



EVALUATION OF THE MENOPAUSAL SYMPTOMS SEVERITY IN WOMEN WITH/WITHOUT CANCER HISTORY AND THEIR EFFECTS ON MENTAL/PHYSICAL HEALTH AND QUALITY OF LIFE

S. OLADI¹, T. GALINI-MOGHADAM², S. OLADI²

¹Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran

²Department of Obstetrics and Gynecology, School of Medicine, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran

Abstract – Objective: A decrease in sexual hormones leads to menopausal symptoms that affect women's physical/mental health and quality of life. Herein, we aim to determine the nature and severity of such symptoms in women with/without a cancer history and their effects on their quality of life.

Patients and Methods: In total, 600 menopausal women with/without a history of cancer were included in this study. Three standardized questionnaires were used to evaluate patients' mental and physical health as well as life quality: FACT-G (Functional Assessment of Cancer Therapy - General), MSNQOL (Menopause Specific Quality of Life), and the Beck's Depression questionnaire. Statistical analysis was done using SPSS v. 16 software.

Results: Out of 600 participants with a mean age of 55.21 (± 8.36) years, 301 have experienced cancer, and 299 individuals are considered controls without a cancer history. The mean age of controls was significantly higher than the cases ($p < 0.001$). Patients with a history of cancer had a higher parity rate ($p < 0.001$) with more children ($p = 0.001$), and they have experienced menopause at a younger age than the control group ($p < 0.001$). According to MSNQOL, physical ($p = 0.027$) and psychological ($p = 0.014$) symptoms were significantly higher in the cases in comparison to controls; whereas, the rate of sexual ($p = 0.225$) and vasomotor ($p = 0.373$) symptoms was not substantially different. Also, logistic regression analysis indicated that odds of physical symptoms is three times higher in patients with cancer history (OR=3.04, 95% CI: 1.47-6.28).

Conclusions: The study indicated that the course of menopause and the management of symptoms have a significant effect on the quality of life of women with a history of cancer.

KEYWORDS: Menopause, Cancer, Women, Quality of life. Menopause, Cancer, Women, Quality of life.

INTRODUCTION

Natural menopause is defined as a menstrual seizure due to the finished ovum storage of the ovaries, which led to the end of a woman's reproductive abilities. A complete course of menopause can take from a few months to even years and is accompa-

nied by symptoms such as hot flushes, change in sleep pattern, fatigue, palpitations, mood changes, and weight gain¹. Currently, most women experience menopause between 48 to 52 years old². After the menopause process, estrogen levels and their relative concentration compared to other hormones decreases. Following ovarian shutdown and reduc-



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tion of sexual hormones, adverse effects of low estrogen levels represent premature menopause, including hot flushes, headaches, vertigo, urinary frequency, depression, and pruritus^{3,4}. Some of the other symptoms of menopause are anger, hostility, and nervousness. In addition to mental problems, menopause can also interfere with patients' daily activities caused by extensive dysregulation of the autonomic and vasomotor systems⁵.

Several studies have shown that the nature and severity of menopausal symptoms differ between patients with cancer history and those who do not. Radiotherapy, used in the treatment of breast cancer, gynecological cancers, colorectal cancers, and hematologic cancers, can damage the delicate and sensitive tissue of ovaries. Menopausal symptoms experienced by cancer patients undergoing extensive therapy are similar to those of the women who have gone through natural menopause. However, the onset of these symptoms is more sudden, and they are generally more lasting⁶.

According to previous studies, 25 million women get menopause each year based on the aging trend worldwide, while in 1990, the number of menopausal women was estimated to be 467 million. It is estimated that this number will rise to one billion and two hundred thousand women by the year 2030^{2,7}.

The calculated age of menopause according to a study done in the north-west of Iran, was 47.7 years, and the only contributing factor to the age at the onset of menopause was suggested to be ethnicity; but in another study performed in mid-west Iran, the average age of menopause was 47.3 years, and the only determining factor was reported to be the occupation of the patient's spouse⁸.

