Efficacy of l-carnitine and silymarin administration on the health-related quality of life in 120 patients with cancer undergoing anthracycline-based chemotherapy

Zeinab Alkasaby Zalat¹, Mohamed M. Abdel-Latif ², Badriyah S. Alotaibi³, Mohamed A. Alm El-Din⁴, Neveen A. Kohaf⁵, and Hosny A. Elewa⁶

¹Department of Clinical Pharmacy, Faculty of Pharmacy (Girlna), Al-Azhar University, Cairo, Egypt. (zeinabalkasaby.pharm@gmail.com)
²Department of Clinical Pharmacy, Faculty of Pharmacy, Assuit University, Assuit, Egypt.
³Department of Pharmaceutical science, Faculty of Pharmacy, Princess of Nourah bint Abdulrahman University, Riyadh, Saudi Arabia
⁴Department of Clinical Oncology, Faculty of Medicine, Tanta University, Tanta, Egypt.
⁵Master degree in pharmaceutical Sciences, Faculty of Pharmacy, Al-Azhar University, Cairo, Egypt.
⁶Department of Pharmacy Practice, Faculty of Pharmacy, Horus University, Dominate City, Egypt.

* Corresponding author: helewa@horus.edu.eg

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Abstract

Objectives: To investigate changes after adding L-carnitine and silymarin compared to anthracycline chemotherapy alone on the health-related quality of life (HRQoL) of women with breast cancer receiving anthracycline-based chemotherapy. Methods: A prospective, randomized comparative study that included 120 women with breast cancer who received anthracycline in their chemotherapeutic regimen. Patients were divided into three groups, anthracycline alone (control group), chemotherapy and l-carnitine (l-carnitine group), and chemotherapy plus silymarin (silymarin group). HRQoL was evaluated using the EORTC QLQ-C30 and EORTC QLQ-BR23 instruments 7 days before chemotherapy and after the third month of chemotherapy. Results: On the application of (EORTC QLQ-C30), there was a significant decrease in global health status/QoL score, functional scale scores from baseline to after three months (P≤0.001) within the control group and a significant increase in symptom scale scores from baseline to after three months. In l-carnitine and silymarin groups, there was a non-significant difference in the scale scores. On the application of (EORTC QLQ-BR23), there was a significant decrease in functional scale scores (p≤0.001) within the control group and a significant increase in symptom scale scores (p≥0.05). In the l-carnitine and silymarin groups, there was a non-significant difference in functional scale scores from baseline to after three months (p≥0.05). Conclusions: QOL was negatively affected by chemotherapy. For BC cases, HRQoL becomes typically worse during the third month of chemotherapy compared with the pretreatment duration. The addition of l-carnitine and silymarin to anthracycline-based chemotherapy showed improvement in the health-related quality of life of cancer patients.

Keywords: Anthracycline, silymarin, l-carnitine, health-related quality of life, breast cancer.
Introduction

The distribution of cancer is currently growing, and the number of new patients is set to grow from 14 million in 2012 to 22 million annually by 2030 [1]. The second most common disease in the world in new cases (1.7 million cases) is breast cancer (BC), and the fifth category is regarded as a cause of death. [2]. With survival rates rising during BC therapy, greater consideration is given to improving health-related quality of life (HRQoL) during and following cancer drugs. Although anthracycline chemotherapy is associated with positive benefits in decreasing the risk of BC recurrence [3], it also affects negatively the HRQoL of survivors [4]. Furthermore, the reality that BC is gradually identified in earlier stages as a result of screening initiatives further increases the number of people who have obtained curative-intent adjuvant chemotherapy. The symptomatology and adverse effects profile of anthracycline chemotherapy on HRQoL should be taken into consideration. For example, chemotherapy induces important effects in BC people, such as exhaustion, febrile neutropenia, depression, dyspnea, discomfort, nausea, and vomiting. [5]. In addition, emotional distress, such as confusion or concern of recurrence and posttraumatic stress, pain, and work strain can include carcinogenic sequelae [6].

In the framework of culture and value systems, the idea of the quality of life (QoL) can be described as a sense of identity in its place in life and in relation to its objectives, desires, values, and concerns [7]. When this term is just linked to health expectations, the expression is titled HRQoL. This expression is a multi-domain term, representing the patient's general perception of the impact of illness and treatment on other aspects of life. [8]. The expression HRQoL is therefore used to include those elements that are usually not addressed in health contexts (such as income independence and environmental quality). Focusing on the development of HRQoL thus requires analyzing nearly all health-related aspects of life [9].

