

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

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Abstract

Breast cancer (BC) is the most frequently diagnosed malignancy and ranks as the leading cause of cancer-related deaths among females worldwide. After lung cancer, it is the second-largest cause of death. Systemic chemotherapy is used to treat more than half of the individuals with BC. They are effective at destroying cancer cells, but they can temporarily display immune dysfunction. The immune system is critical to rebuild and maintain the immune system in optimal fighting shape. **The present study aimed** to evaluate the effect of immune enhancement intervention on clinical outcomes of patients with BC undergoing chemotherapy. **The research design** was quasi-experimental. **Setting:** It was conducted at the oncology center and nuclear medicine at Ain Shams University Hospitals. **Sample:** A purposive sample of 100 patients was sorted into two groups: control and study. **Tools of data collection:** Data were collected using a structured interviewing questionnaire, a Scale for assessing one's quality of life, an Australia-modified Karnofsky performance status scale & a nutritional assessment sheet that includes a lab investigation & tumor marker. **The results:** The study group (60%) and the control group (68%) were married and between the ages of 50 and 70 years old, respectively, and there was a highly significant difference between the two groups in terms of knowledge, quality of life, performance status for usual activities, and nutritional status post-intervention, which led to a highly significant decrease in tumor biomarkers among the study group versus the control group. **Conclusion:** Patients with BC who were undergoing chemotherapy saw a statistically significant improvement in their clinical outcomes after participating in an immune enhancement intervention program. **Recommendations:** More researches are needed to conduct training and instruction, to study the impact of the immune enhancement intervention program on the clinically outcomes and quality of life of the patients.

Keywords: Breast Cancer, Chemotherapy, Immune System Enhancement

Introduction

Breast cancer is cancer that forms in the cells of the breasts. After skin cancer, breast cancer is the most common cancer diagnosed in women in the United States. Breast cancer can occur in both men and women, but it's far more common in women. 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. there were 2.3 million women diagnosed with breast cancer and 685 000 deaths globally (Eraky, 2016). In 2012, BC caused 458,503 deaths worldwide (13.8% 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 prevalence of BC varies widely over the world, with the lowest prevalence in developing countries and the highest prevalence in wealthy

countries (Leer, 2017). Breast cancer is the most common cause of death among Egyptian women, with 65,000 new cancer patients expected in 2012. Carcinoma of the breast is the most common cancer among Egyptian women, accounting for 29 percent of National Cancer Institute cases. (El-Sheshtawy, et al. 2017).

Chemotherapy is a systemic treatment for women with breast cancer. It's commonly used for cancer that's stage II or higher, and it can be used in conjunction with surgery, radiation therapy, or both (Litton, et al. 2012). Chemotherapy is a treatment that uses anti-neoplastic medications to try to kill cancer cells by interfering with biological activities like replication and DNA repair. Chemotherapy drugs are effective at killing cancer cells, but they can also harm fast-growing normal cells and cause major immunosuppressive side effects such as a decrease in white blood cell count, fatigue, weight loss, anemia, nausea, vomiting, and other symptoms that prevent the immune system from contributing to its anti-

cancer effects, which have a significant impact on all aspects of women's quality of life. (Levine & Whelan, 2018).

Despite scientific efforts, clinical oncologists have only given anti-cancer immune treatments a passing glance in the last decade. The immune system is useful for determining BC prognosis, treatment response, and preventing BC metastases (East, 2019). As a result, nurses must develop and implement an immune-boosting intervention program to reduce chemotherapy side effects and increase the rate of response in BC patients.

Chemotherapy kills fast-growing cells, including cancer and bone marrow cells. Damage to bone marrow means it can't produce disease-fighting immune-system cells. Low white blood cell counts (neutropenia) can result.

The recommendations of immune enhancement for anyone who wants to improve his or her health: Exercise, eat a balanced diet, maintain a healthy weight, get good sleep, reduce stress, avoid tobacco and limit the amount of alcohol you drink. (Ramakrishnan, 2020) & (New Hope Cancer Treatment Center, 2020)

Significance of the study:

Breast cancer is the most frequent cancer in women in affluent western countries, accounting for more than one-fourth of all cancer cases, and it is becoming increasingly prevalent in many developing countries. The number of instances has increased dramatically worldwide since the 1970s, which can be attributed in part to modern lifestyles. According to US statistics, 2.8 million women were impacted by BC in 2015. BC accounts for 18.2 percent of all cancer deaths globally, affecting both men and women. According to the National Cancer Institute (NCI), around 232,340 females and 2,240 males are diagnosed with BC each year in the United States, with approximately 39,620 deaths due to the disease. (Zheng, et al.2021) & (American Institute for Cancer Research, 2021).

BC is the most frequent cancer among Egyptian women, accounting for 18.9% of all cancer cases with an age-adjusted prevalence of 49.6 per 100,000 people. According to official NCI (Cairo University) figures, BC accounts for

35.1 % of all cancer cases in Egypt. BC diagnosis comes as a huge shock to women, who say they fear it more than heart illness. According to the Ministry of Health and Population's most recent statistics, one out of every 12 Egyptian women has BC. (El-Sheshtawy, et al., 2017).

Aims of the study

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

Research hypotheses

- Subjects who got an immune enhancement intervention (study group) will report a higher quality of life and performance status than those who did not (control group).
- Study participants who got immune enhancement intervention (study group) have lower levels of possible tumor biomarkers (Cancer Stem Cells) than those who did not (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 for data collection.

*Setting

The study was conducted at the oncology center and nuclear medicine at Ain Shams University Hospitals, which are considered reference hospitals for BC cases.

