Frequency of Lymphedema after Complete Axillary Lymph Node Dissection in Patients with Breast Cancer

Neelma Bukhari, Ghulam Haider, Maryum Nouman, Salahuddin Khan, Areen Yousaf, Zain Abid

Jinnah Postgraduate Medical Center, Karachi Pakistan

ABSTRACT

Objective: To assess the frequency of lymphedema of the arm and forearm after complete axillary lymph node dissection in patients with breast cancer at one year of follow-up and see its association with body mass index among breast cancer patients presenting at a tertiary care hospital in Karachi.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi, Pakistan, from Apr 2019 to 2020.

Methodology: One sixty-eight females of age 25-80 years who underwent complete axillary lymph node dissection for breast cancer were included in the study. A breast surgeon performed the axillary lymph node dissection with more than five years of experience. The patients were followed for one year post-operatively to determine the occurrence of lymphedema. All the demographic details and clinic-pathological findings were reported in the predesigned proforma.

Results: About 168 females (97.6%) out of 172 have undergone complete axillary lymph node dissection. Lymphedema was the most common complication among them (38.1%). Common side effect observed after axillary lymph node dissection was pain (66.1%), followed by heaviness (59.5%), firmness/tightness (46.4%) and numbness. The patients with Body mass index ≥ 25 kg/m^2, right arm involved, exposure to radiotherapy and moderately differentiated tumour (grade-2) had a significantly higher occurrence of lymphedema (p<0.05).

Conclusion: Lymphedema is higher among breast cancer survivors during the first postoperative year. The risk of lymphedema can be reduced by avoiding potential factors like obesity and carefully selecting patients for postoperative radiotherapy.

Keywords: Axillary lymph node dissection, Body mass index, Breast cancer, Lymphedema, Malignancy, Multimodal therapy.

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INTRODUCTION

Approximately two million individuals are diagnosed with carcinoma of breast.[1] However, it remains to be the commonest malignancy among females. Currently, owing to a rise in early screening and initiation of multimodal therapy, the mortality due to breast cancer has reduced to one in twelve (2018) from one in eleven (1970), which has eventually increased the overall survival rate of the breast cancer patients.[2,3]

Multimodal breast cancer treatment involves chemotherapy, radiotherapy, hormonal therapy and surgery. This multimodal strategy has raised the 5-year survival level to 90%, although there are some side effects of these treatments that significantly impact the quality of life of the breast cancer patient.[4,5]

Breast cancer continues to be the most common cancer in women. With the advent of multimodality treatment and early detection methods, there is an overall improvement in survival. For stage IV transformation of the disease into a chronic condition, the focus of attention is recently being directed towards late post-treatment sequelae like lymphedema.[3,6] Lymphedema is a frequent complication leading to significant personal, physical and psychological problems in breast cancer patients.[7] The prevalence of arm lymphedema is 26% (varies from 0-56%) in breast cancer patients after two years following treatment.[3] However, the cumulative incidence of lymphedema differs from 3 to 42.2% in five years of follow up duration.[6,8,9] In Pakistan, the frequency of lymphedema after modified radical mastectomy was reported as 26% in breast cancer patients.[10] Thus, the variations in incidence are due to type of treatment, treatment duration, a lack of standard diagnostic criteria and limited knowledge of the physician.[6]

In Pakistan, significantly fewer researches have been done to evaluate the incidence of lymphedema in breast cancer patients in a 1-year follow up duration. Hence, breast cancer patients have a better prognosis if diagnosed early and patients undergo treatment

Correspondence: Dr Neelma Bukhari, Department of Medical Oncology, Ward-4, TPMC, Karachi-Pakistan

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timely. Knowing the incidence of lymphedema after breast cancer treatment, preventive steps must be adopted in clinical practice. Therefore, the present study aimed to assess the frequency of lymphedema after complete axillary lymph node dissection at one year of follow-up and its association with BMI and postoperative radiotherapy in breast cancer patients at a tertiary hospital in Karachi.

METHODOLOGY

This prospective longitudinal study was conducted at Department of Medical Oncology, Jinnah Postgraduate Medical Center from November 2017 to July 2019. Data collection was initiated after approval from the Ethical Review Committee (No-F.2-81-IRB/2019-GENL/18930/JPMC). The sample size was estimated using the OpenEpi sample size calculator by taking statistics for the prevalence of lymphedema as 26%,[10] the margin of error as 6.7% and 95% confidence level. The calculated sample size came out to 168 patients using a non-random convenience sampling technique.

