in the more-developed countries (**Leer, 2014**).In Egypt, BC is the most common cause of death among women, the number of new cancer patients in the year 2008 is estimated to be 65,000, the BC constitutes 14% of all cases with an annual increases that ranges between 1.5% and 2% and with a median age of 46 years old (**El- Sheshtawy, et al. 2014**).

Chemotherapy offers systemic treatment of BC women. It is usually used for stage II or higher BC and may be combined with surgery, radiation therapy or both (**Litton, et al. 2012**). Chemotherapy involves the use of anti-neoplastic drugs in an attempt to destroy cancer cells by interfering with cellular functions, including replication and DNA repair. Chemotherapy drugs are good at killing cancer cells, but it can damage fast-growing normal cells, and cause major immunosuppressive adverse effects as drop in the number of white blood cells, fatigue, weight loss, anemia, nausea, vomiting, etc, that prevent the immune system from contributing to its anti-cancer effects which has significant effect on all women's quality of life (QoL)dimensions (**Levine &Whelan, 2012**).

The outcome of chemotherapy can be influenced by the functional state of the patient's immune system at multiple

levels as it has a major prognostic and predictive impact on the fate of cancer patients. Immune-relevant biomarkers may guide personalized therapeutic interventions including compensatory measures to restore or improve anticancer immune responses. The efficacy of many of the currently used chemotherapeutic agents depends on the active contribution of immune effectors (**Ramakrishnan, 2010**) & (**New Hope Cancer Treatment Center, 2012**).

Significance of the study:

Breast cancer is the most common cancer among women in developed western countries accounting for more than 1 in 4 cancer cases, and it becoming more significant in many developing countries. The number of cases worldwide has significantly increased since the 1970s, this partly attributed to the modern lifestyles. Based on U.S. statistics in 2015 there were 2.8 million women affected by BC. About 18.2% of all cancer deaths worldwide, including both males and females, are from BC. According to the National Cancer Institute(NCI), about 232, 340 females and 2, 240 males BC are reported in the USA each year, as well as about 39, 620 deaths caused by the disease (**Zheng, et al.2013**) &(**American Institute for Cancer Research, 2013**).

In Egypt, BC is the most common cancer among women, representing 18.9% of total cancer cases with an age adjusted rate of 49.6 per 100, 000 population. According to official statistics of the NCI (Cairo University), the BC accounts for 35.1% of the cases of cancer in Egypt. Diagnosis of BC is a great shock, women report that they fear BC more than heart disease. According to the recent incidence of the Ministry ofHealth and Population, 1 every 12 Egyptian

women has BC(EI- Sheshtawy, et al. 2014).

Despite research efforts, anti-cancer immune therapies have only earned respectful attention by clinical oncologists over the past decade. The immune system is effective in defining BC prognosis, response to different treatment and preventing BC metastases (East, 2013). So it is very important for the nurses to design and conduct immune enhancement intervention program in order to decrease chemotherapy side effects and improve the rate of response among the patients with BC.

However, researches made in this field are very limited. So, more studies are necessary to precisely define the nature and role of immune-modulatory therapy.

Aims of the study:

To evaluate the effect of immune enhancement intervention on clinical outcomes of patients with BC undergoing chemotherapy through assessing patient's knowledge, QoL, performance, and nutritional status.

Research hypotheses

- Subjects received immune enhancement intervention (study group) will report high quality of life and performance status than the subjects who don't receive it (control group).

- Subjects received immune enhancement intervention (study group) will express lower potential tumor biomarkers (Cancer Stem Cells) than the subjects who don't receive it (control group).

Subject and methods:

Research Design:

A quasi-experimental design was utilized to meet the aim of this study.

The present study was carried out through four designs:-

- I - Technical design.
- II - Operational design.
- III - Administrative design.
- IV - Statistical design.

I-Technical design:-

The technical design included setting, subjects and tools of data collection

***Setting**

The study was conducted at the clinical oncology department at Nasser Institute hospital (Cairo), which is one of the Egyptian Ministry of Health Institutes.

***Subjects:**

A purposive sample of 100 adult female patients with diagnosis of BC and undergoing chemotherapy was selected purposive sample with criteria and assigned alternatively into two equal groups of 50 patients (study and control groups) the number in each group is 50 patient. The study group was received immune enhancement intervention program and control group was exposed to routine hospital care. Both groups were selected according to the following inclusion criteria.

***Inclusion Criteria:**

- 1- Full conscious patients who are willing to participate in the study.
- 2- Patients aged over 18 years old.

- 3- Newly admitted to chemotherapy and not attending any educational program.
- 4- There is no metastasis spread.
- 5- No other associated disease.

*** Variables:**

The independent variable in this study was immune enhancement, while the dependent variable was clinical outcomes of patients with BC undergoing chemotherapy.

*** Operational definitions:**

- Immune enhancement intervention is a health education program designed by the researcher based on literature review to enhance the immunity of patients with BC undergoing chemotherapy.

-Clinical outcomes means assessment the level of patient's knowledge, performance status of usual activities, QoL domains (physical, social, psychological, functional and patient's concern related to the disease &its treatment domains), nutritional status in addition to laboratory investigations (hemoglobin, hematocrit, WBC, blood urea nitrogen, serum creatinin & albumin) and tumor biomarkers CD 90 (+ve) CD 45 (+ve) %.

*** Tools for data collection:**

Four tools were utilized for data collection of this study:-

Tool I:- Structured interview questionnaire:

The researcher developed it after reviewing of the related literature. This included the following parts:-

-Part I:- Patient's demographic data such as; age, marital status, educational level, employment status, place of residence, income level, family member & number of children. **(7 Items)**

-Part II:- Patient's knowledge related to BC, chemotherapy side effects & it's management ,the immune enhancement through life style modification.

(21 questions); distributed as the following:-

First:- Multiple choice questions related to definition, causes or risk factors, signs & symptoms and treatment of BC, it also included questions about definition of chemotherapy treatment and it's side effects. **(6 questions)**

Second:- It included true or false questions about the ways of treatment of chemotherapy side effects as (nausea, vomiting, loss of appetite, constipation, diarrhea, stomatitis, infection, platelet deficiency ,anemia, urinary problems, hair loss, & skin problems). **(11 questions)**

Third:- It included true or false questions about the immune system definition and the factors that can enhance and weaken it. **(4 questions)**

***Scoring system** for each question ranging from:-Zero to 1 (Where Zero indicates wrong answers & one indicates correct answer). Total knowledge score was classified as the following;

>75% was considered satisfactory

<75% was considered unsatisfactory.