*Subjects:

A purposive sample of 100 adult female patients with BC who were taking chemotherapy was selected using criteria and

divided into two equal groups of 50 patients (study and control groups), with 50 individuals in each group. The trial group was given an immune-enhancement intervention program, whereas the control group received standard hospital treatment. The following inclusion criteria were used to choose both groups.

The sample size was calculated by adjusting the power of the test to 80% and the confidence interval to 95% with margin of error accepted adjusted to 5% and a known total population of 710 patients using the following equation:

$$X = Z(c/100)2r(100-r)$$

$$N = NX/((N-1)E^2+x)$$

$$E = \text{Sqrt} [(N-n) x/n(N-1)]$$

Where N is the population size, r is the fraction of responses that you are interested in, and Z(c/100) is the critical value for the confidence level (Chau et al., 2017).

*Inclusion Criteria:

- 1- Full-conscious patients who are willing to participate in the study.
- 2- Patients aged over 18 years old.
- 3- Just started chemotherapy and not enrolled in any educational program.
- 4- There is no evidence of metastases.
- 5- There is no other sickness that is linked to it

Variables:

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

Operational definitions:

Immune enhancement intervention is a health education program developed by the researcher based on a literature study to help patients with BC who are undergoing chemotherapy strengthen their immune systems

Clinical outcomes include laboratory tests (hemoglobin, hematocrit, WBC, blood urea nitrogen, serum creatinine & albumin) and tumor biomarkers CD 90 (+ve) CD 45 (+ve) percent, as well as assessment of patient knowledge, performance status of usual activities, QoL domains (physical, social, psychological, functional, and patient's concern related to the disease and its treatment domains), nutritional

status, and tumor biomarkers CD 90 (+ve) CD 45 (+ve).

*Tools for data collection:

The following four tools were used to collect data for this study: -

A tool I: Structured interviewing questionnaire:

After studying the relevant literature, the researcher came up with it. The following parts were included: -

Part I: Demographic information about the patient; including age, marital status, educational level, employment status, residence, income level, family members, and the number of children. (seven items).

(21 questions); distributed as the following:

First, there were multiple-choice questions about the definitions, causes or risk factors, signs and symptoms, and treatment of BC, as well as questions about chemotherapy treatment and its side effects. (6 questions)

Second, it asked true or false questions regarding how to treat chemotherapy side effects, such as (nausea, vomiting, loss of appetite, constipation, diarrhea, stomatitis, infection, platelet deficiency, anemia, urinary problems, hair loss, & skin problems). (A total of 11 questions)

Third, it asked true or false questions about the definition of the immune system and the variables that can strengthen or weaken it. (4 questions).

* For each question, a scoring system ranging from -Zero to 1 is used (Where Zero indicates wrong answers & one indicates correct answers). The following is a breakdown of the total knowledge score:

More than 75% was deemed satisfactory

Less than 75% was deemed unsatisfactory.

Tool II: Australia-modified Karnofsky performance status scale

It was adapted from Abernethy, et al., (2005) and then translated into Arabic by the researchers to measure the ability of patients with BC to do daily activities, as well as to assess the patient's development following the therapy procedure. It was most widely utilized in cancer therapy prognosis, mainly after

chemotherapy. It comprised of 11 components, each of which was graded on a percentage scale ranging from 100 percent normal function to 0%. For most major illnesses, the lower the Karnofsky score, the worse the prognosis.

It was divided into three categories:

- 1- Complete self-independent; (Capacity to do normal activities without any health concerns = 100%, ability to do normal activities with mild discomfort = 90%, and ability to do normal activities with severe discomfort = 80%) are the three options.
- 2- Unable to work and require assistance; three options are scored as follows: (inability to perform regular tasks and require assistance = 70%, inability to perform normal activities and require major assistance = 60%, and need significant assistance with frequent health care = 50%).
- 3- Completely reliant (unable to (Remain in bed more than half of the time = 40%, practically all of the time = 30%, all of the time = 20%, comatose and rarely awaken = 10%, and patient died = 0%).

Tool III: Quality of life assessment scale

Brady, et al. (1997) adapted it, and the researchers changed and translated it into Arabic to assess QoL dimensions for BC patients. It consists of 37 items (seven for the physical domain, seven for the social domain, six for the psychological domain, seven for the functional domain, and ten for the patient's concern about the disease and its treatment domain), all of which are rated on a four-point scale (0 = no affection, one point = mild affection, two points = moderate affection, three points = severe affection). The scale's total score varied from 0 to 111 points, and it was classified as follows:

- **<37 points** representing < 41% was considered no affection which means the 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.

After reviewing the related literature to identify the patient's nutritional status, it included the following:

- A) Dietary history: Included information on the number of meals consumed each day, the frequency of meals, the type of food consumed (meat and chicken), the sorts of foods consumed (fruits and vegetables), and the techniques of cooking and purchasing food. (eight items)
- B) Anthropometric measurements: This includes the patient's current body weight, height in centimeters, and body mass index (BMI) to establish if the patient is underweight or overweight. The BMI is computed by dividing a patient's weight in kilograms by their height in meters squared and is then categorized (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. Hemoglobin, hematocrit, WBCs, blood urea nitrogen, serum creatinine, and serum albumin were among the tests performed.
 2. Laboratory evaluation of putative tumor biomarkers (cancer stem cells): CD 90(+ve) CD45 (+ve) percent were used to assess the remaining cancer stem cells. (seven items)

II- Operational design:

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

* Preparatory phase:

The study's initial step was the preliminary phase. It involved reviewing past and current local and international related literature as well as theoretical knowledge of the various aspects of the study using books, articles, the internet,

periodicals, and magazines to develop data collection tools and to prepare the content of the immune enhancement intervention, as well as designing a colored booklet about (diet, exercise, and lifestyle modification) for BC patients undergoing chemotherapy. This took roughly four months.