Inclusion Criteria: All the females aged 25-80 years presenting at OPD with histologically diagnosed carcinoma of the breast (stage I-III) were included in the study.

Exclusion Criteria: Patients who had a history of oncologic therapy at another hospital, altered function of upper extremities, previous lymphedema, a palliative surgery, and patients who underwent sentinel lymph node mapping were excluded from the study.

Before including in the study, informed consent was taken from all the eligible patients. The axillary lymph node dissection was performed by a breast surgeon with more than five years of experience. Before surgery, the baseline circumference of both sides, arm, and forearm were measured at 10 cm above and 5 cm below the olecranon process. The patients were followed for one year post-operatively to determine the frequency of lymphedema. At two consecutive follow-up clinical examinations, the lymphedema was labelled positive when arm swelling (difference between two arms ≥2 cm) was persistent. All the demographic details and clinic-pathological findings were reported in the predesigned proforma.

SPSS version 23 was used to analyze the data. Frequencies and percentages were calculated for qualitative variables. Mean and SD were calculated for the quantitative variable. Chi-square/Fisher exact test was applied to see the relationship. The *p*-value of ≤0.05 was taken as statistically significant.

RESULTS

The mean age of 168 patients was noted as 49.10 ± 11.18 years. The average BMI was reported as 27.14 ± 6.33 kg/m^2. About 167 patients received chemotherapy (97.1%), whereas 71 (42.3%) females received radiation and 100 (58.7%) females received hormonal therapy, respectively.

Out of 172, about 168 females (97.6%) have undergone axillary lymph node dissection. Lymphedema was the most common complication among them (38.1%), as shown in Figure.

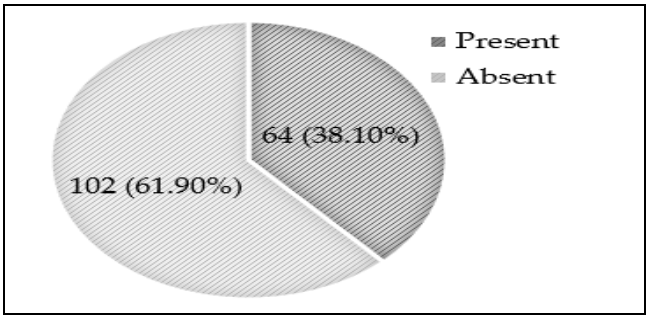

Figure: Frequency distribution of lymphedema.

About 161 (95.8%) females had dominant right arm, 86 (51.2%) had right side of surgery and 107 (63.7%) had left arm involved. The common symptoms observed after axillary lymph node dissection was pain (n=111, 66.1%), followed by heaviness (n=100, 59.5%), firmness/tightness (n=77, 46.4%) and numbness (n=70, 42.2%) as listed in Table-I.

Table-I: Characteristics of patients undergone for axillary lymph node dissection (n=168).

Variables	n (%)
Dominant Arm	
Right	161 (95.8)
Left	7 (4.2)
Side of Surgery	
Right Breast	86 (51.2)
Left Breast	82 (48.8)
Current Arm Involved	
Right Arm	61 (36.3)
Left Arm	107 (63.7)
Symptoms of Lymphedema	
Swelling in Arms	39 (23.5)
Firmness in Arms	77 (46.4)
Numbness	70 (42.2)
Heaviness	100 (59.2)
Tenderness	53 (31.9)
Pain	111 (66.1)

Lymphedema frequency was more among females of age ≥ 50 years; however, no significant difference was observed between the age groups and the

presence of lymphedema (p>0.05). A significant difference was observed when stratified based on Body mass index (p<0.05), the patients with Body mass index ≥ 27.5 kg/m² had a significantly higher frequency of lymphedema. Similarly, the patients with the right arm involved, exposed to radiotherapy, and moderately differentiated tumour (grade 2) had a significantly higher incidence of lymphedema (p<0.05). Whereas no statistical difference was found in the frequency of lymphedema for age and stage of the tumour (p>0.05) (Table-II).

Table-II: Lymphedema stratified by various factors.