Tool II: Australia-modified Karn of sky performance status scale

It was adopted from **Abernethy, et al., (2005)**, then translated into Arabic by the researcher to assess the ability of the patients with BC to perform usual activities, evaluating patient's progress after therapeutic procedure. It was used most commonly in the prognosis of cancer therapy, usually after chemotherapy. It consisted of 11 items, each item scored with percent which ranging from normal function 100% to 0% .The lower the Karnofsky score, the worse the survival for most serious illness.

It included three main categories:-

1- Complete self-independent; Three choices scores as follows:-(Ability to make activities without any health problems = 100%, ability to do normal activities with mild discomfort =90% and ability to do normal activities with severe discomfort = 80%).

2 – Unable to work & need assistance; three choices scores as follows:- (In ability to do normal activities and need assistance = 70%, inability to do normal activities and need significant help = 60% ,need significant help with frequent health care = 50%).

3- Completely dependent (unable to care of self & health care is needed with rapid disease progress); five choices scores as follows:- (Remain in bed more than half of time = 40%, remain in bed almost time = 30%, remain in bed all the time = 20%, unconscious and rarely awaken = 10% and patient died = 0%).

Tool III: Quality of life assessment scale

It was adapted by **Brady, et al. (1997)**, and was modified and translated into Arabic by the researcher to assess QoL domains for patients with BC. It consists of 37 items (7 items for physical domain, 7 items for social domain, 6 items for psychological domain, 7 items for functional domain and 10 items about patient's concern related to the disease & its treatment domain) which rated on 4-points (0 = no affection, 1 point= mild affection, 2 points= moderate affection, 3 points = severe affection). The total score for the scale was ranged from (0-111 points), it was classified as the following:-

<37 points representing < 41% was considered no affection which means highest QoL.

- **37 < 74 points** representing 41% - < 82% was considered mild affection which means good QoL.

- **74 < 111 points** representing 82% - < 100% was considered moderate affection which means moderate QoL.

111 points representing 100 % was considered severe affection which means poor QoL.

Tool IV: Nutritional assessment sheet.

The researcher developed this tool after reviewing of the related literature to identify the patient's nutritional status, it included the following:-

A) Dietary history:- Included information about numbers of meals per day, regularity of meals, way of eaten (meat & chicken), types of (fruits and vegetables taken) methods of cooking and buying food. **(8 Items)**

B)Anthropometric

measurements:- Including current body weight, height in cm, and body mass index(BMI) to determine if the patient is under or over weight. The body mass index is calculated as patient's weight in kilograms divided by their height in meters squared and ranged according to (World Health Organization, 2004).

- Underweight: BMI was lower than 18.5(Kg/m²).
- Normal: BMI was between 18.5-25(Kg/m²).
- Overweight: BMI was between 25-30 (Kg/m²).
- Obese: BMI was 30 or higher (Kg/m²).(**3 Items**)

C)Laboratory investigations:-

1. It included the following laboratory tests: Hemoglobin, hematocrit, WBCs, blood urea nitrogen, serum creatinin and serum albumin.

2. Laboratory assessment of potential tumors biomarkers (cancer stem cells): it included the following CD 90(+ve) CD45 (+ve) %. to evaluate the residual cancer stem cells.(**7 Items**)

II- Operational design:

The operational design includes preparatory phase, content validity, pilot study, fieldwork and the associated limitations.

*** Preparatory phase:**

The preparatory phase was the first phase in the study. It included reviewing past and present local and international related literature and theoretical knowledge of the various

aspects of the study using books, articles, internet, periodicals and magazines to develop tools of data collection and to prepare the content of immune enhancement intervention and designing a colored booklet about (diet, exercise and life style modification) of BC patients undergoing chemotherapy. This period took about 4 months.

Validity and reliability:*

Content validity:

Testing validity of the proposed tools by using face and content validity. Face validity aimed at inspecting the items to determine whether the tools measure what supposed to measure. Content validity was conducted to determine whether the tools cover the aim. Validity was tested by a panel of three experts (Professor of Medical Surgical Nursing department, faculty of Nursing Ain Shams University, assistant professor of Medical Surgical Nursing department , faculty of Nursing Ain Shams University and a lecturer of Medical Surgical Nursing, Faculty of Nursing at Beni-Suef University).The expertise reviewed the tools for clarity, relevance, comprehensiveness and simplicity; minor modifications were done and the final form was developed.

Testing reliability of proposed tools was estimated using the Chronbach's Alpha test to measure the internal consistency of the tools. It was found that, the reliability questionnaire using Chronbach's Alpha equation was ($r = .541$).

1) Reliability of structured interview questionnaire was (0.85).

2) Reliability of Australia-modified Karnofsky performance status scale was (0.94).

3) Reliability of QoL scale related physical condition was (0.92), social condition was (0.83), psychosocial condition was (0.87), functional concern was (0.87), and reliability of patient's concerns related to the disease and its treatment was (0.89).

***Pilot study:**

It was initially carried out prior to data collection on 10% of the study subjects (10 patients) to test the applicability, clarity, efficiency of the tools & estimate the time required for data collection. Some modifications on tools were done based on pilot study. The sample of patients included in the pilot study was not included in the main study sample.

***Field work:**

- Data were collected in the following sequence:-

-Permission to carry out the study from responsible authorities in the faculty of Nursing at Benha University after explanation of the purpose of the study was obtained.

- An official permission from the director of Nasser Institute hospital, to carry out the study after explanation of the purpose of the study was obtained.

- The study was conducted at the clinical oncology department at Nasser Institute hospital, which is one of the Egyptian Ministry of Health Institutes.

-An interview was conducted with head of clinical oncology department of the previous mentioned settings to inform him about the purpose of the study, and request his assistance to facilitate the work.

- Interview with patients before starting data collection procedure was conducted to establish a good relationship.

- Data collection covered a period of 12 months started from the first of November 2015 to the end October of 2016.

Data collection passes throughout two stages as the following:

- Implementation stage
- Evaluation stage

Implementation stage: was divided into two phases

-Phase 1: The first phase of the work was done by meeting the patients in both control and study groups and explaining the aim and nature of the study and take their approval to participate in the study prior to any data collection. Patients were informed about the privacy of their information, nature of the study, their right to withdraw and the confidentiality of the subject data.