Validity and reliability: * Content validity:

Face and content validity are used to test the validity of the proposed instruments. The goal of face validity is to evaluate the things to see if the tools measure what they're designed to measure. The tools were tested for content validity to see if they covered the goal. A team of three specialists examined the validity of the data (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 Ain Shams University). The tools were examined for clarity, relevancy, comprehensiveness, and simplicity, and small changes were made before the final version was created.

The internal consistency of the tools was measured using the Cronbach's Alpha test to determine their dependability. The reliability questionnaire ($r = .541$) was discovered using Cronbach's Alpha equation.

- 1) The structured interviewing questionnaire was shown to be reliable (0.85).
- 2) The Australia-modified Karnofsky performance status measure was found to be reliable (0.94).
- 1) The physical condition on the QoL scale was (0.92), the social condition was reliable (0.83), the psychosocial condition was (0.87), the functional worry was (0.87), and the patient's concerns about the disease and its treatment were (0.87). (0.89).

***Pilot study:**

It was first carried out on 10% of the study subjects (10 patients) before data collection to assess the tools' applicability, clarity, and efficiency, as well as to estimate the time required for data collection. Based on the results of a pilot study, certain tool adjustments were made. The patients who took part in the

pilot trial were excluded in the main study's sample.

***Fieldwork:**

- *Data were collected in the following sequence:*

Permission to conduct the study from appropriate authorities at Ain Shams University's Faculty of Nursing following an explanation of the study's goal was acquired.

Official permission from the director of the oncology center and nuclear medicine, to carry out the study after an explanation of the purpose of the study was obtained.

It was conducted at the oncology center and nuclear medicine at Ain Shams University Hospital

An interview with the head of the clinical oncology department of the above-mentioned settings was held to tell him of the study's goal and to request his aid in facilitating the work.

Interview with patients before starting the data collection procedure were conducted to establish a good relationship.

Data collection covered a period of 12 months starting from the first of March 2019 to the end of March 2020.

Data collection passes throughout two stages as the following:

- Implementation stage
- Evaluation stage

The implementation stage: was divided into two phases

Phase 1: Before any data was collected, the first phase of the work involved seeing the patients in both the control and study groups, explaining the purpose and nature of the study, and obtaining their consent to participate in the study. Patients were told about the confidentiality of their information, the study's nature, their right to withdraw, and the subject data's confidentiality.

To collect necessary data, the study was conducted three days a week from 9 a.m. to 2 p.m. The time required to fill out the study tools was approximately (25-30 minutes) for the structured interview questionnaire, (10 minutes) for the

Australia-modified Karnofsky performance status scale, (25-30 minutes) for the quality of life assessment scale, and (10 minutes) for the nutritional assessment sheet.

Patients in both the study and control groups were questioned to determine their degree of knowledge, performance status for everyday tasks, quality of life, and nutritional status, as well as to gather baseline data utilizing tools (I, II, III & IV).

Before the intervention, each patient in both groups was given a questionnaire, which was filled out by the researchers based on the responses given by the patients. The interview took place in a separate room, and the questions were directed in plain Arabic, with the replies being promptly recorded.

Before the intervention, each patient in both groups had a blood sample taken for laboratory tests to assess hemoglobin, hematocrit, WBCs, blood urea nitrogen, serum creatinine, serum albumin, and possible tumor biomarkers CD90(ve+)CD45(ve+) by flow cytometry.

Phase 2: The study group was only subjected to the second phase of the research by performing the immunological boosting intervention program. The teaching sessions took place in the oncology department's outpatient clinic. The patients were divided into small groups (5-10 patients per session) for the training sessions, with each group experiencing the identical program content and receiving the same teaching tactics and handouts. The overall number of groups was five, and the total number of training sessions for each group of patients was three, to cover all of the information contained in the proposed booklet. It was created by the researcher based on an assessment of the patients' needs

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

- Acquire knowledge regarding BC disease, its treatment & immune enhancement intervention.
- Increase their ability to cope with disease-related self-chemotherapy and its negative effects.

The 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: Information about chemotherapy treatment was included, as well as (a definition of chemotherapy, indications, treatment course routes of administration, and its side effects).

Chapter three: Included information on immunotherapy, such as (the definition of the immune system, factors that weaken and enhance the efficacy of the immune system, and nursing care to strengthen it, through overcoming the side effects of chemotherapy, diet, exercise, and lifestyle modifications to enhance the efficiency of the immune system).

Chapter four: Contained information about how to prevent BC

Patients were answered questions relating to the themes presented in the previous session before the start of each program session to ensure that they remembered the instructions and to reinforce their knowledge. The researcher re-emphasized any aspects that were missed or unclear. In addition, the researcher completed and refreshed the previously mentioned information by asking them some related questions, and gave each patient a booklet of colored pictures containing all of the above information, which discussed with them to capture their attention and motivate them to review it at home. During each session, a PowerPoint presentation was used to explain the intended immune-boosting intervention program, as well as a discussion

The Evaluation stage:

Using the same methods, patients in both groups (study and control) were interviewed again after the intervention to determine any changes from baseline data in terms of the degree of knowledge, performance status for routine activities, QoL, and nutritional status (I, II, III & IV).

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

III: Administrative design:

For authorization to perform the study, the Faculty of Nursing at Ain Shams University wrote an official letter to the head of the oncology center and nuclear medicine at Ain Shams University Hospitals.

After explaining the study's goal to the director of the oncology center and nuclear medicine at Ain Shams University Hospitals., official permission was obtained.

Ethical consideration:

The ethical research consideration in this study included the following:

Before collecting data, the researchers sought informed oral consent from the study's participants.