In order to improve HRQoL and maintain emotional, social, and physical wellness, it is thus essential to understand the requirements of patients, besides the control of clear signs and symptoms throughout the therapy. Therefore, it is important to search for new strategies to improve HRQoL in cancer patients, such as adding L-carnitine and silymarin to patient’s treatment protocols.

L-carnitine is important for the synthesis of long-chain free fatty acids into acylcarnitines and their subsequent transfer to the mitochondrial matrix where they are beta-oxidized in the production of cellular resources. L-carnitine's exogenous supplemental therapies seem to support anorexia, chronic fatigue, cardiovascular disease, diphtheria, hypoglycemia, male infertility, and muscular illness [10].

Silymarin is a nontoxic natural polyphenolic flavonoid extracted from the seeds of the plant milk thistle (Silybum marianum), which is an ancient medicinal plant for the treatment of various liver diseases [11]. Due to its strong antioxidant and tissue regenerative properties, silymarin is being studied as a hepatic, neural, renal, and cardiac protective ingredient. [12]. Silymarin could be helpful in patients with oncology, particularly, for reducing the side effects of cancer chemotherapy [10]. In common cancers such as lung prostatic, stomach, breast, bladder, and hepatocellular carcinoma, even, silymarin has an anti-cancer effect [13].

This research aimed to measure QOL in BC patients and compare the algorithms before and after chemotherapy and determine the impact of L-carnitine and silymarin on HRQoL.

Method
A prospective study to assess HRQoL in 120 Egyptian BC patients who performed the first oncological consultation at the Oncology Department, Tanta University Hospital, Egypt. Women ≥ 18 years of age, histologically documented BC, which has an intervention with breast surgery, and which depends on adjuvant or neoadjuvant chemotherapy as anthracycline, are included.

Patients were divided into three groups: control group (anthracycline- based regimen alone, n=40), l-carnitine group (anthracycline-based regimen + l-carnitine 1 g daily, n=40) and silymarin group (anthracycline- based regimen + silymarin 140 mg daily, n=40)

The evaluation of the patient's HRQoL was evaluated using the EORTC QLQ-C30 (European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire) and EORTC QLQ-BR23 (EORTC BC-specific Quality of Life Questionnaire). The patients performed questionnaires in two stages (i.e., one week before the beginning of the chemotherapy (baseline) and in the third month of therapy, roughly in the 4th period (3-month follow-up), all of these instruments are checked, converted into Arabic, formal, and self-administrative information from medical records such as sociodemographic details (educational level and marital condition), menopause status, family history of cancers, and data were obtained from the Eastern Cooperative Oncology Group scale, measured no more than two weeks before research enrollment. The questionnaire was evaluated according to the systematic approach proposed by the EORTC Group. The research was formulated and performed in compliance with the ethical values of the Standards for Good Clinical Practice and the Helsinki Declaration. The methodology of research was accepted by the National Research Ethics Committee at Tanta University with acceptance number (32551/09/2018), and written informed consent of all patients was received.

**Drugs:**
L-carnitine® 500 mg capsules obtained from (MEPACO)
Silymarin (Legalon ® 140 mg capsule obtained from (MEDA).

One-way analysis of variance test (one-way ANOVA) followed by LSD post hoc test was used to assess any significant differences among the three groups. A paired t-test was used to assess any significant differences within each group at baseline and after chemotherapy. All probability values presented were two-tailed, and p ≤ 0.05 was considered statistically significant.

**Results**

1- Study population
Results concerning sociodemographic and clinical characteristics from the 120 patients included in the study are described in Tables 1, 2, and 3.

There were no significant differences in age, marital status, education level, and menopausal state between the studied groups (p-value ≥0.05) as shown in Table 1.