-The study was conducted 3 days per week from 9 am to 2 pm to collect necessary data and the time needed to fill in the study tools was as follow; about; (25-30 minutes) for structured interview questionnaire, (10 minutes) for Australia-modified Karnofsky performance status scale, (25-30 minutes) for quality of life assessment scale & (10 minutes) for nutritional assessment sheet.

-Patients of both study and control groups were interviewed to assess the level of their knowledge, performance status for usual activities, QoL & nutritional status including laboratory investigations to collect the baseline data using tools (I, II, III & IV).

-The questionnaire was administered to each patient in both groups individually before intervention to fulfill it by researcher according to patient's answers. The interview was carried out in the separate space & the questions were directed in simple Arabic language and the answers were recorded immediately.

-Also ,blood sample for laboratory investigations was taken from each patient in both groups before intervention to assess hemoglobin, hematocrit, WBCs, blood urea nitrogen, serum creatinin, serum albumin and potential tumor biomarkers CD90(ve+) CD45(ve+) by flow cytometry.

- **Phase 2:** the second phase of the work was done on study group only by implementing the immune enhancement intervention program. Teaching sessions were conducted in outpatient clinic of oncology department. For conducting the teaching sessions the patients were divided into small groups (5-10 patients/session) each group perceived the same program content using the same teaching strategies and handout. The total number of groups were (5 groups) and the total number of the teaching sessions for each group of patients were three sessions for covering the information putted in the designed booklet. It was developed by the researcher based on patients' needs assessment.

Program general objectives: At its completion the patients will be able to:-

a.Acquire knowledge regarding BC disease, it's treatment &immune enhancement intervention.

b.Improve their ability to withstand disease self- chemotherapy treatment and its side effects.

This booklet content consisted of four chapters:-

Chapter one:- Contained information about BC including (definition of BC, types, causes & risk factors ,signs and symptoms and methods of treatment).

Chapter two:- Contained information about chemotherapy treatment including(definition of chemotherapy, indications ,treatment course ,routes of administration, and it's side effects).

Chapter three:- Contained information about immunotherapy including (definition of immune system, factors that weaken and enhance the efficacy of immune system and nursing care to strength it, through overcoming the side effects of chemotherapy , diet ,exercise and life style modifications to enhance the efficiency of immune system).

Chapter four:- Contained information about how to prevent BC

Before the start of each program session, the patients were asked questions related to the topics discussed in the previous session to ensure that they remember the instruction given and to reinforce the knowledge. Missed or unclear points were re-emphasized by the researcher. Also the researcher complete and refresh the previous mentioned information by asking them some related questions and gave each patient a booklet of colored picture which included all the information mentioned above and discussed it with patients to grasp their attention and motivate them for reviewing at home. Explanation of the designed immune enhancement intervention program using power point presentation, discussion, were also conducted during each session.

The Evaluation stage:-

- In this stage after intervention the patients in both groups (study & control) were interviewed again to assess any change from the baseline data regarding level of knowledge, performance status for usual activities, QoL and nutritional status using the same tools (I, II, III & IV).

- Blood sample for laboratory investigations was taken from each patient of both groups after intervention to assess hemoglobin, hematocrit, WBCs, blood urea nitrogen, serum creatinin, serum albumin and potential tumor biomarkers CD90(ve+) CD45(ve+) by flow cytometry and comparison between the two groups (study & control) was done to determine the effect of immune enhancement intervention on clinical outcomes of patients with BC undergoing chemotherapy.

III: Administrative design:

An official letter was sent from the Faculty of Nursing at Benha University to the director of Nasser Institute hospital which is one of the Egyptian Ministry of Health Institutes, for permission to conduct the study.

- An official permission from the director of Nasser Institute hospital, after explanation of the purpose of the study was obtained.

Ethical consideration:

The ethical research consideration in this study included the following:

- The researcher obtained informed oral consent from patients included in the study prior to data collection.

- patients informed about their rights to participate or withdraw from the study at any time without given a reason and they were assured that anonymity and confidentiality of information was protected. Ethics, values, culture, and beliefs were respected.

IV) Statistical design:

Data was coded and transformed into specially designed form to be suitable for computer data entry process. The data collected was tabulated and analyzed by SPSS statistical package version 22 on IBM. Quantitative data were expressed in the form of mean and standard deviation ($\bar{X} \pm SD$) and analyzed by applying Chi-Squared (χ^2) and paired t test and independent t test for comparison mean score between both study and control group & Pearson correlation r test. Qualitative data was expressed as number and percentage and the analysis by applying p-value. Level of significance was set as P-value < 0.05 and highly significant difference if P < 0.001.

Results:

Table (1): Frequency distribution of demographic characteristics for both study and control groups.

Variables	Control group(N=50)		Study group(N=50)		X ²	P value
	No	%	No	%		
Age in years					0.196	>0.05
>18< 30	6	12.0	6	12.0		
30 < 50	20	40.0	18	36.0		
50-70	24	48.0	26	52.0		
Mean ±SD	54.2400±9.307		48.4000±12.8142			
Marital status					4.45	>0.05
Single	6	12.0	14	28.0		
Married	34	68.0	30	60.0		
Widow	10	20.0	6	12.0		
Educational qualification					2.75	>0.05
Illiterate	17	34.0	16	32.0		
Primary	11	22.0	11	22.0		
Secondary	14	28.0	9	18.0		
University	8	16.0	14	28.0		
Occupation					1.09	>0.05
Working	15	30.0	20	40.0		
House wife	35	70.0	30	60.0		
Residence					0.360	>0.05
Rural	23	46.0	26	52.0		
Urban	27	54.0	24	48.0		
Number of children					5.24	>0.05
No	8	16.0	0	26.0		
1	4	8.0	0	0.0		
2	10	20.0	9	18.0		
≥ 3	28	56.0	28	56.0		
Family income					1.47	>0.05
Enough	26	52.0	32	64.0		
Not enough	24	48.0	18	36.0		

In-significant (P>0.05) Significant* (P<0.05)

Highly significant**(P<0.001) X²=

chi-square test

Effect of Immune Enhancement Intervention on Clinical Outcomes of Patients with Breast Cancer Undergoing Chemotherapy