Variables	Lymphedema		*p*-value
	Present	Absent	
Age Groups			
<50 years	30 (38.5%)	48 (61.5%)	0.999
≥50 years	34 (37.8%)	56 (62.2%)	
Grade of Tumor			
Grade 1 (Well Differentiated)	-	7 (100%)	0.027*
Grade 2 (Moderately Differentiat)	48 (44.4%)	60 (55.6%)	
Grade 3 (Poorly differentiated)	16 (30.8%)	36 (69.2%)	
Undifferentiated	-	1 (100%)	
Stage of Tumor			
Stage 1	3 (60%)	2 (40%)	0.554
Stage 2	24 (33.3%)	48 (66.7%)	
Stage 3	35 (40.2%)	52 (59.8%)	
Stage 4	2 (50%)	2 (50%)	
Body Mass Index Groups			
<27.5 kg/m²	30 (31.3%)	66 (68.8%)	0.038*
≥ 27.5 kg/m²	34 (47.2%)	38 (52.8%)	
Radiotherapy			
Yes	41 (57.7%)	30 (42.3%)	0.001*
No	23 (23.7%)	74 (76.3%)	
Affected Arm			
Right	33 (54.1%)	28 (45.9%)	0.001*
Left	31 (29%)	76 (71%)	

DISCUSSION

Lymphedema is a highly reported complication post complete axillary lymph node dissection. It affects the quality of life, but it also restricts the ability to work. The present study found that 96.5% underwent axillary lymph node dissection and lymphedema was the most common complication among 38.1% of patients. Similarly, in a prospective study, lymphedema was the only factor associated with post lymph node dissection with a p-value <0.05.[11]

In another study, lymphedema was reported post-mastectomy, and in a similar study, it was found that lymphedema is somewhat associated with seroma formation.[12] In a Pakistani study, the breast cancer patients were randomized into three groups. Results showed that in all three groups, less than 30% developed metastatic disease, some developed skin toxicities, and other patients developed lymphedema in less than 27% of patients in all three groups.[13] Lymphedema was found among almost 31% of survivors of breast cancer during three year period.[14,15] Literature has also confirmed the prevalence of lymphedema being double in patients who underwent axillary surgery.[8,16] The results of the current study are also validated by Meek *et al,* Ozaslan *et al,* and Beaulac *et al*.[17-19] Also, in a study conducted in Karachi, patients undergoing axillary dissection with mastectomy reported complications related to post axillary node dissection and lymphedema in the arm was found in approximately twenty-six percent of the patients.[10]

In the current study, the results showed a significant association of lymphedema with the site of the arm. The right arm was more involved, and there was a difference in the size of the swelling in both arms, which was also found significant. This could be due to the slightest difference in the size of both arms. The current study also showed a significant association between lymphedema with increased body mass index. This explains that patients having border line obesity or higher BMI index are at greater risk of having lymphedema, which could be due to a variety of factors.[20,21] The study conducted by Johansson *et al,* found that factors related to lymphedema and higher BMI index were one of factor that was found significant.[22] In addition, literature has found that lymphedema could be present as an early complication and late complication. It has been evident in a study that lymphedema can be evaded by avoiding obesity.[23] However, in a study conducted by Larson et al., the results showed no significant association with BMI index.[24] The current study also showed a significant association of lymphedema with tumour grade (p<0.05). The majority of the patients with moderate to poorly differentiated tumours developed lymphedema. Warren *et al*. found that 6.8% of the patients developed lymphedema after 60 months post-operatively, wherein the incidence of lymphedema was higher among the radiotherapy group.[9] The similar results were observed in the current study.

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CONCLUSION

The incidence of lymphedema of the ipsilateral arm and forearm is high after complete axillary lymph node dissection in Breast cancer patients. The risk of lymphedema increased further with exposure to postoperative radiotherapy and raised BMI. Risk factors identified in this study

offer opportunities for intervention (weight loss, use of sentinel node biopsy where possible, careful selection of patients for postoperative radiotherapy) to reduce the incidence of lymphedema and control the symptoms associated with this condition.

Conflict of Interest: None.

Authors' Contribution

NB: Conceptual design, methodology development, manuscript writing, GH: Supervision, reviewed, MN: Analysis, interpretation of data, Sk: Literature review, manuscript writing, AY: Data collection, ZA: Results interpretation.

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