In Tables 2 and 3, there were also non-significant differences regarding family history of cancer (Eastern Co-Operative Oncology Group) ECOG performance, a model of breast cancer detection, and stage of breast cancer between the studied groups (p-value ≥0.05)
Table (1): Demographic data of the studied groups

| Variable                  | Groups                  | Control Group N=40            | l-carnitine group N=40      | Silymarin group N=40  | P-value |
|---------------------------|-------------------------|-------------------------------|-----------------------------|-----------------------|---------|
| Age (years) Mean ±SD      |                         | 44.455 ± 9.47                | 45.64 ± 9.941               | 44.68 ± 12.44         | 0.61    |
| Marital status            |                         |                               |                             |                       |         |
| Married                   | 43(71.6%)               | 18(72%)                      | 19(76%)                     | 0.775                 |
| Single                    | 17(28.3%)               | 7(28%)                       | 6(24%)                      |                       |
| Education level           |                         |                               |                             |                       |         |
| Elementary or middle school| 55(91.6%)              | 21(84%)                      | 22(88%)                     | 0.726                 |
| High school               | 3(5%)                   | 3(12%)                       | 2(8%)                       |                       |
| College                   | 2(3.33%)                | 1(4%)                        | 1(4%)                       |                       |
| Menopausal state          |                         |                               |                             |                       |         |
| Premenopausal             | 10(16.6%)               | 3(12%)                       | 4(16%)                      | 0.700                 |
| Perimenopausal            | 33(55%)                 | 18(72%)                      | 17(68%)                     |                       |
| Postmenopausal            | 17(28.3%)               | 4(16%)                       | 4(16%)                      |                       |

Age represented in mean ± standard deviation
Data are represented as number and percentage. p ≤0.05 value considered significant

Table (2): Demographic data of the studied groups

| Variable                                    | Groups                  | Control Group N=40         | l-carnitine group N=40       | Silymarin group N=40   | P-value |
|---------------------------------------------|-------------------------|----------------------------|------------------------------|------------------------|---------|
| Family history of cancer                    |                         |                            |                              |                        |         |
| No                                          |                         |                            |                              |                        |         |
| Yes (breast)                                | 25(41.6%)               | 10(40%)                    | 11(44%)                      | 0.815                  |
| Yes (breast and other)                      | 20(33.3%)               | 5(20%)                     | 6(24%)                       |                        |
| Yes (other)                                 | 5(8.3%)                 | 6(24%)                     | 5(20%)                       |                        |
| ECOG performance status                     |                         |                            |                              |                        |         |
| 0                                           | 55(91.6%)               | 23(92%)                    | 22(88%)                      | 0.850                  |
| 1                                           | 5(8.33%)                | 2(8%)                      | 3(12%)                       |                        |
| Model of breast cancer detection            |                         |                            |                              |                        |         |
| Screen detected                             | 30(50%)                 | 16(64%)                    | 15(60%)                      | 0.674                  |
| Symptomatic                                 | 20(33.3%)               | 5(20%)                     | 6(24%)                       |                        |
| Unknown                                     | 10(16.6%)               | 4(16%)                     | 4(16%)                       |                        |

ECOG: Eastern Cooperative Oncology Group
Table (3): Distribution of patients regarding pathology and stage in the studied groups

| Variable           | Control | L- Carnitine | Silymarin | P-Value |
|--------------------|---------|--------------|-----------|---------|
|                    | N   | %     | N   | %     | N   | %     |
| **Stage:**         |       |       |       |       |       |       |
| Breast adjuvant    | 27   | (67.5%) | 33  | (82.5%) | 31  | (77.5%) |
| Breast neoadjuvant | 4    | (10%)  | 2   | (5%)   | 6   | (15%)  |
| Breast metastatic  | 4    | (10%)  | 1   | (2.5%) | 2   | (5%)   |

Data are represented as number and percentage. p ≤0.05 value considered significant

Age represented in mean ± standard deviation
p ≤0.05 value considered significant

**2-HRQoL scores**

Application of (EORTC QLQ-C30). There was a significant decrease in global health status/QoL score, physical functioning, role functioning, emotional functioning, and social functioning scores from baseline to after three months (p≤0.001) within the control group. There was a significant increase in symptoms scale include fatigue, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, and diarrhea scores from baseline to after three months. Table (4) and figures 1-3

In the L-carnitine group, there was a non-significant difference in global health status/QoL score, physical functioning, role functioning, emotional functioning, and social functioning scores from baseline to after three months (p≥0.05). There was also a non-significant change in symptoms scale include pain, insomnia, appetite loss, and constipation scores from baseline to after three months. Table (4) and figures 1-3