Some studies have shown that there is a direct correlation between the quality of life and different stages of menopause, indicating that the quality of life decreases as the symptoms become more severe⁹. Symptoms such as irritability, anger, and depression are dominant during menopause, and it is estimated that 26% to 33% of women experience their first depressive episode during this time⁵.

Menopause is one of the most critical periods of a woman's life, marking the end of her reproductive capabilities, which is why complications and problems regarding this stage of life should be taken seriously as a health issue that directly affects half the population. Developing countries such as Iran should employ educational programs and conduct scientific studies to improve women's health.

More than 15 million women worldwide are cancer survivors (a person with any type of cancer who is still living^{10,11}). Based on the data provided by the center for cancer statistics of Iran, 24,495 cases of cancer in women were documented between 2005 to 2006. The corrected incidence rate

in the Mazandaran province during this period is 74 in 100,000. Hence, we aim to evaluate the nature and severity of menopausal symptoms following their effect on the quality of life among patients with a history of cancer.

MATERIALS AND METHODS

This study is a descriptive and comparative investigation aiming to determine the nature and severity of menopausal symptoms and their subsequent effects on the quality of life, either physical or emotional, in patients with a history of cancer and those who do not. The study population is 600 patients including menopausal women with a history of cancer that referred to the oncology ward of the Tuba Clinic, Mazandaran University of Medical Sciences, Sari, Iran; and menopausal women that do not have a history of cancer, who referred the Mostafavian Clinic, Mazandaran University of Medical Sciences, Sari, Iran. The Ethics Committee of Mazandaran University of Medical Sciences approved the study protocol due to the code I.R.MAZUMS.REC.1395.216.

We used three standardized questionnaires to evaluate patients' mental and physical health and quality of life: FACT-G (Functional Assessment of Cancer Therapy - General), MSNQOL (Menopause Specific Quality of Life), and the Beck's Depression questionnaire. The patient's demographic data were also collected in a separate questionnaire.

The nature and severity of menopausal symptoms were evaluated using the MSNQOL questionnaire, a standardized questionnaire including 29 multiple-choice questions addressing menopausal symptoms in four categories: 1) Vasomotor; 2) Emotional; 3) Physical; and 4) Sexual. For each question, the patient gives each symptom a grade between 0-6 to determine the severity of each symptom. Grading zero means that the patient has not experienced that specific symptom.

Since the severity of menopausal symptoms has a Likert scale of 7, patients over the midpoint of this range are classified as having moderate to severe symptoms. The severity of symptoms is classified as 1. No symptoms (score=1), 2. Moderate to severe ($2 \leq \text{scores} \leq 5$) and 3. Severe ($6 \leq \text{scores} \leq 8$) and 4. Very severe (scores>8).

Physical and emotional health was assessed using the FACT-G questionnaire. This questionnaire includes 27 questions that evaluate a cancer patient's life from four perspectives of physical, social, functional, and emotional health. Each of these questions has a Likert score of 5, ranging from 0 (not at all) to 4 (very much). A higher score indicates a better state of physical and emotional health. The validity and

reliability of the Persian translated version of this questionnaire were proved.

Signs of depression were evaluated using Beck's Depression Inventory (BDI-II). Each of the 21 items of this questionnaire points to a specific sign of depression. Each question can be scored 0 to 3, and the sum of the scores ranges between 0 to 63, which can be classified as follows: 1) No depression (0-13); 2) Mild depression (14-19); 3) Depression (20-28); 4) Severe depression (29-63). Cronbach's alpha was reported to be 0.87.

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate the normal distribution of data. Due to the large sample size (over 100) and the high precision of these tests, kurtosis and skewness values were examined to evaluate the normality of the variable with a higher accuracy rate, and the variables that were not normally distributed were manipulated using a logarithmic pattern.

