

Lymphedema

A significant health problem for women with breast cancer in Jordan

Basem B. Morcos, MD, Firas Al Ahmad, MD, Iyad Anabtawi, MD, Abdel-Munem Abu Sba', MD, Hisham Shabani, MD, Rawya Yaseen, MD.

ABSTRACT

الاهداف: النظر في معدلات تورم الذراع اللمفوي نتيجة لسرطان الثدي في منطقتنا، ورفع مستوى الوعي حول هذه الظاهرة عند العاملين في القطاع الصحي.

الطريقة: أجريت دراسة مقطعية للمريضات المتعالات من سرطان الثدي في مركز الحسين للسرطان خلال الفترة من يناير 2004م إلى ديسمبر 2009م. اشتملت المجموعة على 515 مريضة. تم تهيئة استبانة حول أية أعراض خاصة بالذراع من قبل المريضات أنفسهن. وتم تعريف التورم اللمفوي بالتالي: (أي اختلاف في محيط الذراع بما يساوي أو يزيد عن 2 سم).

النتائج: وجد في الدراسة أن نسبة حدوث تورم الذراع اللمفوي هي 21.1%. رفع تقييم المريضات الخاص بأنفسهن من هذه النسبة لتصل إلى 35%. معظم المريضات (75%) شكون من أعراض مثل: ألم في الذراع، و الاخذار، ومحدودية الحركة. كانت الأعراض بسيطة لدى معظم المريضات اللاتي يعانين من تورم الذراع اللمفوي إلا أن 17 مريضة (15.6%) كانت أعراضهن شديدة.

خاتمة: ما زالت مشكلة التورم اللمفوي تعتبر مشكلة صحية منتشرة في منطقتنا من العالم. معظم المريضات يعانين من تورم بسيط، إلا أن بعضهن يعانين من تأثيرات شديدة تحد من أنشطة الحياة اليومية. إنه من المهم للعاملين في القطاع الطبي تفهم أهمية هذه المشكلة ومضاعفاتها على المريضات.

Objectives: To investigate the frequency of breast cancer related lymphedema in our region, and to heighten its awareness among health workers.

Methods: This is a cross-sectional study of patients treated with breast cancer at King Hussein Cancer Center, Amman, Jordan, between January 2004 and December 2009. We excluded patients with bilateral breast cancer. A total of 515 patients were included.

We asked the patients to complete questionnaires that included questions related to arm symptoms. Lymphedema was defined as 2 cm or more difference between the 2 upper limbs' girths.

Results: The incidence of lymphedema was 21.1%. The subjective evaluation by the patients overestimated the figure (35%). Most patients (75.3%) had limb symptoms, such as pain, numbness, and limitation of movement. In most patients with lymphedema, the symptoms were mild, but in 17 patients (15.6%) the effects were severe.

Conclusion: Lymphedema continues to be a common health problem in our region. Most patients have mild lymphedema, but in some patients the effects on daily activities are severe. It is important for health workers to understand the significance of this problem and its associated morbidity.

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From the Department of Surgery, King Hussein Cancer Center, Al-Jubeiha, Amman, Jordan.

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Address correspondence and reprint request to: Dr. Basem B. Morcos, Department of Surgery, King Hussein Cancer Center, Al-Jubeiha, Amman, Jordan. Tel. +962 (6) 5300460. Fax. +962 (6) 5353001. E-mail: bmorcos@doctor.com