Table 1: Represents frequency distribution of demographic characteristics for both study and control groups. This table shows that, (52%) of the study group and (48%) of control group were aged (50 - 70 years old) with their mean ages were (48.4000±12.8142) for study & (54.2400±9.307) for control group with 60% and 68% respectively of both groups were married. Regarding to level of education, (32% & 34%) of both study and control groups were illiterate, and (60%&70%) of them were house wife respectively. In relation to place of residence; (52%) of study group were lived in rural area compared to (54%) of control group were lived inurban area and (56%) of both groups had equal to or more three children. In addition to monthly income (64%) of the study group and (52%) of control group had enough family income. There were no statistical significant difference existed between the two groups regarding (age, marital status, education, occupation, number of children and family income) P > 0.05

Table (2): Comparison between patients in the study and control groups regarding their total knowledge level at pre and post intervention

Knowledge	Pre intervention										ΣI	Pvalue	Post intervention								ΣI	Pvalue
	Control group				Study group				Control group				Study group									
	Satisfactory		Un satisfactory		Satisfactory		Un satisfactory		Satisfactory				Un satisfactory		Satisfactory		Un satisfactory					
	No	%	No	%	No	%	No	%	No	%			No	%	No	%	No	%				
Breast cancer	9	18.0%	41	82.0%	8	16.0%	42	84.0%	10	20.0%	40	80.0%	46	92.0%	4	8.0%	52.59	<0.001 **				
Chemotherapy side effects	10	20.0%	40	80.0%	8	16.0%	42	84.0%	7	14.0%	43	86.0%	37	74.0%	13	26.0%	36.52	<0.001 **				
immune system	21	42.0%	29	58.0%	14	28.0%	36	72.0%	15	30.0%	35	70.0%	45	90.0%	5	10.0%	37.50	<0.001 **				
Total knowledge	5	10.0%	45	90.0%	4	8.0%	46	92.0%	4	8.0%	46	92.0%	44	88.0%	6	12.0%	64.10	<0.001 **				

Table 2: Represents comparison between patients in the study and control groups regarding their total knowledge level at pre and post intervention. This table illustrated that 92% of study and 90% in control groups had unsatisfactory level of knowledge pre intervention compared to post intervention that 88% of study group had a satisfactory knowledge level than 92% in control group had unsatisfactory knowledge. This table also showed that there were no statistical significant difference existed between both study and

control groups regarding their total knowledge level pre intervention $P>0.05$. But there were a highly significant difference between the two groups post intervention $P<0.001$.

Figure 1: Percentage distribution of studied patients' total knowledge score regarding the effect of immune enhancement intervention on clinical outcomes of patients with BC undergoing chemotherapy of both study and control groups at pre and post intervention phase.

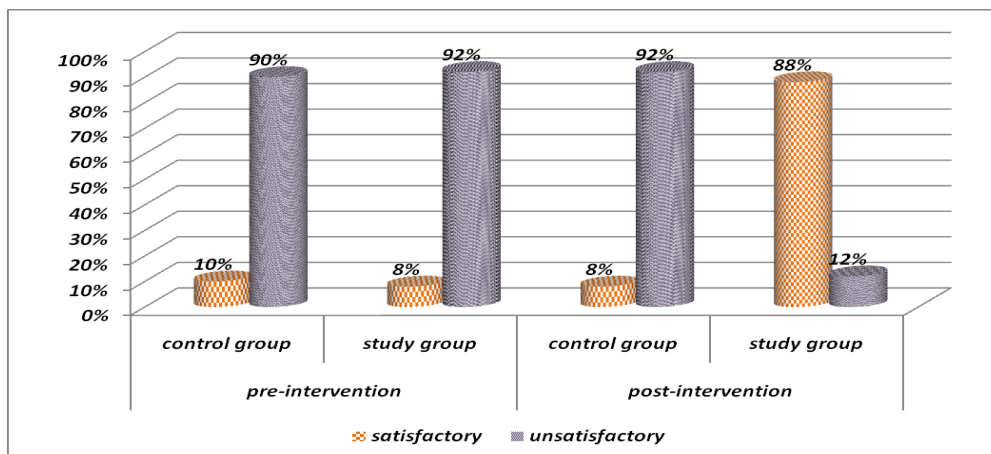


Figure 1: Percentage distribution of studied patients' total knowledge score regarding the effect of immune enhancement intervention on clinical outcomes of patients with BC undergoing chemotherapy of both study and control groups at pre and post intervention phase. This figure shows that, (90% & 92 %) of control group had unsatisfactory knowledge regarding breast cancer, chemotherapy treatment, and immune system respectively at pre and post intervention, Meanwhile (92%) of study group had unsatisfactory knowledge pre intervention compared to post intervention that (88%) of them had satisfactory knowledge.

Table (3): Mean score of performance status for usual activities between study and control groups at pre &post-intervention phase.

Performance status	Pre intervention				Post intervention			
	Control group	Study group	T	P value	Control group	Study group	T	P value
	Mean ±SD	Mean ±SD			Mean ±SD	Mean ±SD		
Completely self-independent	27.60±7.70	30.00±6.709	1.66	>0.05	27.0000±9.09137	34.6000±7.05951	-4.669	<0.001**
Unable to work & need assistance	56.40±6.92	59.20±8.53	1.80	>0.05	53.6000±9.84782	63.4000±7.45326	-5.611	<0.001**
Completely dependent (unable to care of self & health care is needed with rapid disease progress).	81.20±4.35	82.80±4.53	1.80	>0.05	79.8000±6.84821	86.6000±5.57326	-5.446	<0.001**

In-significant (P>0.05) Significant* (P<0.05) Highly significant**(P<0.001) X²= chi-square test

Table 3: Mean score of performance status for usual activities between study and control groups at pre &post-intervention phase. This table shows that there were no statistical significant difference existed between both study and control groups regarding their performance status of usual activities at pre-intervention P > 0.05 compared to post intervention that ,there were highly significant improvement of mean score of study group than the control group P< 0.001.