Patients were advised of their right to withdraw from the study at any time without giving a reason, and they were guaranteed that their anonymity and confidentiality would be preserved. Ethics, values, culture, and beliefs were all held in high regard.

IV) Statistical design:

Data was coded and translated into a particularly designed form that could be entered into a computer. The data were tabulated and analyzed using IBM's SPSS statistical program version 22. Quantitative data were reported as mean and standard deviation (X₂SD) and analyzed using Chi-Squared (2), paired t-test, and independent t-test for comparing mean scores between study and control groups, as well as correlation r test. The p-value was used to analyze qualitative data, which was expressed as numbers and percentages. P-values less than 0.05 (P-value < 0.05) were considered significant, and P-values less than 0.001 (P < 0.001) were considered extremely significant.

Results

Table (1): Represents the frequency distribution of demographic characteristics for both study and control groups. This table shows that **52%** of the study group and **48%** of the control group were aged (50 - 70 years old) with their mean ages being **48.4000±12.8142** for the study & **54.2400±9.307** for the control group with **60%** and **68%** respectively of both groups were married. Regarding the level of education,

32% & 34% of both the study and control groups were illiterate, and **60%&70%** of them were housewives respectively. In relation to place of residence; **52%** of the study group were lived in a rural area compared to **54%** of the control group were lived in urban areas and **56%** of both groups had equal in having more than three children. In addition to monthly income **64%** of the study group and **52%** of the control group had enough family income. There were no statistically significant differences existed between the two groups regarding (age, marital status, education, occupation, number of children, and family income) P > 0.05

Table 2: - Represents a 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 the study and **90%** of the control groups had an unsatisfactory level of knowledge pre-intervention compared to post-intervention **88%** of the study group had a satisfactory knowledge level and **92%** in the control group had unsatisfactory knowledge. This table also showed that there was no statistically significant difference existed between both study and control groups regarding their total knowledge level pre-intervention P>0.05. But there was a highly significant difference between the two groups post-intervention P<0.001.

Figure 1 Pre- and post-intervention percentage distribution of study patients' overall knowledge score on the influence of immune enhancement intervention on clinical outcomes of patients with BC having chemotherapy in both the study and control groups. This graph shows that the control group had unsatisfactory knowledge about breast cancer, chemotherapy treatment, and the immune system before and after intervention **90 % and 92 %**, respectively, whereas the study group had unsatisfactory knowledge pre-intervention **92 %** compared to post-intervention **88 %**.

Table 3: Mean score of performance status for usual activities between study and control groups at the pre-&post-intervention phase. This table shows that there was no statistically 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 was a highly

significant improvement of mean score of the 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 the post-intervention phase. This table illustrated that **70%, 64% & 82%** of the control group had moderate QoL affection regarding psychological, functional & concerns related to the disease and its treatment domains and **70%** of them had severe QoL affection for the disease and its 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 the control group had moderate QoL affection post-intervention compared to **76%** of the study group had mild QoL affection and there was a highly statistically significant difference existed between the two groups $P < 0.001$.

Figure (2): Pre- and post-intervention percentage distribution of the total quality of life score of the patients investigated in both the study and control groups. This graph demonstrates that the control group had moderate QoL affection at pre-intervention **82%** and post-intervention **72%**, respectively, whereas the study group had moderate QoL affection at pre-intervention **72%** and mild QoL affection at post-intervention **76%**.

Table 5: Between the study and control groups, the mean score of laboratory investigation findings pre-and post-intervention. Hemoglobin, hematocrit, WBCs, urea, creatinine, albumin, and CD90 (+ve) CD45 (+ve) % pre-intervention laboratory tests revealed no statistically significant difference between study and control groups with a P-value > 0.05 . However, the study group's mean hemoglobin **11.87801.07329**, hematocrit **37.3544**

± 5.04343 , and albumin **36.1300 \pm 4.46621** were statistically substantially higher than the control group's hemoglobin **11.0720 \pm .90171**, hematocrit **34.6848 \pm 3.87934**, and albumin **41.4002 \pm 3.84722**. Concerning potential tumor biomarkers, (CD90 (+ve) & CD45(+ve) %), this table illustrated that there was statistically significant decrease in mean value **10.5800 \pm 1.81928 & 7.5000 \pm 2.29685** of the study group than **11.4400 \pm 1.63083 & 9.5400 \pm 1.69284** of control group respectively at post-intervention. So it was clear that there was a statistically significant difference existed between the two groups regarding laboratory investigations & tumor biomarkers at post-intervention than pre-intervention.

Table 6:- Correlation between quality of life score, level of knowledge, performance status for usual activities, and potential tumor biomarkers among the study group post-intervention. This table illustrated that there was a positive correlation between patients' 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 a negative significant relationship between patients' 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 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 patients' total QoL score and their knowledge and performance scores at different phases of intervention. In addition, there was a positive association between patients' total quality of life score and their tumor biomarkers.