Breast cancer related lymphedema (LE) is a common clinical problem. It usually follows axillary surgery, but may be related to radiotherapy or tumor metastasis in the axilla. It is the most feared long-term complication after axillary dissection. Lymphedema has been reported since the beginning of last century. In 1908, Handley described a method for the relief of this condition.¹ In 1921, Halsted described the condition and referred to it as 'elephantiasis chirurgica'.² Although the condition

is extensively described in the literature, no agreement exists on its definition. However, it can be described as a chronic, usually progressive condition associated with an arm or hand swelling. It is usually an irreversible condition. In many patients, it starts with pitting edema, but later may progress to non-pitting edema. The later changes are related to chronic inflammatory fibromatosis and hypertrophy of the hypodermal and dermal connective tissue.³ During Halsted radical mastectomy era, LE rates high, reaching up to 62.5%.⁴ Later, as the surgical approach for breast cancer became less aggressive, the rate of LE declined. In 1966, Hughes and Patel did an extensive review and found an incidence of 49.2%.⁵ Two more recent series, however, noted a LE rate of 24% and 28%.^{6,7} Lymphedema is a much-feared complication by surgeons and patients alike. It is associated with physical and psychological morbidity. The LE is unsightly, especially if severe, and may limit the patient's ability to wear suitable clothes.⁸ Lymphedema is also associated with other physical symptoms, such as pain, numbness, and limitation of movement of the arm. These problems usually affect the quality of life.⁹ This study aims to look at how frequent this complication is in our breast cancer patient population and to gain an insight into how patients are physically affected by it.

Methods. Study population. This is a cross-sectional study of patients diagnosed with carcinoma of the breast at King Hussein Cancer Center, Amman, Jordan, between January 2004 and December 2009. The study was approved by the Institutional Review Board of the Center. Eligibility criteria in this study were first breast carcinoma diagnosis (both invasive and in-situ), surgery carried out at the center, surgery carried out at least 6 month prior to accrual, and patients capable of informed consent. Patients should have finished their chemotherapy and radiotherapy, if any, at least one month prior to accrual.

Between January 2004 and December 2009, 1205 women fit the eligibility criteria. They had their surgery carried out by one of the 4 surgical oncologists at the center. During the period from December 2009 to December 2010, a nurse practitioner approached 540 of these eligible patients during their surgical outpatient visit and explained the study objectives. Five hundred

and thirty-one patients gave their informed consent. Sixteen patients were excluded from the analysis due to a diagnosis of bilateral breast cancer. The final study population therefore consisted of 515 women.

Data collection and lymphedema assessment. After obtaining informed consent, eligible patients were asked to answer a questionnaire containing questions related to arm symptoms and LE. After filling the questionnaire, both upper limbs were examined visually and the examiner gave his subjective impression about the presence of LE. Objective measurement of LE was performed after that so as not to affect the subjective impression of the examiner. The method used to detect LE was mid-arm and forearm circumference (MAC) measurements. We considered a ≥ 2 cm difference in the limb girth between the affected and non-affected limbs as a definition of LE in our patients. A difference more than 5 cm was arbitrarily considered as severe LE. Other signs, such as redness, pitting, and nail changes were also recorded.

The medical records of all recruited patients were reviewed. Demographic data and weights of patients were collected. Tumors characteristics as well as therapeutic interventions were also recorded.

Statistical analysis. Descriptive statistics were calculated for participants' demographics, arm swelling characteristics as well as other symptoms. Lymphedema incidence was calculated for the total patient population. The time elapsing from the date of surgery and date of accrual in the study was calculated for all patients and was divided into 6 months intervals, starting from 6 months after operation. Incidence of LE in each of those time intervals was calculated. The association between LE and other symptoms were tested using the Fisher exact test, Chi-square test, and t-test. All analyses were performed using SAS version 9.1 (SAS institute Inc, Cary, NC).

Results. The characteristics of the 515 patients enrolled in this study are presented in Table 1. The mean age of the patients at diagnosis was 50.1 years (range=23.9-83.4). Most (81.4%) had a body mass index (BMI) of more than 25. Only 22 patients (4.3%) had ductal carcinoma in situ (DCIS), the rest had invasive carcinoma.

The treatment received by the patients is also shown in Table 1. Most of the patients (81.9%) underwent axillary dissection (AD), and only 18.1% had sentinel lymph node biopsy. Most of the participants received chemotherapy (88.5%), radiotherapy (74.6%), and

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Table 1 - Characteristics of the participants (N=515).

