Original article

The impact of chemo-induced menopause on the quality of life of young women with non-metastatic breast cancer in Algeria

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ABSTRACT

Background: Breast cancer is the most common cancer in females worldwide. Young women with breast cancer are treated with chemotherapy, which may exhibit gonadotoxicity thus inducing chemo-induced menopause with a risk of deterioration in their quality of life.

Method: A prospective study first of its kind in Algeria was carried out on 57 patients aged between 30 and 49 years that went for consultation at the oncology department of Pierre and Marie Curie Medical Centre Algiers. The medical files obtained and criteria of questionnaires: Quality of Life Questionnaire for Breast Cancer (QLQ-BR23) and the Quality of Life Questionnaire-Core 30 (QLQ-C30) were used to assess the quality of life in patients.

Results: From the medical files, patients had a dominant histological type of invasive ductal carcinoma at 96% and Scarff-Bloom-Richardson (SBR) II grade and luminal B profile were the most frequent. The (QLQ-C30) having averages of global health status, symptom score, and functional score with 56.34, 63.7, and 45.75 respectively. QLQ-BR23 having averages for symptom, functional score of 61.6 and 49.71 respectively.

Conclusion: Chemotherapy induces gonadotoxicity, which results in chemo-induced menopause that has a negative impact on the quality of life of young women. QLQ-BR23 is more suitable than QLQ-C30 to access the context of this study.

Key words: breast cancer, chemo-induced menopause, quality of life, young women

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INTRODUCTION

Breast cancer is the most common cancer in females worldwide, with 40% of diagnosed cases under 49 years [1]. This cancer in young women is frequently familial, with almost half of the reported cases harboring a germ line mutation in genes; tumor protein 53 (TP53), breast cancer genes 1 and 2 (*BRCA1* and *BRCA2*) [2]. One in 196 women is diagnosed with breast cancer under the age of 40.

ADOLESCENTS AND YOUNG ADULTS

Breast cancer is the second cause of female death from cancer [3]. The death of breast cancer is often linked to local recurrence and evolution of the disease that cannot be indefinitely eradicated by treatment. Young women with breast cancer have the poorest prognosis due to the aggressiveness of the tumors [4].

Cancer treatments have adverse effects on ovarian function, such as delayed or arrested puberty, infertility, subfertility, and premature ovarian insufficiency (POI: menopause before age of 40) [1]. Chemotherapy damages the reproductive system by destroying the hypothalamic-pituitary axis, the uterus. The primordial or growing follicles within the ovaries significantly impact the fertility of young women [5]. The ovarian function is determined by the hormone levels such as estrogen (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone, and anti-Müllerian hormone in the early phase of the menstrual cycle [6]. Anti-Müllerian is an indicator of ovarian reserve widely used in obstetrics and gynecology because of its ability to fluctuate less in physiological cycles. Previous studies report that anti-Müllerian hormones are an efficient marker for predicting post-cancer ovarian function in premenopausal young female patients with breast cancer [7] with implications for future fertility and reproductive lifespan. There is therefore a need for a biomarker than can usefully provide an assessment of the ovary and its potential for long-term function after cancer treatment, and ideally also be of value pre-treatment, for the prediction of post-treatment function. In this review we assess the value of anti-Müllerian hormone. Several other common effects linked with treatment, such as alopecia, hematology toxicity, etc., can be observed at their age. The effect of chemo-induced menopause concerns most young women on how to continue with life, especially the quality of their life.

Young women who have attained breast cancer are at great risk of deterioration of their life, psychological troubles, sexual problems, or physical changes [4]. In Algeria, there are no studies to examine the specific cases of young women suffering from chemo-induced menopause. The aim of this study is to assess the impact of chemo-induced menopause on the quality of life of young women diagnosed with non-metastatic cancer in Algeria. This study used a specific questionnaires QLQ-C30 and QLQ-BR23 as the principal criteria for evaluation and measuring the impact of chemo-induced menopause on the quality of life.

MATERIALS AND METHODS

Patients

Eligible patients were women aged 18–49 years with stages SBR I–III, genitally active at the moment of breast cancer diagnosis, with non-metastatic breast cancer, received adjuvant chemotherapy, monotherapy, and targeted therapy, the normal initial rate of anti-Müllerian hormone and those with post-chemotherapy amenorrhea.

Non-eligible patients were women 50 years and above with menopause, low rates of an anti-Müllerian hormone, and metastatic breast cancer.

Study design

This is a prospective study, approved by the done on 57 patients who were registered from February 1st to of March 31st 2020 for consultation at oncology department of Pierre and Marie Curie Medical Centre of Algiers subjected to questionnaires.