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

Variables	Control group(N=50)		Study group(N=50)		X2	P value
	No	%	No	%		
Age in years						
18 < 30	6	12.0	6	12.0	0.196	>0.05
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						
Single	6	12.0	14	28.0	4.45	>0.05
Married	34	68.0	30	60.0		
Widow	10	20.0	6	12.0		
Level of education						
Illiterate	17	34.0	16	32.0	2.75	>0.05
Primary	11	22.0	11	22.0		
Secondary	14	28.0	9	18.0		
University	8	16.0	14	28.0		
Occupation						
Working	15	30.0	20	40.0	1.09	>0.05
Housewife	35	70.0	30	60.0		
Residence						
Rural	23	46.0	26	52.0	0.360	>0.05
Urban	27	54.0	24	48.0		
Number of children						
No	8	16.0	13	26.0	5.24	>0.05
1	4	8.0	0	0.0		
2	10	20.0	9	18.0		
≥ 3	28	56.0	28	56.0		
Family income						
Enough	26	52.0	32	64.0	1.47	>0.05
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

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

Knowledge	Pre-intervention								X ²	P-value	Post-intervention								X ²	P-value
	Control group				Study group						Control group				Study group					
	Satisfactory		Unsatisfactory		Satisfactory		Unsatisfactory		Satisfactory		Unsatisfactory		Satisfactory		Unsatisfactory		Satisfactory		Unsatisfactory	
No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	
Breast cancer	9	18	41	82	8	16	42	84	0.071	>0.05	10	20	40	80	46	92	4	8	52.59	<0.001**
Chemotherapy- side effects	10	20	40	80	8	16	42	84	0.271	>0.05	7	14	43	86	37	74	13	26	36.52	<0.001**
Common system	21	42	29	58	14	28	36	72	.215	>0.05	15	30	35	70	45	90	5	10	37.50	<0.001**
Total knowledge	5	10	45	90	4	8	46	92	.122	>0.05	4	8	46	92	44	88	6	12	64.10	<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 in both study and control groups at pre and post-intervention phases.

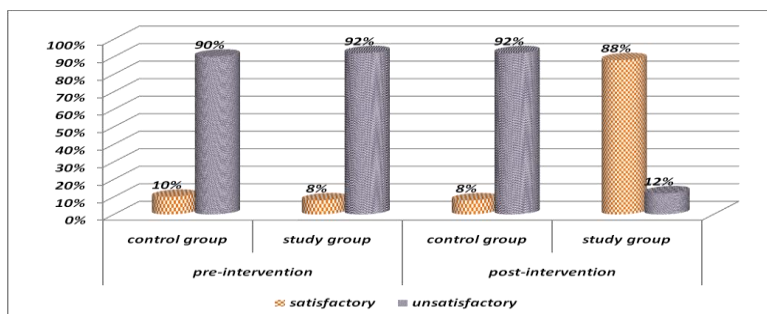


Table (3): Mean score of performance status for usual activities between study and control groups at the pre- & post-intervention phase.

Performance status	Pre-intervention				Post-intervention			
	Control group Mean±SD	Study group Mean±SD	T	P-value	Control group Mean±SD	Study group Mean±SD	T	P-value
Completely self-independent	27.60±7.70	6.709±30.00	1.66	>0.05	27.000±9.09137	34.6000±7.05951	4.669	<0.001**
Unable to work& need assistance	56.40±6.92	8.53±59.20	1.80	>0.05	53.6000±9.84782	7.45326±63.4000	5.611	<0.001**
Completely dependent (unable to care of self& health care is needed with rapid disease program)	81.20±4.35	4.53±82.80	1.80	>0.05	79.8000±6.84821	5.57326±86.6000	5.446	<0.001**

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

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

Quality of life domains	Control group								Study group								T	P-value
	No affection		Mild affection		Moderate affection		Sever affection		No affection		Mild affection		Moderate affection		Sever affection			
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%		
Physical	0	0	6	12	9	18	35	70	36	72	9	18	5	10	0	0	40.89	<0.001**
Social	0	0	5	10	28	56	17	34	3	6	10	20	36	72	1	2	50.48	<0.001**
Psychological	0	0	6	12	35	70	9	18	22	44	11	22	13	26	4	8	34.80	<0.001**
Functional	0	0	5	10	32	64	13	26	17	34	17	34	15	30	1	2	35.54	<0.001**
Patients' concerns related to the disease& its treatment	0	0	1	2	41	82	8	16	35	70	7	14	7	14	1	2	69.02	<0.001**
Total	0	0	0	0	36	72	14	28	0	0	38	76	12	24	0	0	64.00	<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

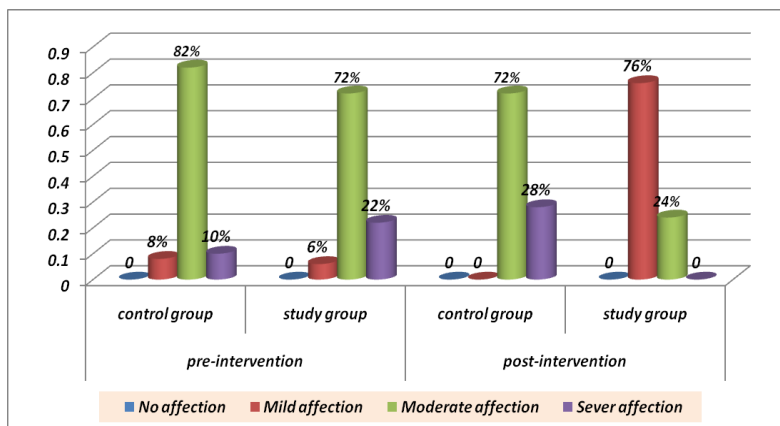


Table (5): Mean score of laboratory investigations findings between study and control groups at pre-&post-intervention phase

Laboratory result	Pre-intervention		T	P-value	Post-intervention		T	P-value
	Control group	Study group			Control group	Study group		
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±5.04343	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
Urine	10.6396±8.23190	12.2964±8.63968	.982	>0.05	10.5598±7.800476	8.4520±5.02704	1.605	>0.05
Creatinine	.8128±.15886	.8652 ±.25429	.1236	>0.05	.8264±.13609	.7420±.11445	.611	>0.05
Albumin	40.8956±4.01060	41.7600±5.61340	.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 (6): Correlation(r) test between the 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 (7): Correlation (r) test between the quality of life score, level of knowledge, 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