A Q-Q chart was used to re-evaluate the data, the kurtosis, and the variables' skewness. Chi-square test was used to examine the relationship between qualitative variables, and independent *t*-test

was used to compare the qualitative data between the case and control groups. Also, logistic regression was used to study the variables' predictive values in the classification of patients in the two study groups. Collected data were analyzed using SPSS software version 16 (SPSS Inc., Chicago, IL, USA).

RESULTS

Out of 600 patients with a mean age of 55.21 ± 8.36 ranged from 34 to 87, 301 were cancer survivors, and 299 patients were in the control group. For the total of 600 patients, the average age at the onset of menopause was 46.55 ± 6.15 years, the mean body mass index (BMI) was 28.08 ± 4.98 , the mean number of pregnancies was 4.38 ± 2.33 , the mean number of children was 3.67 ± 1.96 , and the mean age of menarche was 13.44 ± 1.60 years. Other variables such as Beck's questionnaire, FACT-G and MEN-QOL results, physical activity, pregnancies that reached over 20 weeks, and comparative statistical analysis are presented in Table 1.

TABLE 1. Baseline characteristics of participants.

Variables	With/without a cancer history								p-value	
	Cancer survivors (cases)				No history of cancer (controls)					
	Mean	Max.	Min.	S.D.	Mean	Max.	Min.	SD		
Age	52.83	77	34	7.77	57.59	87	39	8.28	<0.001	
BMI	27.91	44.44	15.62	5.06	28.27	42.06	19.56	4.92	0.377	
Weekly exercise time (hr.)	42.29	180	10	29.66	50.34	180	10	33.47	0.031	
Number of pregnancies	3.92	9	0	2.16	4.84	15	0	2.42	<0.001	
Number of pregnancies over the age of 20	3.42	9	0	1.93	4.23	12	0	2.13	<0.001	
Number of children	3.31	9	0	1.87	4.03	12	0	1.98	0.001	
Menarche age	13.44	19	11	1.60	13.33	18	9	1.67	0.410	
Age at the onset of menopause	45.15	62	25	5.88	47.95	63	28	6.12	<0.001	
Years under cancer treatment	6.98	30	1	6.70	-	-	-	-	-	
FACT-G Score	38.33	84.00	17.00	8.37	40.45	84.00	26.00	11.76	0.008	
Beck Score	9.31	40.0	.0	7.25	8.05	37.0	.0	6.69	0.027	
MENQOL	Vasomotor menopausal symptoms	3.71	8	1	2.48	3.53	8	0.1	2.47	0.373
	Psychologic menopausal symptoms	3.25	8	1	1.47	2.59	7	1	1.50	0.014
	Physical menopausal symptoms	3.26	8	1	2.24	2.86	8	1	2.19	0.027
	Sexual menopausal symptoms	3.44	8	1	1.17	3.32	8	1	1.25	0.225

BMI: body mass index, SD: standard deviation.



Descriptive variables such as occupation, the status of employment, housing condition, history of smoking, educational status, physical activity, the type of physical activity, marital status, prematurity and possible cause of menopause, drug history, use of vitamin supplements, the stage of menopause at the time of evaluation, type of cancer, endotherapy (any therapeutic procedure that involves the use of an endoscope to localize the intervention to a location inside the body) and the use of antidepressants were compared between the case and the control group, which presented in detail in Table 1. Housing conditions ($p=0.016$), type of physical activity ($p=0.001$), marital status ($p=0.027$), causes of menopause ($p<0.001$), the onset of menopause ($p<0.001$), drug history ($p=0.001$), type of vitamin supplements ($p<0.001$), stage of menopause ($p<0.001$), type of cancer ($p<0.001$), and endotherapy ($p<0.001$) had a statistically significant correlation with the presence of a history of cancer (Table 1). In the case of cancer types, the most prevalent and probable cancers related to the matter are breast (39.53%) and uterine (31.89%) cancers. Also, no correlation was observed between having a history of cancer and educational status, level of physical activity, the type of exercise, and more use of vitamin supplements regardless of the type. The analysis of all the variables and their relationship is demonstrated in detail in Table 2.