Quality of Life Questionnaire for Breast Cancer (QLQ-BR23) one of the first breast cancer specific questionnaires with 23 items developed in 1996 [8]. Since 1996 major changes in BC treatment have occurred, requiring an update of the EORTC BC module. This study presents the results of the phase IeIII update of the QLQ-BR23 questionnaire.

Patients and methods

The update of the EORTC QLQ-BR23 module followed standard EORTC guidelines. A systematic literature review revealed 83 potential relevant QoL issues during phases I and II. After shortening the issues list and following interviews with patients and health care providers, 15 relevant issues were transformed into 27 items. The preliminary module was pretested in an international, multicentre phase III study to identify and solve potential problems with wording comprehensibility and acceptability of the items. Descriptive statistics are provided. Analyses were qualitative and quantitative. We provide a psychometric structure of the items. The phase I and II results indicated the need to supplement the original QLQ-BR23 with additional items related to newer thera-

peutic options. The phase III study recruited a total of 250 patients (from 12 countries).

Quality of Life Questionnaire-Core 30 (QLQ-C30) a questionnaire designed to assess the quality of life of cancer patients, physical, psychological and social functions [8].

Data collection

After enrollment, the eligible patient's medical files were obtained to extract the demographic information (name of the patient, number of the file, age of the patient), tumor node metastasis classification, histological types, anatomopathology classification, immunohistochemistry and molecular classification.

Estimation of the quality of life

The quality of life was assessed using 2 questionnaires: QLQ-C30 functional score and QLQ-BR23.

QLQ-C30

This was used to evaluate the impact of chemo-induced menopause on the functional quality of life. This questionnaire is divided into 3 dimensional scales: global health status, functional (physical, role, cognitive, emotional and social functioning) and symptom (fatigue, pain, nausea/vomiting) containing the overall of 30 questions.

Physical functioning and role functioning scales employs "yes" or "no" response choices. Global scale health status comprises of two items that use a modified 6 point linear analogue scale. The rest of the items used a 3 point categorical scale; 0 "lowest" to 3 "highest". The scales has linearly transformed to a 0–100 scale. For the global health status and the functional scale, the higher the score means better the level of functioning while for the symptom scale, the high score represents a high level of symptoms. The pain intensity was assessed with a 5 point scale ranging from "no pain" to "severe pain".

QLQ-BR23

This was used to address breast cancer specific issues, it had 2-dimensional scales: functions (body image, sexual activity, sexual life, future perspective) and symptoms (systemic side effect, breast symptoms, arm symptoms, hair loss) with overall of 23 questions with a raw score ranging from 1 to 4. All scales and single items measures range in score from 0 to 100. A high score for the functional scale representing a healthy level of functioning while a high score for the symptom scale represent a high level of symptoms.

The scores of both questionnaires were calculated separately and were obtained from the calculation of averages of the item.

Table 1. The question numbering of different items in the questionnaires.

QLQ-C30	Item (question) number
The global health status/QoL	29, 30
Function scale	
Physical functioning	1–5
Role functioning	6, 7
Emotional functioning	21–24
Cognitive functioning	20, 25
Social functioning	26, 27
Symptom scale	
Fatigue	10, 12, 18
Nausea and vomiting	14, 15
Pain	9, 19
Dyspnea	8
Insomnia	11
Loss of appetite	13
Constipation	16
Diarrhea	17
Financial difficulties	28
QLQ-BR23	Question number
Functional scale	
Body image	9–12
Sexual activity	14, 15
Sexual life	16
Future perspective	13
Symptom scale	
Systemic side effect	1–4, 6–8
Breast symptoms	20–23
Arm symptoms	17–19
Hair loss	5

Average score

Raw score (RS) was calculated for each sub dimensional scale. This score corresponds to a result of each question divided by the number of questions in each sub dimension scale.

$$RS = \frac{(Q_1 + Q_2 + \ldots + Q_n)}{n}$$

N is the number of questions in the sub dimension scale.

$Q_1, Q_2 \ldots$: results of each question.

Then application of the equation, RS is normalized to obtain the score of the scale.

To obtain the score (S) standardize the raw score to 0–100 range following the transformation.

$$\text{Quality of life, symptom scale: S score} = \left(\frac{RS - 1}{\text{Range}}\right) \times 100$$

$$\text{Functional scale S} = \left(1 - \frac{RS - 1}{\text{Range}}\right) \times 100$$

Range is the difference between the minimum and maximum values possible for each response .6, 3, 3 for quality of life scale, functional and symptoms, respectively. The average of dimension was determined. The average of each scale was calculated in order to compare with the next. Each scale corresponded to a score of 100.

Sexuality (question 16) and hair loss (question 5) were not included in the calculation if the patients answered (not at all), the questions 15 and 4.

The scores of scales were calculated separately. Therefore there wasn't the overall score for the questionnaire QLQ-C30.