In the silymarin group, there was a non-significant difference in global health status/QoL score, physical functioning, role functioning, emotional functioning, and social functioning scores from baseline to after three months (p≥0.05) and there was also a non-significant change in symptom scale include fatigue, pain, insomnia, appetite loss, and constipation scores from baseline to after three months. Table (4) and figures 1-3

**Application of (EORTC QLQ-BR23).**

There was a significant decrease in functional scale include body image score and a significant decrease in sexual functioning, sexual enjoyment scores from baseline to after three months (p≤0.001) within the control group, and there was a significant increase in symptoms scale include systemic therapy side effects and breast symptom scores from baseline to after three months(p≥0.05). Table (5) and figures 4,5

In the L-carnitine group, there was a non-significant difference in functional scale include body image
score, sexual functioning, and sexual enjoyment scores from baseline to after three months (p≥0.05). Table (5) and figures 4, 5

In the silymarin group, there was a non-significant difference in functional scale include body image score, sexual functioning, sexual enjoyment, and arm symptom scores from baseline to after three months. Table (5) and figures 4, 5

Table 4. Comparison of HRQoL between the study segments (EORTC QLQ-C30).

| Variable                  | Groups                                      |
|---------------------------|---------------------------------------------|
|                           | Control Group N=40 | L-carnitine Group N=40 | Silymarin Group N=40 |
|                           | At base line | After 3 months | At base line | After 3 months | At base line | After 3 months |
| Global health status/ QoL | 77.6 ± 16.02 | 55.18±15.3    | 76.7 ± 15.6 | 71.2 ± 13.2 | 78.7±13.5 | 77.4±14.6 |
| P-value                   | 0.001*       | 0.1847        | 0.745       |
| functional scales         |               |               |             |               |             |               |
| Physical functioning      | 89.73 ± 4.51  | 67.5±10.33    | 90.1 ± 4.88 | 88.3±4.093 | 88.6±2.89 | 87.8±11.3 |
| P-value                   | 0.001*       | 0.1641        | 0.7331      |
| Role functioning          | 80.78±19.6   | 52.3±18.3     | 79.3±15.4  | 73.1±14.6  | 80.4±16.8 | 79.6±14.5 |
| P-value                   | 0.001*       | 0.1506        | 0.8577      |
| Emotional functioning     | 72.3±19.3    | 48.32±20.5    | 70.8±17.5  | 58.3±25.6  | 71.6±18.7 | 68.4±23.4 |
| P-value                   | 0.001*       | 0.0495*       | 0.595       |
| Cognitive functioning     | 83.4±20.2    | 75.6±19.8     | 85.1±21.3  | 83.6±16.8  | 80.6±17.5 | 80.3±20.6 |
| P-value                   | 0.1744       | 0.783         | 0.956       |
| Social functioning        | 87.3±15.4    | 59.6±20.14    | 88.6±19.5  | 89.3±18.6  | 86.7±17.5 | 88.4±21.4 |
| P-value                   | 0.001        | 0.897         | 0.759       |
| Symptom scales            |               |               |             |               |             |               |
| Fatigue                   | 14.8±2.3     | 58.7±14.3     | 13.6±5.3   | 18.6±1.3   | 15.3±2.2 | 16.4±1.3 |
| P-value                   | 0.001        | 0.001         | 0.0346      |
| Nausea and vomiting       | 1.02±0.02    | 12.6±1.5      | 1.5±1.1    | 5.6±2.1    | 1.8±1.2 | 4.7±3.2  |
| P-value                   | 0.001        | 0.001         | 0.001       |
| Variable                | Control Group N=40 | 1-carnitine Group N=40 | Silymarin Group N=40 |
|------------------------|--------------------|------------------------|----------------------|
|                        | At base line       | After 3 months         | At base line         | After 3 months |
| Pain                   | 28.3±23.2          | 36.3±24.2              | 27.3±12.5            | 30.5±21.2      | 29.1±15.6 | 31.2±18.3 |
| P-value                | 0.239              |                        | 0.518                | 0.664          |
| Dyspnoea               | 7.6±4.3            | 18.2±5.7               | 7.9±2.6              | 15.2±1.8       | 7.5±2.8  | 10.6±3.5  |
| P-value                | 0.001              |                        | 0.001                | 0.0011         |
| Insomnia               | 28.3±19.3          | 52.6±23.2              | 29.2±12.5            | 33.5±18.6      | 28.7±21.2 | 32.4±18.7 |
| P-value                | 0.001              |                        | 0.001                | 0.452          |
| Appetite loss          | 7.4±3.2            | 22.3±14.3              | 6.5±2.8              | 8.6±5.2        | 7.6±1.5  | 6.6±12.5  |
| P-value                | 0.001              |                        | 0.0818               | 0.0928         |
| Constipation           | 18.6±14.5          | 33.5±17.6              | 17.5±12.2            | 20.3±14.8      | 19.3±14.3 | 17.2±12.3 |
| P-value                | 0.002              |                        | 0.469                | 0.5803         |
| Diarrhoea              | 1.02±2.2           | 9.3±4.9                | 1.3±2.1              | 6.2±5.3        | 1.5±2.1  | 3.5±2.5   |
| P-value                | 0.001              |                        | 0.001                | 0.0036         |
| Financial difficulties | 27.3±26.3          | 31.2±21.3              | 26.3±19.8            | 30.2±27.3      | 25.6±21.3 | 32.1±28.3 |
| P-value                | 0.567              |                        | 0.568                | 0.363          |