Table (4): Comparison between patients in the study and control groups regarding their total quality of life score at post intervention phase

Quality of life domains	Control group								Study group								T	P value
	No affection		Mild affection		Moderate affection		Severe affection		No affection		Mild affection		Moderate affection		Severe affection			
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%		
Physical	0	0.0%	6	12.0%	35	10%	20.0	70.0%	36	72.0 %	9	18.0%	4	8.0%	0	0.0%	40.89	P<0.001* *
Social	0	0.0%	5	10.0%	27	0%	0.0	54.0%	14	28.0%	10	20.0%	36	72.0%	8	16.0 %	50.48	P<0.001* *
Psychological	0	0.0%	6	12.0%	35	70.0%	31	62.0%	0	0.0%	11	22.0%	13	26.0%	4	8.0%	34.80	P<0.001* *
Functional	0	0.0%	5	10.0%	32	64.0%	30	60.0%	0	0.0%	17	34.0%	15	30.0%	1	2.0%	35.54	P<0.001* *
Patient's concerns related to the disease & its treatment	0	0.0%	1	2.0%	41	82.0%	1	2.0%	35	70.0 %	7	14.0%	14	28.0%	1	2.0%	69.02	P<0.001* *
Total	0	0.0%	0	0.0%	36	72.0 %	14	28.0%	0	0.0%	38	76.0%	12	24.0%	0	0.0 %	64.00	P<0.001 **

Table 4: Comparison between patients in the study and control groups regarding their total quality of life score at post intervention phase. This table illustrated that (70%,64%&82%) of control group had moderate QoL affection regarding psychological, functional &their concerns related to the disease and its treatment domains and 70% of them had severe QoL affection of the disease and it's treatment regarding physical domain at post intervention compared to the study group that (72% &70%) of them had no QoL affection regarding physical and patients concerns related to the disease and its treatment domain. In relation to total QoL, this table showed that 72% of control group had moderate QoL affection post intervention compared to 76% of study group had mild QoL affection and there was highly statistical significant difference existed between the two groups P<0.001.

Figure (2) :-Percentage distribution of studied patient's total quality of life score in both study and control groups at pre and post intervention

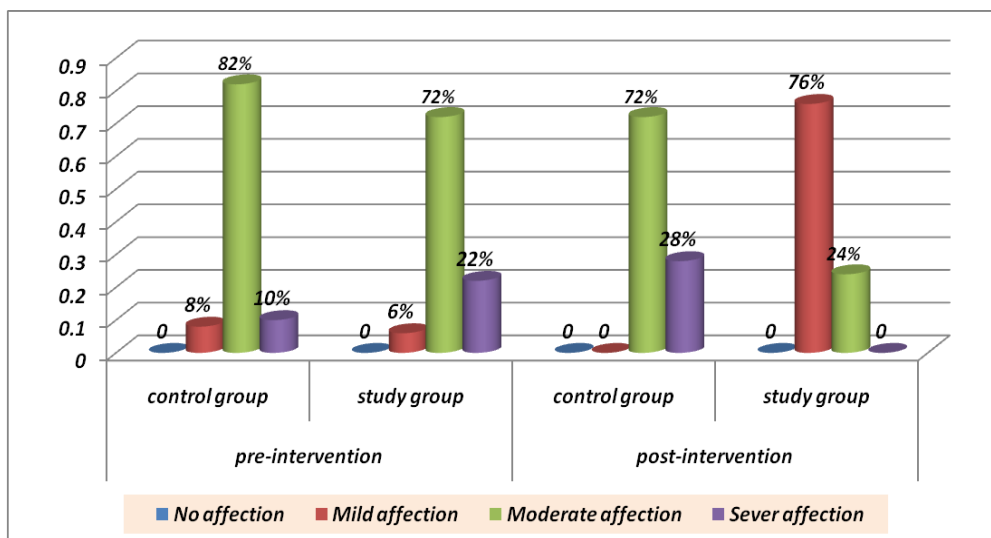


Figure (2):Percentage distribution of studied patient's total quality of life score in both study and control groups at pre and post intervention. This figure shows that (82% & 72%) of control group had moderate QoL affection at pre and post intervention respectively, Meanwhile (72%) of study group had moderate QoL affection at pre intervention compared to post intervention that (76%) of them had mild QoL affection.

Table (5):Mean score of laboratory investigations findings between study and control groups at pre & post-intervention phase.

Laboratory results	Pre intervention				Post intervention			
	Control group	Study group	T	Pvalue	Control group	Study group	T	Pvalue
	Mean ±SD	Mean ±SD			Mean ±SD	Mean ±SD		
Hemoglobin	11.0120±.91577	10.7000±1.16637	1.488	>0.05	11.0720±.90171	11.8780±1.07329	-4.066	<0.001**
Hematocrit	33.9324±4.13129	32.1000±5.91215	1.796	>0.05	34.6848±3.87934	37.3544±5.04848	-2.965	<0.001**
WBCs	7.3156±1.54936	7.1080±1.08380	.776	>0.05	7.2476±1.43045	7.6744±1.30542	-1.558	>0.05
Urea	10.6396±8.23190	12.2964±8.63968	-.982	>0.05	10.5598±7.80476	8.4520±5.02704	1.605	>0.05
Creatinin	.8128±.15886	.8652±.25429	-1.236	>0.05	.8264±.13609	.7420±.11445	.611	>0.05
Albumin	40.8956±4.01060	41.7600±5.61940	-.379	>0.05	41.4002±3.84722	36.1300±4.46621	3.439	<0.001**
Tumor biomarker CD90(+ve)	11.6400±1.53543	12.1000±2.05287	-1.269	>0.05	11.4400±1.63083	10.5800±1.81928	2.489	<0.05*
Tumor biomarker CD45(+ve)	9.6800±1.73134	9.0400±1.81783	1.803	>0.05	9.5400±1.69284	7.5000±2.29685	5.056	<0.001**

Table 5: Mean score of laboratory investigations findings between study and control groups at pre & post-intervention phase. This table showed that there were no statistically significant difference existed between study and control groups regarding to laboratory investigations for hemoglobin , hematocrit, WBCs, urea, creatinine, albumin, and CD90 (+ve) CD45 (+ve) % at pre intervention as P value >0.05. But there was a statistical significant increase in mean value of hemoglobin (11.8780±1.07329), hematocrit (37.3544±5.04848), and albumin (36.1300±4.46621) of the study group than hemoglobin (11.0720±.90171), hematocrit (34.6848±3.87934) & albumin (41.4002±3.84722) of the control group at post intervention. Concerning to potential tumor biomarkers, (CD90 (+ve) & CD45(+ve)%), this table illustrated that there were statistical significant decrease in mean value (10.5800±1.81928)& (7.5000±2.29685)of the study group than (11.4400±1.63083)& (9.5400±1.69284) of control group respectively at post intervention. So it was cleared that there were statistical significant difference existed between the two groups regarding to laboratory investigations & tumor biomarkers at post intervention than pre intervention.

Table (6):-Correlation(r) test between quality of life score ,level of knowledge ,performance status for usual activities and potential tumor biomarkers among the study group pre and post intervention.