The highest score of scale of quality of life indicated highest level of quality of life.

The highest score of the functional score corresponded to the highest level of functional health.

The highest score of the scale symptoms corresponded to the highest level of symptomology.

Statistical analysis

We used SPSS software version 22 to calculate the frequencies, averages, median and for the diagrams and histograms.

RESULTS

General characteristics of the population.

Patients according to age

This study had patients of age varying between 30 and 49 with an average of 42.60 years and median of 43 years.

The histological type of breast cancer

The most dominant histological type is the invasive ductal carcinoma in 55 patients with frequency of 96%. The other minor histological types; 2% invasive lobe carcinoma and 2% invasive colloid carcinoma.

Grouping according to grade

The grouping according to the grade has high existence of different grades where we had:

- SBR grade II with 35 patients (61.4%)
- SBR grade III with 16 patients (28.1%)
- SBR grade I with 6 patients (10.5%)

Number of ganglions

The values of ganglion status was obtained from 53 patients, the 4 patients had no values.

A total of 20 patients had number of ganglions below 3 (35.1%). A total of 7 patients had number of ganglions between 3 and 7 (12.3%). A total of 26 patients had number of ganglions above 7 (45.6%).

Grouping the patients according to hormone receptors

The hormonal receptors (estrogen receptor) was expressed by 44 patients (77.2%) and not expressed by 13 patients (22.8%).

Molecular classification

The classification of tumors according to their molecular profile showed that luminal B is the most frequent with 29 patients (51%), 8 patients with luminal A (14%), 11 patients with TNBc (19%), 9 patients with HER2+ (16%).

The score of the quality of life for patients

The score of the different scales is between 0 and 100.

Table 2. Results of the questionnaire QLQ-C30.

QLQ-C30	Global health status score	Symptom score	Functional score
Total	57	57	57
Average	56.34	63.7	45.75
Median	66	66.6	42.00

Table 3. Results of the questionnaire QLQ-BR23.

QLQ-BR23	Symptom score	Functional score
Total	57	57
Average	61.6	49.71
Median	62	50.00

DISCUSSION

This prospective study was conducted for a short period of time due to the coronavirus pandemic however 57 patients that had enrolled at the oncology department was a good inclusion rate. In this study, we found out that the age groups most affected were between 40 and 45 years. Questionnaire QLQ-C30 had the global state of health and functional score averages 56.34 and 45.75 respectively indicating a far from perfect thus a bad quality of life for the young women. The symptom scale had 63.7 that is very close to 100 representing a high symptomology level from the patients. Questionnaire QLQ-BR23 had a functional score, symptom score with averages 49.71 and 61.6 respectively, this is evidence for de-

creased quality of life similar to results from a study done by Jahanmohan [9]. Therefore, there is a significant difference between the patients' chemo-induced menopause and the non-chemo-induced menopause and the decreased quality of life. Results from this study had significant correlations with those published from studies of [10] and [6] that implies chemo-induced menopause had negative effects on the patients and therefore decreased the quality of life. From this study we noted that QLQ-BR23 represented the specific problems of breast cancer than the body image and the sexuality while QLQ-C30 is more general. QLQ-BR23 is more precise and more adequate to value the quality of life of patients and in particular this study.

CONCLUSION

This study shows an alteration in the quality of life, at this stage a study of the quality of life is more and more privileged. We suggest that there should be several other prospective studies that can provide a better understanding of the chemo-induced menopause, its impact on the quality of life and also the role of anti-Müllerian hormone in the prediction of menopause. Another study can be put in place with more samples thus more representation, longer duration with several other parameters such as follicle-stimulating hormone, the stage TNM and also the genetic parameters such as BRCA, PTEN.

LIMITATION

Due the global pandemic of corona virus, there was a review in the consultation criteria of the cancer patients by the medical oncology society of Algeria to avoid patient contamination from coronavirus that limited the number of patients in this study.

Due to strict measures to enforce the lock down, we could not access the laboratories to measure the anti-Müllerian hormone of the patients as a second criteria of the study, to verify the correlation between the gonadotoxicity and variations of anti-Müllerian hormone.

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Ethical consideration

This study was approved by the scientific and ethical committee of Saad Dahlab Blida 1 University. Ethical consent was acquired from the chief of the oncology department of Pierre and Marie Curie Medical Centre Algiers with complete confidentiality of the patient's data sustained during the whole work.

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Authors' contributions:
Imene Bedhrani and Sidi Mousa Nesrine conceived and designed the study, collected data. Samuel Mulondo, Sidi Mousa Nesrine analyzed and interpreted the data. All authors drafted, edited, reviewed and approved the final manuscript.

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The authors had full access to the data and take full responsibility for its integrity.
All authors have read and agreed with the content of the manuscript as written.
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