Table 5. Comparison of HRQoL between study segments. Specific questionnaire for BC (EORTC QLQ-BR23).

| Variable                  | Control Group N=40 | 1-carnitine Group N=40 | Silymarin Group N=40 |
|---------------------------|--------------------|------------------------|----------------------|
|                           | At base line       | After 3 months         | At base line         | After 3 months |
| Functional scales         |                    |                        |                      |                |
| Body image                | 90.66 ± 8.51       | 65.5±12.33             | 90.1± 8.88           | 88.3± 8.093    | 87.6± 7.89 | 88.8±18.3 |
| P-value                   | 0.001*             |                        | 0.4575               | 0.7647         |
| Sexual functioning        | 52.78±19.6         | 16.3 ±15.3             | 52.3±16.4            | 44.1±15.6      | 51.3 ±14.8 | 48.3 ±19.5 |
| P-value                   | 0.001*             |                        | 0.0763               | 0.542          |
| Sexual enjoyment*         | 69.3±19.7          | 28.32±21.5             | 70.7 ±17.5           | 33.3 ±25.6     | 71.7 ±15.7 | 66.4 ±13.4 |
| P-value                   | 0.001*             |                        | 0.001*               | 0.02054        |
| Variable                          | Control Group (N=40) | l-carnitine Group (N=40) | Silymarin Group (N=40) |
|----------------------------------|----------------------|--------------------------|------------------------|
|                                  | At base line         | After 3 months           | At base line           | After 3 months           | At base line           | After 3 months           |
| Future perspective               | 33.4±20.2            | 39.6±19.8                | 34.1±21.3              | 35.2±16.8                | 32.6±17.5              | 33.3±20.6                |
| *P*-value                        | 0.278                | 0.8402                   | 0.8975                 |                         |                         |                         |
| Symptom scales                   |                      |                          |                        |                          |                          |                         |
| Systemic therapy side effects    | 8.8±9.3              | 58.7±18.3                | 7.6±6.3                | 48.6±16.3                | 8.3±7.2                | 36.4±20.3                |
| *P*-value                        | 0.001                | 0.001                    | 0.001                  |                          |                         |                         |
| Breast symptoms                  | 32.3±23.2            | 18.6±21.5                | 33.5±21.1              | 17.6±22.1                | 32.8±21.2              | 19.3±23.2                |
| *P*-value                        | 0.035                | 0.0123                   | 0.0406                 |                          |                         |                         |
| Arm symptoms                     | 34.3±23.2            | 20.3±24.2                | 35.3±12.5              | 22.5±21.2                | 33.1±15.6              | 25.2±18.3                |
| *P*-value                        | 0.0421               | 0.0123                   | 0.107                  |                          |                         |                         |
| Upset by hair loss*              | NA                   | 68.2±35.7                | NA                     | 65.2±31.8                | NA                     | 62.6±35.5                |
| *P*-value                        |                      |                          |                        |                          |                         |                         |

* Statistically significant *p*-value from the Wilcoxon test.