To evaluate the predictive value of the data in determining whether the patient belongs to the case or the control group, a logistic regression test was used. The overall percentage of correct classification in this model is 73.6%. The results show that odds ratios of age, B.M.I., age at the onset of menopause, and the severity of physical menopausal symptoms as continuous predictors are greater than 3. Other variables did not have a statistically significant coefficient p -value ($p>0.05$). Odds Ratios of menopausal symptoms are shown in Table 3.

DISCUSSION

The age at the onset of menopause in this study population ranged from 25 to 63 and had a mean of 46.5 years. The mean BMI scores of the patients recovering from cancer and the control group were not different in any statistically significant manner, which is compatible with a similar study by Marino *et al*¹². Logistic regression showed that age, BMI, age at the onset of menopause, and severity of physical symptoms were significant continuous predictors (Odd Ratios>3). According to

our data, other variables did not show a statistically significant coefficient ($p>0.05$).

In this study, the most prevalent malignancy in the case group was breast cancer (39.53%), followed by malignancies of the uterine (31.89%) and colon cancer (11.96%), whereas Marino *et al*¹² reported a 90% rate of malignancy in the case group.

Comparison of the weekly physical activity of the two groups showed that while the number of patients that had weekly exercises regardless of the type and duration of the activity was not significantly different between the case and control groups, the duration and form of exercise was a distinguishing point. The mean 42.29 minutes of weekly exercise recorded by the case group was lower than the 50.34 minutes of exercise recorded by the control counterparts significantly ($p=0.031$); the specific form of exercise was also a key factor between the two groups as it was shown that 23.08% of patients who had physical exercise only indulged in light exercise and warm-up while the remaining 76.92% routinely hiked which is to be compared with the 91.30% of the case group ($p=0.001$).

The evaluation of the underlying cause of menopause showed that 2.00% of patients in the case group experienced natural menopause whereas 58.13% experienced post-surgical menopause, 38.54% became menopausal after receiving chemotherapy and 1.33% after radiotherapy treatment. In the control group except for two patients who became menopausal post-surgery, all other patients experienced natural menopause. Marino *et al*¹² reported that the prevalence of post-surgical menopause between survived cancer patients is 41%. Furthermore, 50.17% of patients in the case group experienced early-onset menopause, 41.20% of patients became menopausal around the expected age, and only 26 patients (8.63%) experienced late-onset menopause; which was statistically significant ($p<0.001$).

The highest prevalence of menopausal symptoms was recorded in patients aged 46 to 50 years, and women who were over 65 years old reported the lowest rate of menopausal symptoms. We also concluded that chemotherapy, immunotherapy, and tamoxifen administration affect menopausal symptoms, whereas radiotherapy did not affect the symptoms. Overall, compared to the control group, the case group experienced more symptoms by 5.3% and used replacement treatments 7.4 times more than the control group.

Burger *et al*¹³ reported that 56% of patients diagnosed with breast cancer experienced menopausal symptoms in the first six months after diagnosis, which lasted for at least one month.

TABLE 2. Classification of the qualitative data and the results of the statistical tests.