Characteristic	N	(%)
Age		
≤50	282	(54.8)
>50	233	(45.2)
Body mass index		
≤25	95	(18.6)
>25	417	(81.4)
Tumor type		
Invasive carcinoma	493	(95.7)
DCIS	22	(4.3)
Tumors size		
Tx	7	(0.0)
T1	139	(27.4)
T2	274	(53.9)
T3	95	(18.7)
Lymph node stage		
N0	210	(40.8)
N1	137	(26.5)
N2	75	(14.6)
N3	93	(18.1)
Lymphovascular invasion		
Present	203	(40.4)
Absent	299	(59.6)
Grade		
I	19	(3.7)
II	141	(27.8)
III	348	(68.5)
Surgery-breast		
Mastectomy	334	(65.1)
Wide local excision	179	(34.9)
Surgery-axilla		
Axillary dissection	409	(81.9)
Sentinel lymph node biopsy	90	(18.1)
Chemotherapy		
Yes	456	(88.5)
No	59	(11.5)
Radiotherapy		
Yes	384	(74.6)
No	131	(25.4)
Hormonal therapy		
Yes	398	(77.3)
No	117	(22.7)
Trastuzumab		
Yes	68	(13.2)
No	447	(86.8)

Some data are missing for some of the patients, DCIS - ductal carcinoma in situ

hormonal therapy (77.3%). Adjuvant trastuzumab was given to 68 patients (13.2%).

Lymphedema incidence. Participants had their surgery at a median of 26.2 months (range=6-82) before accrual. Overall, 110 patients (21.4%) had LE at the time of enrollment using MAC measurement. Most of the patients (81.3%) had mild to moderate LE and in 18.7% it was more severe, with a limb girth difference of more than 5 cm. The incidence of LE based on the subjective evaluation by the examiner and patients were 22.1% and 35%. The incidence of LE in those who were examined between 6 and 12 months from surgery

Table 2 - Distribution of the participants' symptoms (N=515)

Symptom	N (%)	Patients without LE n=405	Patients with LE n=110	P-value
Swelling	180 (35.0)	98 (24.2)	82 (74.5)	0.00
Heaviness	185 (35.9)	131 (32.3)	54 (49.1)	0.00
Pain	199 (38.6)	148 (36.5)	51 (46.4)	0.06
Numbness	220 (42.7)	163 (40.2)	57 (51.8)	0.03
Limitation in movement	135 (26.2)	89 (22.0)	46 (41.8)	0.00
Any symptom	388 (75.3)	290 (71.6)	98 (89.1)	0.00

LE - lymphedema

was 16.3%. The corresponding figure for 12-18 months was 20.8%. For all patients who were examined after 18 months, the average figure was 22.7% (the numbers in each time period was too low to obtain meaningful results). Translating those figures into cumulative incidence indicates that 72% of patients who develop LE do so within the first 12 months and 92% within 18 months from surgery.

Physical morbidity. Most patients in our series (75.3%) had symptoms in the ipsilateral upper limb. The symptoms included pain (38.6%), numbness (42.7%), heaviness (35.9%), and decrease in shoulder range of movement (26.2%). Only 127 patients (24.7%) did not have any symptoms. With a median follow-up of over 2 years, numbness was the most common symptom. Symptoms as a whole were more common in patients with LE (Table 2). Most of the 110 patients with LE stated that their LE and other symptoms had no effect (48.6%) or minimal effect (35.8%) on their daily activities. Seventeen patients (15.6%); however, said that their symptoms severely affected their daily activities and work.

Discussion. Incidence of lymphedema. Breast cancer is one of the most common malignancies in women. It is the most common cancer in Jordan and accounts for 36.7% of all female malignancies.¹⁰ Considering the incidence of LE in breast cancer patients, it becomes clear that LE is a relatively common health problem.