NA, not applicable; there was no valid information available. # According to the EORTC Scoring Manual [14], the variation in the number of responses in EORTC QLQ-BR23 is predicted since the fields ‘sexual enjoyment’ and ‘upset by hair loss’ do not apply when the responses related to these scales are ‘no’.

Figure (1): Comparison between studied groups regarding global health status (EORTC QLQ-C30)
Figure (2): Comparison between studied groups regarding functional scale: A: physical functioning, B: role functioning, C: emotional functioning, D: cognitive functioning, E: social functioning (EORTC QLQ-C30)
Figure (3): Comparison between studied groups regarding symptom scales - A: fatigue, B: nausea and vomiting, C: pain, D: dyspnoea, E: insomnia, F: appetite loss, G: constipation, H: diarrhoea, I: Financial difficulties (EORTC QLQ-C30)
Figure (4): Comparison between studied groups regarding functional scales - A: body image, B: sexual functioning, C: sexual enjoyment, D: future perspective, (EORTC QLQ-BR23)
Discussion

The measurement of HRQoL is a valuable feature to determining the impact of medical care on diseases, psychological problems, lifetime happiness, and the well-being of patients. [15]. BC patients are at an increased risk for general HRQoL therapies (e.g., exhaustion, sleep problems, and pain) and psychological disorders (depression, anxiety, apprehension of recurrence, issues related to sex and body image) as well and general HRQoL. [16,17]. Chemotherapy often affects the patient's HRQoL expectations, as symptoms escalate and the functioning level declines. [18–20]. It is necessary to add a new strategy to deal with chemotherapy's undesirable effects on patients' quality of life.

Our research is the first to examine the impact of silymarin and l-carnitine on the wellbeing of cancer patients undergoing anthracycline-based protocols and could also help oncologists assess classic symptoms that chemotherapy activates as well as the influence of chemotherapy, has psychosocial characteristics.

Our results showed that anthracycline has a negative effect on HRQoL, represented by a decline in global health status score, functional scales, and symptoms scale. This influence may be clarified by chemotherapy, which indicates that the
health status of women with BC is worsened during therapy. Binnoto et al. stated that global health worsened also with the rising complications of chronic medication during chemotherapy therapy [21] In fact, BC patients have a high risk of developing behavioral changes that adversely affect HRQoL [22]. According to previous studies [23, 24], the levels of psychological activity and body image during chemotherapy are substantially decreased, and modified body image is known to be a critical psychosocial issue for women with BC [25]. This can be understood because the body image is influenced by the context of what others think and thus affects the trust of the individual. Psychological factors were strongly linked to global HRQoL and decreased social and emotional functioning in BC patients [26]. On comparing the results of the baseline scores and after 3 months, there was also a significant decline between the periods in cognitive functioning, pain, dyspnöea, and constipation between the two evaluations in the control group. These measures deal with physical effort, health, and support with basic needs and the ability to work or do daily work. This result is growing in patients with BC because of physical disabilities linked to illness and medication. The literature records similar results [18, 27]. As the physical performance of the target is consistently better earlier than the end of the procedure, if exhaustion progresses [19]. Regarding the hair loss scale disturbance, segments cannot be contrasted. In line with the EORTC Rating Manual [14], a variance in the EORTC QLQ-BR23 answers is expected as measures disrupted by hair loss and sexual pleasure are not valid where the responses correlated with this measure are ‘no.’ However, a high score on this examination suggests that the disorder adversely affected HRQoL [14]. Alopecia is therefore life-altering and patients perceive these side effects as distressing [21]. This modification may create discomfort as to how others see it or evaluate it, causing social interaction to disappear because it feels uncomfortable in public places. [18]. The social isolation of BC patients is associated with a number of reasons. Social stigmatization of the disease can affect BC woman's interactions with other people. Our research has affected the social functioning of chemotherapy, indicating that a patient's physical condition and treatment interferes with family relations and social activities [21]. Similar results were reported in other studies [18], demonstrating the effect of chemotherapy on social relationships. On the other hand, larger social networks are linked to greater HRQoL when patients get better social support from family and friends after a BC diagnosis. [28]. It is known that attraction can be affected by shifts in hormone levels and changes in body image after a cancer diagnosis [29]. Our findings are in agreement with the study of Hall et al [30]. which revealed that, in the short and long term, the majority of systemic effects of chemotherapy tend to affect women's sexuality. The findings of elevated systemic adverse effects (systemic medication side effects, exhaustion, nausea and vomiting, depression, loss of appetite, and diarrhea) in patients treated with chemotherapy are compatible with the expected results of toxicity for the drug. Chemotherapy may also worsen toxicity at low levels [31] such as diarrhea, which may be enough to worsen patients' HRQoL. In cancer patients, insomnia is also a common problem. Chemotherapy's concomitant effect on insomnia symptoms is mediated by various oncological symptoms, such as urinary symptoms, nausea, and night and digestive symptoms. [32]. Smell and taste alterations also take place as a side effect of chemotherapy. These changes affect food behavior, reduce food consumption, or limit food intake [33].
As illustrated in our results, the addition of l-carnitine to anthracycline-based chemotherapy protocol showed non-significant changes in the global health status scale score, functional scale scores, and symptom scale scores of insomnias, appetite loss, and diarrhea from baseline values. This may be due to that l-carnitine (LC) plays an important role in the metabolism of fatty acids, and LC deficiency is associated with a feeling of weakness or general fatigue. Cancer patients receiving chemotherapy often develop l-carnitine deficiency, which is considered to be a factor contributing to general fatigue. [35]. There also was an improvement in body image score compared to the control group this explained as chemotherapy-induced damage of the carnitine system, and secondary deficiency of this molecule may cause fatigue due to impaired energy metabolism and thus bad impact on the self-confidence of women with breast cancer [35]. Thus, restoration of the carnitine pool may alleviate the body image score of cancer patients. Our results are in harmony with Shindo et al. who studied the effect of l-carnitine on the quality of life of cancer patients receiving chemotherapy and reported significant improvement from the control group [36].