Variables	Level of knowledge				Level of performance status				Tumor biomarkers			
	Pre-intervention		Post intervention		Pre intervention		Post intervention		CD90(+ve)		CD45(+ve)	
	r	P value	r	P value	r	P value	r	P value	r	P value	r	P value
Quality of life pre-intervention	.163	.258	-	-	.062	.511**	-	-	-.018	.024*	-	-
Quality of life post-intervention	-	-	.053	.714	-	-	.798	.023*	-	-	-.424**	.002*

Table 6:- Correlation between quality of life score, level of knowledge, performance status for usual activities and potential tumor biomarkers among the study group pre and post intervention. This table illustrated that there was positive correlation between patient's total QoL score and their level of knowledge & their performance status for usual activities at pre intervention P<0.05 and post intervention P<0.001. But there was negative significant relation between patient's total QoL score and their potential tumor biomarkers among the women in the study group at different phases of intervention P<0.05.

Table (7):- Correlation(r) test between quality of life score , level of knowledg, performance status for usual activities and potential tumor biomarkers among the control group pre and post intervention

Variables	Level of knowledge				Level of performance status				Tumor biomarkers			
	Pre-intervention		Post intervention		Pre intervention		Post intervention		CD90(+ve)		CD45(+ve)	
	r	P value	r	P value	r	P value	r	P value	r	P value	r	P value
Quality of life pre-intervention	.109	.453	-	-	-.414**	.058	-	-	.193	.018*	-	-
Quality of life post-intervention	-	-	.003	.984	-	-	.314	.559	-	-	.835	.584

Table 7: Correlation between quality of life score, level of knowledge, performance status for usual activities and potential tumor biomarkers among the control group pre and post intervention. This table showed that there was a significant positive correlation between patient's total QoL score and their knowledge and performance scores at different phases of intervention. In addition there was a positive association between patient's total quality of life score and their tumor biomarkers.

Discussion

Breast cancer is a chronic disease, and patients have to deal with the consequences of its treatment that changes women's life forever. Although BCs are living longer, they often experience late effects from either the disease or treatment, which may affect daily functioning and QoL domains. The outcome of chemotherapy can be influenced by the host immune system at multiple levels (Ibrahim, 2012). Now We appreciate that the immune system plays a dual role in cancer. It cannot only suppress tumor growth by destroying cancer cells or inhibiting their outgrowth but also promote tumor progression either by selecting for tumor cells that are more fit to survive in an immune-competent host or by establishing conditions within the tumor micro environment that facilitate tumor outgrowth. Today, the

immune system is under a lot of pressure not only from environmental factors, but also from poor eating habits and lack of sleep and lack of exercise. So that if the immune system is weakened enough, cancer cells can survive and multiply (Gartner, et al. 2009). The professional health care givers play an important role in promoting and maintaining health through education. Such education is effective in promoting proper self-care to maintain healthy life style and attain better QoL for improving patient's outcomes and facilitate effective inter-professional collaboration. Despite promising results, few studies have tested this efficacy (American Joint Committee on Cancer, 2010). The overall goals when planning care for the patient with BC will actively participate in the decision making process related to treatment options, fully comply with the therapeutic plan, manage the side effects of chemotherapy and be satisfied with the

support provided by significant others and health care providers (**MacDonald, 2002**).

The findings of the present study illustrated that in relation to age, about half of both study and control groups were aged (50 - 70 years old) with their mean ages were (48.4000 ± 12.8142) for study & (54.2400 ± 9.307) for control group. This study finding was in agreement with **Ibrahim, (2012)** in his study about effect of breast cancer on women's quality of life, who revealed that, more than half of the studied women were ranging between 40 to less than 60 years old with mean of $46.4 + 11.2$. Also, this study finding is supported with **El-Saghir, et al. (2006)**, in his study about trends in epidemiology and management of breast cancer in develop Arab countries who concluded that BC is the most common cancer among women in Arab countries with a young age of around 50 years at presentation. In this respect **Hussein, (2007)** revealed that a highest percentage of women under the study of nurses role in early detection of BC in Egypt were above 40 years old women. Therefore **Bickley, (2008)** in his study about Bates Guide to Physical Examination and History Taking: Health Promotion and Counseling recommended that, clinical physical examination annually by the age of 40, in conjunction with mammography, that it improves the detection of BC by 5%-20%. Also, this study finding was supported with **Ibrahim, (2011)** in his study about Quality of life of adult patient with burn injury who noted that BC in Egyptian patients has a younger age distribution with the majority of cases occurring at 30-60 years of age, the median age is 46 years old, and this study finding was in contrast with that of **Abosereal, et al. (2011)** in his study about early detection of breast cancer among females at Facous District, Sharqia Governorate, Egypt, who noted that the most frequent interviewed age groups for early detection of BC

women at Faskous district were (30-39 years) with mean age (38,7) years old. This study finding explained by the researcher's opinion may be due to this subjects under study were not detected and diagnosed the breast tumor early but, it was discovered accidentally. There are other potential causes such as exposure to sedentary activities and obesity.

Regarding to marital status: The present study, revealed that slightly more than two thirds of both study and control groups were married. Supporting this study finding is **Hussein, (2007)** in his study about nursing Role in Early detection of Breast Cancer through Mammography and Genetic Screening and its Impact on Patient's Outcomes who reported that the majority of BC women were married. This study finding explained by the researcher's experience could be due to our cultural habits and beliefs especially among rural or low socioeconomic people with less education to encourage early marriage.

In relation to level of education: The present study demonstrated that about one third of both study and control groups were illiterate. This study result is consistent with **Abdelaleem, (2014)** who found that Egyptian females seeking medical advice at late stage, especially for cancer symptoms. Moreover, they are less educated which had its impact in decreasing awareness and delayed promptness to respond to their initial symptoms. Also on the same line **Hass, (2011)** in his study about Immune system who stated that most participants were illiterate. This study finding explained by the researcher's experience could be due to the stressors related to family responsibilities due to lack of health services that can be offered to them & lack of income. This study result was also in line with **Abdelaleem, (2014)** in his study about effect of immune enhancement on clinical outcomes of mastectomy patients undergoing

chemotherapy who stated that it is very important for the nurse to assess level of education of the patients to know their learning capability and retention because providing patient who is unable to read and write with written educational materials could pose a severe threat to him. This study result was in line with **Abd El Razik, (2010)**, in his study about the effect of educational program on QoL for patients with cancer undergoing chemotherapy, who reported that, the highest percentage of the studied groups were coming from rural areas weren't interested with education. Nevertheless, this result was congruent with **Rowe, et al.(2006)** in his study about quality of Life among women undergoing hysterectomies who mentioned that women, who are highly educated have technical access to the internet. The use of additional sources of health information like, the internet may reflect the desire of these women to become more informed, and to participate more actively in decision making regarding their care. Their active participation is important in improving their quality of life.