Discussion

Breast cancer is a long-term illness, and patients must deal with the long-term effects of treatment, which alter women's lives forever. Even though BCS are living longer, patients frequently face late effects from the disease or therapy, which can have an impact on daily functioning and QoL dimensions. At numerous levels, the host immune system can influence the outcome of chemotherapy. (Ibrahim, 2017). Now it is understood that the immune system performs two roles in cancer. It can both repress tumor growth and promote tumor advancement by selecting tumor cells that are better suited to live in an immune-competent host or by creating conditions in the tumor microenvironment that favor tumor propagation. Today,

Environmental influences, as well as bad food habits, lack of sleep, and lack of exercise put a lot

of strain on the immune system. So that cancer cells can live and thrive if the immune system is sufficiently weakened. (Gerbershagen, et al. 2018). Through education, professional health providers play an essential role in promoting and maintaining health. Such education is beneficial in promoting good self-care to maintain a healthy lifestyle and achieve a higher quality of life, which improves patient outcomes and facilitates successful inter-professional collaboration. Despite promising results, this efficacy has only been explored in a few types of research. (American Joint Committee on Cancer, 2010). When planning care for a patient with BC, the overall goals are for the patient to actively participate in the treatment decision-making process, fully comply with the therapeutic plan, manage chemotherapy side effects and be satisfied with the support provided by significant others and health care providers. (Marmor, 2017).

The results of this study revealed that nearly half of both the study and control groups were between the ages of 50 and 70, with mean ages of (48.4000 ± 12.8142) for the study and (54.2400 ± 9.307) for the control group. This study's findings were consistent with **Ibrahim's (2017)** findings in study on the impact of breast cancer on women's quality of life, which found that more than half of the women tested were between the ages of 40 and 60, with a mean age of $46.4 + 11.2$ years. Also, this study's findings are supported by **El- Saghir, et al. (2019)**, 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 their study about trends in epidemiology and management of breast cancer in developed Arab countries. In this regard, **Hussein (2020)** found that the majority of women in Egypt who participated in a study on nurses' role in the early identification of BC were over 40 years old. As a result, in a study about Bates' Guide to Physical Examination and History Taking: Health Promotion and Counseling, **Bickley (2021)** recommended that clinical physical examinations be performed annually by the age of 40, in conjunction with mammography, to improve the detection of BC by 5% to 20%. Also, this study finding was supported by **Ibrahim, (2017)** in a study about the Quality of life of an 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 **Abo serial, et al. (2017)** in a study about early detection of breast cancer among females at Facous District, Sharqi Governorate, Egypt, who noted that the most frequent interviewed age groups for early detection of BC

Women in the Facous district ranged in age from 30 to 39 years old, with an average age of 38.7 years. This study finding, according to the researcher's perspective, could be attributable to the fact that the breast tumors in the people under study were not recognized and diagnosed early, but were discovered accidentally. Other factors that may have a role include sedentary behavior and obesity.

In terms of marital status, slightly more than two-thirds of both the study and control groups were married, according to the findings. **Hussein (2020)** found that the majority of BC women were married in his study about the nursing role in the

early detection of breast cancer using mammography and genetic screening and its impact on patient outcomes. This study finding could be related to our cultural habits and beliefs, especially among rural or low socioeconomic people with less education, to urge early marriage, as indicated by the researchers' point of view.

In terms of educational attainment, the current study found that roughly one-third of both the study and control groups were illiterate. This study's findings are congruent with those of **Abd Elalem (2019)**, who discovered that Egyptian women sought medical guidance late in life, particularly for cancer symptoms. Furthermore, they are less informed, which has resulted in a decrease in awareness and a delay in responding to their initial symptoms. In a similar vein, **Hass (2019)** noted in a study on the immune system that the majority of the participants were illiterate. This study finding could be attributed to tensions connected to family duties due to a lack of health services available to them and a lack of finances, as indicated by the researchers' opinion. This study's findings were in line with those of **Abd Elalem, (2019)**, who stated in a study on the effect of immune enhancement on clinical outcomes of mastectomy patients undergoing chemotherapy that the nurse must assess the level of education of the patients to determine their learning capability and retention because providing a patient who is unable to read and write with written educational materials could pose a serious risk to him. This study's findings were consistent with **Abd El Razik's (2021)** findings in his study on the impact of educational programs on QoL for cancer patients receiving chemotherapy, who found that the majority of the study groups came from rural areas and were uninterested in education. Nonetheless, this finding was consistent with **Rahkola, et al. (2019)**, who found that women with a high level of education have technical access to the internet in their research of quality of life among women following hysterectomies. The desire of these women to become more informed and participate more actively in decision-making regarding their treatment may be reflected in their use of extra sources of health information, such as the internet. Their active involvement is critical to improving their quality of life.

Housewives made up somewhat more than two-thirds of both the study and control groups,

according to occupation. **Brown, et al. (2020)**, in their study on the efficacy of exercise therapies in regulating cancer-related fatigue among adult cancer survivors: a meta-analysis, noted that a shift or adjustment of the prior occupation may be required, either temporarily or permanently. This study finding can be attributed to housewives are less physically active and live a more sedentary lifestyle. Also, this study's findings were consistent with **Ibrahim's (2017)** findings that the majority of the women surveyed were not employed; this might be explained by the fact that the majority of the women were illiterate and housewives. **Yi, et al. (2017)** revealed that roughly two-thirds of the analyzed samples were illiterate and housewives in their study about the informational needs of Korean women with BC. Women were not working; this may be attributed to the fact that the majority of women were illiterate and housewives. **Yi, et al. (2017)** revealed that roughly two-thirds of the analyzed samples were illiterate and housewives in their study about the informational needs of Korean women with BC.