Variables		With/without a cancer history				p-value
		Cancer survivors		No history of cancer		
		N.	%	N.	%	
Occupation	Teacher	11	42.30	15	41.66	0.080
	Healthcare	9	34.61	0	0.00	
	Manual worker	0	0.00	4	11.12	
	Office worker	2	7.69	8	22.22	
	Marketer	4	15.40	9	25.00	
Occupational status	Employed	26	8.64	36	12.04	0.449
	Housewife	275	91.36	263	87.96	
Housing condition	Owner	277	92.02	293	98.00	0.016
	Rental	24	7.98	6	2.00	
	Lease	0	0.00	0	0.00	
History of smoking	Currently smoker	0	0.00	0	0.00	0.450
	Non-smoker	299	99.33	295	98.66	
	History of smoking currently a non-smoker	2	0.67	4	1.34	
Educational status	Middle school or less	201	67.33	219	73.24	0.490
	High school diploma	60	20.00	52	17.39	
	University	38	12.67	28	9.37	
Physical activity	Yes	156	51.83	134	44.82	0.204
	No	145	48.17	165	55.18	
Type of physical activity	Professional	0	0.00	0	0.00	0.001
	Jogging	120	76.92	122	91.30	
	Warm-up	36	23.08	12	8.70	
Marital status	Married	267	88.70	259	86.62	0.027
	Divorced	4	1.34	0	0.00	
	Widowed	28	9.30	40	13.38	
	Single	2	0.66	0	0.00	
The underlying	Natural menopause	6	2.00	297	99.33	<0.001
	Menopause following surgery	175	58.13	2	0.67	
	Menopause following chemotherapy	116	38.54	0	0.00	
	Menopause following radiotherapy	4	1.33	0	0.00	
Onset of menopause	Early onset	151	50.17	84	28.09	<0.001
	On-time	124	41.20	153	51.17	
	Late onset	26	8.63	62	20.74	
History of taking medication	Yes	36	11.96	8	2.68	0.001
	No	265	88.70	291	97.32	
Type of medication	Calcium	9	25.0	0	0.00	0.601
	Letrozole	9	25.0	0	0.00	
	Aromasin	9	25.0	0	0.00	
	Tamoxifen	9	25.0	0	0.00	
	Progesterone	0	0.0	4	50.00	
	Oral contraceptive pill	0	0.0	4	50.00	
Vitamin supplements	Yes	135	44.85	126	42.14	0.605
	No	166	55.15	173	57.86	
Type of supplement	Folic acid	4	2.96	2	1.59	<0.001
	Calcium	77	57.04	24	19.05	
	Iron supplement	16	11.85	22	17.46	
	Vitamin	24	17.79	22	17.46	
	Folic acid - Calcium	2	1.48	2	1.59	
	Pharmaton	2	1.48	0	0.00	
	Calcium - Vitamin	4	2.96	26	20.63	
	Calcium - Iron	2	1.48	12	9.52	
	Vitamin – Folic acid	2	1.48	0	0.00	
	Folic acid	2	1.48	6	4.76	
	Iron - Vitamin	0	0.00	6	4.76	
	Iron – Vitamin – Omega 3	0	0.00	2	1.59	
	Vitamin – Omega 3	0	0.00	2	1.59	

Continued



TABLE 2 (CONTINUED). Classification of the qualitative data and the results of the statistical tests.

Variables		With/without a cancer history				p-value
		Cancer survivors		No history of cancer		
		N.	%	N.	%	
Staging of menopause at the time of evaluation	Regular menses with no symptom of menopause	209	69.43	0	0.00	<0.001
	Irregular menses and hot flushes	78	25.91	0	0.00	
	Completed menopause	14	4.66	0	0.00	
Type of cancer	Breast cancer	119	39.53	0	0.00	<0.001
	Uterine cancer	96	31.89	0	0.00	
	Ovarian cancer	26	8.64	0	0.00	
	Colon cancer	36	11.96	0	0.00	
	Lung cancer	4	1.33	0	0.00	
	Lymphoid cancer	10	3.32	0	0.00	
	Hematologic cancer	2	0.67	0	0.00	
	Others	8	2.66	0	0.00	
Endotherapy	Yes	49	16.28	0	0.00	<0.001
	No	252	83.72	0	0.00	
Use of antidepressants	Yes	55	18.27	38	13.04	0.060
	No	246	81.73	261	86.96	
Beck's depression index	No depression	247	82.06	257	85.95	0.413
	Mild depression	28	9.30	24	8.03	
	Depression	20	6.64	16	5.35	
	Severe depression	6	2.00	2	0.67	
MENQOL score (vasomotor aspect)	No symptoms	93	30.90	101	33.78	0.533
	Mild symptoms	123	40.86	109	36.45	
	Moderate to severe symptoms	85	28.24	89	29.76	
MENQOL score (psychological aspect)	No symptoms	74	24.58	112	37.46	0.002
	Mild symptoms	143	47.51	109	36.45	
	Moderate to severe symptoms	84	27.91	78	26.09	
MENQOL score (physical aspect)	No symptoms	92	30.56	123	41.14	0.010
	Mild symptoms	110	36.54	105	35.12	
	Moderate to severe symptoms	99	32.89	71	23.74	
MENQOL score (sexual aspect)	No symptoms	119	39.53	142	47.49	0.139
	Mild symptoms	122	40.53	103	34.45	
	Moderate to severe symptoms	60	19.93	54	18.06	