MATSUI et al. also studied the impact of l-carnitine on the quality of life of cancer patients with chemotherapy reporting improvement [35].

These studies open the way for more research on the l-carnitine impact on health-related quality of life of cancer patients, as it is a constrain of chemotherapy.

Regarding the administration of silymarin with anthracycline contains chemotherapy, our results showed that there was a non-significant change in global health status score, functional scale scores, and symptom scale scores including (fatigue, insomnia, appetite loss, and constipation) from the baseline. This may be interpreted as silymarin has been found to be a very potent antioxidant, supporting native cellular antioxidant mechanisms such as glutathione (GSH) and superoxide dismutase by scavenging free radicals and reactive oxygen species (ROS) [37]. This can partly explain the efficacy of silymarin in hepatic damage due to disease or poisons because this antioxidant action may reduce oxidative stress associated with lipid insults that suppress lipid peroxidation (and thus cell death). The general anticancer effects of flavonoids collectively as well as the high antioxidant ability of silymarin, there was a strong interest in modifying silymarin for use as a chemoprotective agent. [37].

Our study is the first to study the effect of silymarin on the health-related quality of life of cancer patients. There was also a non-significant improvement in body image score compared to the control group, which may be due to the ability of silymarin to eliminate toxins that have undesirable effects on the mental status and self-pride sense of the patients.

More studies should be done in a similar population in order to analyzes the long-term HRQoL effects of silymarin and l-carnitine on anthracycline-based chemotherapy

Physicians and healthcare professionals should often evaluate patients for side effects of preventive treatment and use symptom scales. Screening can also take into account patients' views of global health status and QoL, physical functioning, job functioning, and emotional and social functioning. In this context, basic communication skills and sympathy in the psychosocial evaluation are significant.
It is important to understand the patient and the family objectives in order to help the therapy tailor to its needs and to make ensure that we support the entire person, including cancer care and wellbeing preferences into consideration during therapy. Minimizing the adverse effects of medication and introducing strategies to help the patient overcome this process is critical for enhancing HRQoL. We must adapt our care strategy to the needs of each patient with this awareness.

Conclusions
In BC cases, the HRQoL of chemotherapy is usually worse during the third month relative to the time before therapy starts. The addition of L-carnitine and silymarin to anthracycline-based chemotherapy showed improvement in health-related quality of life of cancer patients and provided the basis for the design of future placebo-controlled supplementation studies in this population.

Conflicts of interest
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