In terms of domicile, the current study found that more than half of the study group lived in rural areas, whereas more than half of the control group lived in urban areas. Women in rural areas want more health-related information about their BC. This research supports **Mansour's (2019)** findings in his study on the impact of counseling on the quality of life of patients with bladder cancer. Undergoing urinary diversion revealed that the majority of the participants in the study came from rural areas. This study finding may be due to the lack of health and educational services in rural areas; also, patients' cultures, norms, beliefs, and place of residence influence their behaviors and patterns of lifestyle, the nature of life, and beliefs to accept the illness and modify their lifestyle according to the prescribed therapeutic regimen. However, this study finding is in disagreement with **Dey, et al. (2019)** who study about Urban-Rural Differences 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, which found that urban incidence of BC was three to four times

higher than rural incidence. This study's findings are also at odds with **Pakseresht, et al. (2020)**, who claimed in their study about risk factors for breast cancer among women in the Delhi Indian Journal of Cancer that a substantial number of BC patients live in metropolitan areas, maybe due to radiation exposure.

This indicates that the environment has a deleterious impact on the development of BC.

In terms of the number of children, more than half of both groups had three or more; this conclusion was consistent with **Abd Elalem's (2019)** study, which indicated that the majority of the patients evaluated had more than three children. This study's finding, as described by the researchers' opinion, could be attributable to the fact that increasing family size reduces per capita income while increasing the responsibility and effort required of mothers to care for their children, resulting in poor health and illness exposure. The findings of this study correspond with those of **Abd El Razik (2021)**, who indicated that two-thirds of the patients were having children.

About two-thirds of the study group and more than half of the control group had enough family income every month. This study found, as indicated by the researchers, point of view, could be related to the fact that the majority of the samples were illiterate and unemployed, preventing the patients from visiting private or specialized clinics for high-quality care and accurate information. This study's findings are in line with those of **Abd El Razik (2021)**, who reported that approximately two-thirds of the women tested had sufficient income. However, these findings contradict **Ibrahim's (2017)** findings, which stated that slightly more than three-quarters of the women surveyed had insufficient income. Low income and the occurrence of cancer have a negative association. This is in line with **Chaul- Woung, et al. (2016)**, who highlighted the relative risk of cancer incidence in the lowest income group and stated that low socioeconomic status is an important factor affecting QoL in the normal population and patients with medical illness in their study in equations in Cancer Incidence and Mortality across Income Groups and Policy Implication in South Korea.

According to the **Breast Cancer Organization (2012)**, the poorest patients are more likely to report poor health, feel less content and in control of their life, and have higher healthcare demands.

The current study found that there was a highly statistically significant difference between the study and control groups in terms of patient knowledge of BC, chemotherapy, and management of its side effects, as well as the immune system, post-intervention. There was also a noticeable difference in the study group's knowledge compared to the control group. This study finding may be due to patient education about what symptoms to expect or watch for, when and how to contact their doctors or nurses, and how to manage their diseases, which can help ensure that the adverse effects of cancer and its treatment are regulated, relieved, or averted. Such education can empower patients and caregivers, improve treatment results, reduce side effects, office visits, and hospitalizations, and cut costs in an already overburdened health system. This study result can be explained as follows: patients in the study group enroll in the educational program and follow the instructions in the booklet, which improves their awareness and knowledge of the disease and its treatment, which in turn helps them modify their lifestyle, which improves and strengthens their immune system, allowing them to fight the disease and overcome chemotherapy side effects. This study result was supported by **Oncology Nursing Society, (2021) &** according to **Karim-kos (2021)**, a nurse-led educational intervention before the commencement of chemotherapy may help women with BC have a better understanding of the treatment, improve their ability to handle side effects, and improve their coping mechanisms. This study's findings were also consistent with **Williams and Schreier's (2018)** findings in a study on the effect of education in managing side effects in women receiving chemotherapy for breast cancer treatment, who stated that teaching effective self-care behaviors improves patients' independence, comfort, control, and quality of life.

Following the intervention, patients in both the study and control groups had the following performance status for their typical activities: - The current investigation revealed that the study group's mean score improved significantly more than the control groups. After the intervention, the overall QoL domains of patients in both the study and control groups were as follows: -The current study

found that the study group's mean score in the physical, psychological, functional, patient worries about the disease and its treatment, and social domains was significantly higher than the control groups. Because the majority of the study participants exhibited modest affection compared to the control group, they had moderate affection on their QoL. This study finding is explained by the researcher's experience that the improvement in performance status and QoL of the study group can be attributed to their response to intervention and that they follow the instructions given to them through teaching sessions or information found in the booklet, which includes health teaching about the disease, its treatment, management of chemotherapy side effects, and immune enhancement through (diet, exercise, and alteration of one's way of life).

As each item was related to the others, this represented a development in their knowledge, which in turn led to an improvement in their performance status and QoL domains. This study result was supported by **Reiger, (2018)** 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 perform normal activities of daily living. Cancer has been found to have a significant effect on a patient's ability to function in the usual role and activities. So physical and functional well-being are essential components for overall QoL. As cancer has a negative effect on QoL, exercise during cancer treatment may improve QoL in addition, **Dorneles (2020)** claimed in his study on the effects of exercise on cancer-related fatigue that physical activity has the most supporting evidence for non-pharmacological therapies for fatigue and other chemotherapy side effects during cancer treatment. On the same line, Aerobic exercise has been reported to minimize fatigue and improve performance status throughout chemotherapy and radiation therapy, as well as after cancer treatment has been completed, according to **Schwartz (2020)**. Furthermore, **Ingram and Visovsky (2016)** stated in their study on Exercise intervention to modify physiologic risk factors in cancer survivors that "evidence of the benefits of lifestyle modification through eating a healthy diet and exercising for cancer survivors has steadily mounted over the past two decades, particularly in the areas of psychological and QoL outcomes and cancer-related fatigue, which can enhance the immune