According to occupation; slightly more than two thirds of both study and control groups were house wives .This study finding was consistent with **Brown, et al. (2011)** in his study about efficacy of exercise interventions in modulating cancer-related fatigue among adult cancer survivors: a meta-analysis. who suggested that change or modification of previous occupation may be necessary either temporarily or perhaps permanently. This study finding explained by the researcher's experience may be due to the fact that the house wife people tend to be less physically active and tend to have more sedentary life. Also, this study result was congruent with **Ibrahim, (2012)** who showed that the majority of the studied

women were not working; this could be explained as the highest percentages of women were illiterate, and housewife. The present study is in accordance with **Yi, et al. (2007)**, in his study about informational needs of Koreans women with BC, who reported that about two thirds of the studied samples were illiterate and house wife.

Regarding the place of residence: The present study showed that more than half of study group were lived in rural area compared to more than half of control group were lived in urban area. Rural women desire greater health-related information about their BC. This study finding is congruent with that of **Mansour, (2005)**, in his study about impact of Counseling on Quality of Life of Patient with Bladder Cancer Undergoing Urinary diversion who documented that the highest percentage of the included sample were from rural areas. This study finding explained by the researcher's experience may be due to people who lived in rural areas lack health and educational services; also cultures, norms, beliefs and place of living of patients has an effect on behaviors and patterns of life style ,the nature of life and beliefs of patients to accept the illness and modify their life style according to prescribed therapeutic regimen. However, this study finding is in disagreement with **Dey, et al. (2009)** in his study about Urban- Rural difference in Breast Cancer Incidence by Hormone Receptor Status across 6 years in Egypt: Breast Cancer Research and treatment, who studied urban-rural differences in BC incidence by hormone receptor status across 6 years in Egypt, and reported that urban incidence of BC was three to four times higher than rural incidence. This study finding is also inconsistent with **Pakseresht, et al. (2009)** in his study about risk factors with breast cancer among women in Delhi,

Indian Journal of Cancer who stated that large number of BC patients were living in urban areas, it may be due to exposure to radiation. This means that environment has a negative effect on the occurrence of BC.

Regarding to number of children, more than half of both groups had equal to or more than three children, this study finding was consistent with study performed by **AbdElalem, (2014)** who found that the majority of the studied patients had more than three children. This study result explained by the researcher's experience may be due to that the increase in family size might reduce per capita income and increase responsibility and effort on women to serve her children this lead to poor health and exposure to illness. This present study is in agreement with **Abd El Razik, (2010)**, who stated that two thirds of participated patients were having children.

In relation to monthly income about two thirds of the study group and more than half of control group had enough family income. This study finding explained by the researcher's experience may be due to that most of the samples were illiterate, not working which can't allow the patient to visit private, or specialized clinics to get high quality of care, and get correct information. This study finding is consistent with **Abd El Razik , (2010)**, who stated, that about two thirds of the studied women were having sufficient income. However, these study findings are in disagreement with **Ibrahim, (2012)** who denoted that slightly more than three quarters of the studied women were having insufficient income. There is a negative relation between low income, and occurrence of cancer. This is congruent with **Chul-Woung, et al. (2007)**, in his study about Inequations in Cancer Incidence and Mortality across Income Groups and Policy Implication in South Korea, who

highlighted that the relative risk of cancer incidence in lowest income group and stated that low socioeconomic status is an important factor affecting QoL in normal population and inpatient with medical illness. **Breast Cancer Organization, (2012)**, reported that the most economically deprived patients are more likely to report poor health and to feel less satisfied and less control of their lives and having higher health care needs.

Regarding to the patients knowledge about BC, chemotherapy & management of its side effects & the immune system post intervention ,the current study revealed that there was highly statistical significant difference existed between study and control groups regarding patient's knowledge about BC, chemotherapy and management of its side effects and the immune system. And there was visible improvement in patient's knowledge of study group than in control group. This study finding explained by the researcher's experience might be due to that education of patients about what symptoms to expect or watch for, when and how to contact their physicians or nurses, and how to manage their conditions can help ensure that the side effects of cancer and its treatment are moderated and alleviated or prevented. Such education can empower patients and their caregivers, help to optimize treatment outcomes, decrease adverse effects, office visits , hospitalizations and substantially reduce costs in an already burdened health system .This study result may be explained that the study group patients apply the educational program and follow instructions found in the booklet, this lead to improvement of their awareness and knowledge about the disease and it's treatment and this in turn help them to modify their life style which in turn improve and strength the immune system to be able to fight the disease and overcome the chemotherapy side effects. This study result was supported by **Oncology Nursing Society, (2010)&**

Keller, (2006) who stated that an educational intervention provided by nurses before the start of chemotherapy may assist women with BC to increase their knowledge of chemotherapy treatment, enhance their ability to manage side effects, and improve their coping strategies. This study finding was also in line with Williams and Schreier, (2004) in their study about the effect of education in managing side effects in women receiving chemotherapy for treatment of breast cancer who stated that teaching effective self-care behaviors enhances patient's independence, comfort, control, and improvement in their QoL.

Regarding to performance status for usual activities of patients in both study and control groups post intervention:- The present study showed that there were highly significant improvement of the mean score of the study group than control group. Regarding to total QoL domains of patients in both study and control groups post intervention:-The present study revealed that there were highly significant improvement of the mean score of the study group related to physical, psychological, functional, patient's concerns related to the disease and its treatment & social domain than control group. As the majority of the study group had mild affection compared to control group that majority of them had moderate affection on their QoL. This study finding explained by the researcher's experience that the improvement in performance status and QoL of patients in the study group may be attributed to their response to intervention and that they follow the instructions given to them through teaching sessions or through the information found in the booklet that include health teaching about the disease, its treatment, management of chemotherapy side effects and immune enhancement through (diet, exercise and