In our series of patients, 21.4% developed LE within a median of 26.2 months from the time of their surgery. This incidence is well within the incidence cited in the literature, which ranges between 3% and 83%,¹¹ although figures between 20% and 30% are more typical. This wide range in incidences is attributed to more than one factor. There is no clear and universal definition of LE and there are variations in the methods of its diagnosis and measurement. Some methods depend on circumference measurements, but other methods exist, including

water displacement, bioelectrical impedance, or bio-impedance spectroscopy,¹²⁻¹⁴ which reflects increased water content. Since those tests do not completely agree with each other,^{13,15} the results are expected to be different. Although water displacement and circumference measurement are both reliable techniques in clinical practice, the use of arm circumferences is the most popular method for assessing LE. This is probably related to its simplicity and practicality. It is; however, associated with some limitations. Water displacement is messy and impractical in the clinic.

Despite the importance of patients' perception, LE defined solely by patient perception is not accurate and many studies showed a difference between measured and perceived LE.¹⁶⁻¹⁸ This might be related partly to the associated sensory changes resulting from surgery. In our patients, the perceived LE rate was 35%, which is significantly higher than the measured LE rate (21.4%). Patients also differ in stage and grade of their disease, and in the adjuvant treatment received. Patients with more advanced tumors usually receive more aggressive treatment, including mastectomy, axillary dissection, and radiotherapy, which have been shown in different studies to be associated with increased risk of LE,^{11,17,19} Our patients, at a median of 50.1 years, are younger than the Western average and have more advanced stages of disease at the time of diagnosis. The rate of mastectomy is 65.1% and that of axillary dissection is 81.9%. Also, most of our patients (74.6%) received adjuvant radiotherapy. Comparing our patients' characteristics to those from a recent population based study at the US shows that our patients have more advanced disease stages, and that they undergo more aggressive treatment, including surgery, radiotherapy, and chemotherapy.²⁰ Another factor explaining the varying incidence of LE is related to the fact that patients are evaluated at different time periods following their surgery. Although LE usually develops within the first 2-3 years after surgery, it is well known that it can develop many years later.²¹ Our results indicate that most LE (92%) occurred within the first 18 months. Other series showed that 75-80% of patients who develop LE do so within the first year or 2 after surgery.^{6,7,18,22-25} Approximately 10% develop LE after the third year.¹⁸ Thus, the follow up period has to be at least between 2-3 years to represent the true incidence of LE.

Morbidity of lymphedema. Upper limb LE is a feared complication by both patients and physicians. It is associated with physical and psychological morbidity. The most obvious problem of LE is cosmetic. For

most patients with LE, the swelling is noticeable and may be unsightly. It usually affects clothing options, and patients may avoid certain social situations.²² That explains part of the psychological morbidity. Although we have not studied the psychological effects, the literature shows that self-esteem and sexuality are also impaired.⁸ Concerns on the recurrence of the tumor add to the psychological distress.

Physical problems range from discomfort to life threatening malignancy.^{26,27} Although most of the symptoms are mild, they are present in most of patients.¹⁸ Three quarters of our breast cancer participants (75.4%) had one or more of upper limb symptoms, including swelling, heaviness, pain, numbness, and limitation of shoulder movement. It is worth noticing that symptoms can be present even without the presence of LE, as our data indicate. However, they are more common in patients with LE. The effect of LE has on daily activities and work depend on the severity of LE and on the associated symptoms. Women with severe LE have significantly worse physical functioning.¹⁸ Our data indicate that in about half of the patients with LE (48.6%), their symptoms affected their daily activities and worked. In 15.6%, the effects were severe. Although we did not quantify those effects, the results provide an accurate reflection of what patients feel. Those effects are especially important for young, active women, who are expected to care for their families at home and at work.

In conclusion, lymphedema continues to be a significant health problem for patients with breast cancer. Incidence varies between different series due to differences in definition, tumor stage, and follow-up period, among others. The incidence in our region is similar to that cited in the literature, which is commonly between 20% and 30%. Although most patients with LE have minor swelling and symptoms, it is still associated with significant physical and psychological morbidity. Understanding the extent of this problem as well as its morbidity is essential for those working with patients with breast cancer.

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