system. Physical functioning, body weight, and composition, muscle strength and endurance, and immunological function have all improved in recent years. In a study about exercise and the immune system, **Blannin (2020)** found that people who exercise regularly have a stronger immune system than those who do not. This study finding may be due to moderate-intensity physical activity having a protective effect, as stated by the researcher's experience. **Ashley (2020)**, in a study on the powerful impact of omega-3 fatty acids in preventing illnesses of inflammation, claimed that fatigue and poor performance status linked with cancer are likely caused by both physical and psychological factors; the physical causes include anemia, various metabolic disturbances and inappropriate 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 contributes to the severity of fatigue in some patients. Congruent with this study finding was Untreated cancer tiredness and other chemotherapy side effects, according to **Lawrence (2021)**, may result in a decline or discontinuation of normal physical, social, interpersonal, and recreational activities, as well as interfere with home, family, work, and educational role performance. Uncontrolled chemotherapy side effects can affect all aspects of quality of life, including physical, psychological, social, and spiritual well-being, and can result in a loss of productivity, self-esteem, a significant reduction in physical functioning, and QoL, as well as difficulty adhering to and finishing treatment regimens.

In terms of comparing the total knowledge level and quality of life score of patients in the study and control groups before and after the intervention, Pre-intervention, the majority of patients in both the study and control groups had an unsatisfactory level of knowledge, however post-intervention, the majority of the study group had satisfactory knowledge whereas the majority of the control group had unsatisfactory knowledge.

There were no statistically significant relations between the patients in both study and control groups regarding their total knowledge level pre-intervention $P > 0.05$. But there was a strongly highly significant relationship between the two groups post-intervention $P < 0.001$. This study concluded, according to the researcher's

perspective, can be related to the effect of educational programs among study groups that achieve knowledge and proper self-care practices as well as lifestyle changes for enhancing their QoL. **Ahmed (2021)** discovered that elements over which nurses have some control, such as the environment, the information supplied to patients and family members, symptom management, and nursing intervention, all influence QoL. Nurses are in a unique position to deliver outpatient education because they are the healthcare providers who are in constant touch with patients and their families, and they are often the most accessible source of information for patients. Furthermore, the majority of patients in both the study and control groups had moderate QoL affection before the intervention, whereas the majority of patients in the study group had mild QoL affection after the intervention. In terms of overall QoL affection post-intervention, there was a clear and strongly highly significant relationship between the study and control groups $P < 0.001$. However, there was no pre-intervention relationship between the two groups ($P > 0.05$).

The following is a comparison of the control and study groups in terms of total knowledge and quality of life scores, performance status for everyday activities, and probable tumor biomarkers at pre and post-intervention: - In regards to the patients in the research group; Pre and post-intervention, there was a statistically significant positive connection between total QoL and performance status for routine activities. That is, patients with a high level of performance status for regular activities had a good level of total QoL domains.

Meanwhile, at different stages of treatments, there was a negative significant connection between total QoL score and possible tumor biomarkers. Meanwhile, there was a negative significant relationship between total QoL score and their potential tumor biomarkers at different phases of intervention $P < 0.05$. Patients with a high level of overall QoL domains had a lower occurrence of possible tumor biomarkers, which meant they had a lower risk of developing cancer. There was a favorable link between patients' total QoL score and their knowledge and performance scores at different phases of intervention when compared to patients in the control group. Furthermore, there was a link between the patients' overall quality of life and their tumor biomarkers. In addition, there was a statistically significant beneficial connection

between patient knowledge and QoL. That is, patients with a high level of knowledge had an excellent overall quality of life. This study finding may be attributable to patients who had good information related to effective self-care and lifestyle adjustment or modification, which minimizes physical, psychological, emotional, and social problems, as indicated by the researchers, point of view. In a similar vein, **Mohammed (2018)** found a highly positive correlation between women's knowledge and their QoL in his study on the effect of Instructional for Relieving Chemotherapy Side Effects on Women with Ovarian Cancer. This underlines the importance of health education in improving women's quality of life and reducing life-threatening conditions. Finally, the findings of the study backed up the research hypothesis, confirming that the immune-boosting intervention program had a statistically significant positive impact on the clinical outcomes of BC patients following chemotherapy. Because it was proven that patients in the study group who underwent an immune enhancement intervention program had a higher quality of life, had a better performance status, and had lower levels of possible tumor biomarkers than patients in the control group who did not. As a result, nutritional support, physical activity, and lifestyle modification components of immune enhancement interventions are becoming more widely recognized as critical concerns for cancer patients undergoing chemotherapy who want to strengthen their immune system and reduce the disease's negative consequences. side effects of chemotherapy

Conclusion

Based on the results of this study, it can be concluded that an immune enhancement intervention program had a statistically significant positive effect on clinical outcomes (level of patient knowledge, performance status of usual activities, QoL domains, nutritional status, as well as laboratory investigations (hemoglobin, hematocrit, WBC, blood urea nitrogen, serum creatinine & albumin) and tumor biomarkers CD 90(+ve) CD45 (+ve) percent) of patients with breast cancer.

Recommendations

The current study concluded that patients with breast cancer should be given the generated guided booklet about immune enhancement intervention to improve their level of knowledge, awareness, and

management of chemotherapy side effects, as well as immune system enhancement. In addition, more research is needed to conduct training and instruction of nurses about the immune enhancement intervention program, as well as to assess its impact on their performance and, as a result, on patient outcomes over time.

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