They also reported a low quality of life, a history of a chronic illness, treatment with tamoxifen, positive estrogen receptors, and history of immunotherapy in patients who suffered from menopausal symptoms. In this study, the severity of sexual symptoms between the two groups was not significant ($p=0.225$), whereas the reported rate of such symptoms was significantly different ($p=0.03$).

According to a study performed in Australia, the severity of menopausal symptoms of the vasomotor system was significantly higher in cancer recovering patients on three different occasions at the time of the referral, 12 hours prior to the referral, and 24 hours prior to the referral ($p<0.05$). Nevertheless, the severity of symptoms such as nocturnal hyperhidrosis, sleep irregularities, and cold sweats was not different between the two groups. They also concluded that psychological symptoms such as irritability and low mood and

sadness are more common in the group without a cancer history¹².

In this study, 82.06% of the patients in the case group did not suffer from depression while 17.94% required medical intervention, which was greater than the 14.05% rate of depression of the control group, the relationship between the group variable and Beck's score category was not statistically significant ($p=0.413$).

Marino *et al*¹² concluded that patients who were cancer survivors showed a higher rate of mental illness and depression ($p<0.05$); they also reported that menopausal symptoms and their effects on the quality of life were statistically different, and they suggested that hot flushes are among the most troublesome symptoms of menopause. They proposed that proper management and prevention of menopausal symptoms can help increase the quality of life for patients with a history of cancer and should be included in the standard treatment regimen of these patients.

TABLE 3. Odds Ratios of menopausal symptoms in Logistic regression.

Symptoms	Odds Ratio (95% CI)	p-value
Vasomotor	1.02 (0.69-1.51)	0.89
Psychological	1.01 (0.51-1.99)	0.95
Physical	3.04 (1.47-6.28)	0.003
Sexual	0.96 (0.61-1.49)	0.86

According to a study conducted by Javadian *et al*¹⁴, hot flushes, night sweats, and insomnia with a prevalence of 63.8%, 55%, and 55%, respectively, were the most common, menopausal symptoms experienced by patients with a history of cancer. They also reported that 36.3% of patients had a good quality of life, 6.3% showed secondary physical disabilities, and 3.8% had consequent social impairments.

A small study population and the significant age difference between the case and the control groups were the limitations of our study. Since the use of replacement treatments such as acupuncture, herbal medicine, and vitamin E supplements was more prevalent in patients in the case group, we propose that more information and awareness should be directed towards cancer survived patients to help reduce the menopausal symptoms.

CONCLUSIONS

In summary, this study indicated that for women with a history of cancer, the course of menopause plays an important role in determining their quality of life. Since most women have adequate access to healthcare centers, these centers should provide women with proper training regarding management and control of menopausal symptoms. Educational classes and professional consultation can reduce the negative effects of menopause on women's quality of life. Education should also focus on helping women understand the process of menopause and accept it as a natural and positive stage of life. They should also encourage women to seek appropriate medical care regarding their health-related issues. On the other hand, considering the significant effect of social support in increasing the quality of life in menopausal women, encouraging family members, especially spouses to attend these

classes and using social networks to increase the general awareness and emotional support can help increase these women's quality of life.

CONFLICT OF INTERESTS:

The authors declare that they have no conflict of interests.

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