life style modification). Which reflected improvement of their knowledge that in turn lead to improvement in their performance status and QoL domains as each items related to others. This study result was supported by **Reiger, (2001)** in his study about Assessment and epidemiologic issues related to fatigue who stated that physical function has been defined as the ability to ambulate and to perform normal activities of daily livings. Cancer has been found to have a significant effect on patient's abilities to function in usual role and activities. So that physical and functional well-being are essential components for overall QoL. As cancer has a negative effect on QoL, so exercise during cancer treatment may improve QoL. Also, **Dimo, (2001)** in his study about effects of exercise on cancer-related fatigue stated that on the non-pharmacological interventions for fatigue and other chemotherapy side effects during cancer treatment, physical activity has the strongest supporting evidence. On the same line **Schwartz, (2000)** who stated that aerobic exercise has been found to reduce fatigue and improve performance status during chemotherapy and radiation therapy and after cancer treatment has been completed. Moreover, **Ingram and Visovsky, (2007)** in their study about Exercise intervention to modify physiologic risk factors in cancer survivors, who stated that evidence of the benefits of life style modification through eating healthy diet & practicing exercise for cancer survivors has mounted steadily over the past two decades particularly in the areas of psychological and QoL outcomes and cancer related fatigue that in turn can enhance the immune system. More recently, improvements in physical functioning, body weight and composition, muscle strength and endurance, and immune function have been reported. On the same line **Brolinson and Elliott, (2007)** in their study about exercise and the immune

system stated that the immune system of people who exercise regularly is stronger than of those who don't. This study finding explained by the researcher's experience may be due to engaging in moderate intensity physical activity can have a protective effect. This study result was supported by **Adams, (2009)** in his study about the powerful role of omega-3 fatty acids in preventing diseases of inflammation who stated that fatigue and poor performance status associated with cancer probably has both physical and psychological causes; the physical causes include anemia, various metabolic disturbances and in appropriate nutrition due to anorexia, nausea and vomiting and the psychological causes may contribute to fatigue and poor performance status include depression, anxiety, and lack of sleep. Finally the release of endogenous inflammatory cytokines contribute to the severity of fatigue in some patients. Congruent with this study finding was **Nail, (2002)** in his study about fatigue in patients with cancer who stated that untreated cancer fatigue and other chemotherapy side effects may result in a decrease or discontinuation of normal physical, social, interpersonal and recreational activities and interfere with home, family, work and educational role performance. Uncontrolled chemotherapy side effects may affect all QoL domains, that is; physical, psychological, social and spiritual wellbeing, and may lead to loss of productivity, self-esteem and significant reduction in physical functioning and QoL and difficulty adhering and completing treatment regimens.

Concerning the comparison between patients in the study and control groups regarding their total knowledge level and quality of life score at pre and post intervention, The present study showed that most of the patients in both study and control groups had unsatisfactory level of knowledge pre intervention compared to post

intervention that majority of the study group had a satisfactory knowledge versus most of them in the control group had unsatisfactory knowledge. There was no statistical significant relations between the patients in both study and control groups regarding their total knowledge level pre intervention $P > 0.05$. But there were a strongly highly significant relation between the two groups post intervention $P < 0.001$. This study finding explained by the researcher opinion may be attributed to the effect of using educational program among study group that attain knowledge and proper self-care practices and life style modifications for improving their QoL. In this respect **Ahmed, (2011)** who found that QoL is influenced by factors over which nurses have some control, for example, the environment, information provided to patients and family members, symptoms management and nursing intervention. Nurses are in a key position to carry out patient education, since they are the health care providers who have continues contact with the patient and family and are usually most accessible source of information for patients. Also, the present study revealed that the majority of patients in both study and control groups had moderate QoL affection pre intervention compared to post intervention that majority of patients in control group had moderate QoL affection versus to mild QoL affection on majority of patients in study group. It was clear that there was a strongly highly significant relation between study and control groups regarding the total QoL affection post intervention $P < 0.001$. But there was no relation between the two groups pre intervention $P > 0.05$.

The relation between control and study groups regarding their total knowledge level & quality of life score, performance status for usual activities and their potential tumor biomarkers at pre and post intervention: -Regarding patients in study group; There was a statistical positive significant relation between the

total QoL score and performance status for usual activities pre and post intervention .That means patients with good level of total QoL domains were having high level of performance status for usual activities .Meanwhile ,there was negative significant relation between total QoL score and their potential tumor biomarkers at different phases of intervention $P < 0.05$. That means patients with good level of total QoL domains were having decrease in the incidence of potential tumor biomarkers. Compared to patients in control group that there was positive relation between patient's total QoL score & their knowledge and performance scores at different phases of intervention. In addition there was a positive association between patient's total quality of life score and their tumor biomarkers. There were also a statistical significant positive relation between patients' level of knowledge and their QoL. That means patients with high level of knowledge were having good level of total QoL domains. This study finding explained by the researcher's experience may be due to patients who had good knowledge associated with proper self-care and life style change or modification and reduces the physical, psychological, emotional, and social problems. In the same-line **Mohammed, (2011)**, in his study about effect of Instructional for Relieving Chemotherapy Side Effects on Women with Ovarian Cancer who stated that there was a highly positive correlation between women's knowledge and their QoL. This emphasizes effect of health education on the priority of QoL and decrease of life threatening problem for women. Finally, the study findings supported the research hypothesis which confirmed that the immune enhancement intervention program had statistical significant positive effect on clinical outcomes of patients with BC undergoing chemotherapy. Because it was proofed that the patients in study group who

received immune enhancement intervention program reported high QoL ,better performance status and expressed lower potential tumor biomarkers versus the patients in control group who don't receive it. Therefore nutritional support, physical activity and life style modification components of immune enhancement intervention are increasingly recognized as a fundamental concern for cancer patients undergoing chemotherapy that can strengthen the immune system and reducing bad consequence of the disease chemotherapy side effects.

Conclusion

Based on the findings of the current study, it can be concluded that immune enhancement intervention program had statistical significant positive effect on clinical outcomes (level of patient's knowledge, performance status of usual activities, QoL domains, nutritional status in addition to laboratory investigations(hemoglobin, hematocrit, WBC, blood urea nitrogen, serum creatinin & albumin) and tumor biomarkers CD 90(+ve) CD45 (+ve) %) of patients with breast cancer undergoing chemotherapy.

Recommendations

The current study recommended the need to provide the developed guided booklet about immune enhancement intervention for patients with breast cancer to increase their level of knowledge, awareness about breast cancer, management of chemotherapy side effects and immune system enhancement. Also ,further study is recommended to conduct the training and teaching of nurses about the immune enhancement intervention program and evaluate its impact on their performance

and consequently on patients outcomes on the long run.

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