

FREQUENCY OF SEROMA FORMATION AFTER MODIFIED RADICAL MASTECTOMY IN PATIENTS WHO RECEIVE NEO-ADJUVANT CHEMOTHERAPY

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Abstract

Background: Breast cancer is among the commonest of causes of the death caused due to cancer in the females throughout the world.

Objective: To determine the frequency of Seroma formation in patients undergoing Modified Radical Mastectomy after neoadjuvant therapy.

Methodology: Study Design: Comparative cross-sectional study. Place and Duration of Study: Department of Surgery, Chandka Medical College Hospital, Larkana from November 2019 to January 2022. A total of 217 diagnosed cases of breast carcinoma patients who underwent a modified radical mastectomy after initially receiving neoadjuvant chemotherapy were selected for this study. Pre-designed proforma was used to collect information related to different variables.

Results: The average age of the women was 47.29±8.38 years. Frequency of seroma formation in patients undergoing modified radical mastectomy with neo- adjuvant therapy was found in 41.94% (91/217). Average seroma Volume and number of resected lymph nodes was 56.64±5.64 ml and 7.59±1.08.

Conclusion: Seroma formation following Modified Radical Mastectomy with neo – adjuvant therapy was almost 42%. We identified no potential risk factors other than the pathological status of tumor which was associated with increased frequency of seroma formation.

Keywords: Breast cancer, Modified radical mastectomy (MRM), Neo – adjuvant therapy, Seroma formation.

Article Citation: Rabab U, Shaikh A, Fatima S, Sandano M. Frequency of seroma formation after modified radical mastectomy in patients who receive neo-adjuvant chemotherapy. JSZMC 2022;13(3):03-07. DOI: <https://doi.org/10.47883/jszmc.v13i3.218>

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Introduction

Breast cancer is the most common cancer in the United States and is the second commonest cancer in Indo-Pak. It is also the commonest cause of deaths due to cancer in females throughout the world.¹⁻³ Depending upon initial stage of tumor at the time of diagnosis various surgical treatment options ranging from Breast Conservation therapy to mastectomies are available. Such surgical treatment options can be used upfront or after a neo-adjuvant chemotherapy (NAC) to downstage the initial tumors so as to facilitate subsequent surgery with negative margins. Worldwide trend of breast conserving surgery is increasing due to advances in chemotherapy regimen and timings as well as use of various oncoplastic procedures, however, Modified radical mastectomy (MRM) is still the more widely used treatment modality in Pakistan because of delayed presentation of patients with tumors of relatively large size and nodal involvement, vague surgical practices and unreliable patient follow up.¹⁻² Post surgery, various complications may ensue. The most

frequent complication of the procedure is seroma formation.

Seroma is a sterile serous collection develops under the skin flaps or in the axillary dead space after surgical intervention.³

Seroma occurs in almost every patient post-mastectomy and now mostly perceived as a side effect of surgical procedure rather than a surgical complication.⁴

Although it is not a life threatening complication but it significantly increases days of hospital admission and compromises quality of life of patient and ultimately increase burden of disease and over stretch health budget.⁵ The reported incidence of seroma formation varies widely between 15 to 18%. There are differing opinions with regard to exact etiology of seroma formation. Several factors have been implicated in seroma formation like the extent of lymph node clearance, number of positive nodes, the use of postoperative radiation and whether intraoperative lymphatic channel ligation was done or not. Other factors like age, hypertension and weight are also associated with Seroma formation

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Received: 05-04-2022

Published: 10-08-2022

and reported by many researchers⁶⁻⁹ Other school of thought suggest that increased frequency of seroma formation is possibly related to early removal of drains, but this is not a well-accepted concept for the pathogenesis.¹⁰

Literature shows that with conservative breast surgery chances of seroma formation are lower because less dead space forms with this procedure. Similarly there is evidence of decreased seroma formation with immediate implant based reconstructions is carried out.⁸

Researchers also observed relation between neo-adjuvant therapy prior to MRM and seroma formation. In this regard, different studies showed contrasting results whereby some studies concluded low volumes of seroma formation with NAC, whereas other studies showed no such association. This factor therefore needs to be validated by various studies for a better evidence generation.⁹

While the small seroma formation responds to expectant management or aspiration, it can also lead to further complications ranging from infective complications to dehiscence of wound and flap necrosis which may result in increase in overall recovery period and delay to start subsequent adjuvant treatments.¹¹

This aim of this study was to determine the frequency of seroma formation in patients who underwent MRM after neo adjuvant therapy; besides it also explored association of seroma formation with other factors as identified in literature.

Methodology

This descriptive case series was conducted at Department of surgery, Chandka Medical College Hospital Larkana from November 2019 to January, 2022.

The sample size of 217 subjects was calculated by WHO sample size calculator using 95% confidence interval 95%, 5 % margin of error and anticipated proportion of patients with Seroma formation as 17.2%.

It included all consenting female patients of 15-65 years of age with biopsy proven non stage IV breast cancer who initially received neo-adjuvant chemotherapy followed by modified radical mastectomy and thus were managed with curative intentions. Exclusion criteria included patients with stage IV disease at the time of diagnosis and

those patients with early breast cancers in whom surgery was performed upfront without prior NAC. Patients older than 70 years of age and with severe, comorbid who did not receive treatment and the patients who lost to follow up.

Using non – Probability consecutive sampling technique, all consecutive patients admitted to the surgical ward units I,II and III of Chandka medical college teaching hospital for surgical intervention who met inclusion criteria were enrolled in this study. Written informed consent was obtained from all. Exclusion criteria were followed strictly to avoid confounding variables. All information of variables was recorded in pre designed proforma.

Data was analyzed on SPSS, Version 20. Percentage and frequency was calculated for categorical variables.

Mean and standard deviation was calculated for quantitative variables like age of patient, height, weight, BMI and duration of disease, Seroma volume, no of resected lymph nodes, tumor size, duration of disease and categorical variables.

Effect modifiers such as age of patient, height, weight, BMI, tumor size, duration of disease, residence, educational status, occupation, marital status was controlled by stratification. Post stratification chi square test was applied. A P-value less than or equal to 0.05 was considered to be statistically significant.

Results

A total of 217 histologically proven female patients of breast carcinoma were selected for this study. All underwent modified radical mastectomy after receiving neo-adjuvant chemotherapy. The average age of the women was 47.29±8.38 years. Other demographics like average weight, height, BMI and duration of disease are given in table I. 8.76% women had less than 2 cm tumor, whereas 46.5% had tumour size of 2-5cm and 44.7% had more than 5cm. The average weight of resected mammary tissue was 97.34±11.74 gram and average size of tumour within the specimen was 4.60±1.77 cm.

Frequency of seroma formation in patients was 41.94% (91/217). Average seroma Volume was 56.64±5.64 ml and number of resected lymph node was 7.59±1.08. Stratification analysis was performed and it was observed that rate of seroma formation had no significant correlation with different age groups (p=0.877) as shown in table II. Similar observations were also noted for BMI and

size of tumor. Seroma formation was significantly high in stage III as shown in table 3.

Table I: Demographic characteristics of patients

Variables	Mean	Std. Deviation	95% Confidence Interval for Mean	
			Lower Bound	Upper Bound
Age (Years)	47.29	8.38	46.17	48.42
BMI (kg/m ²)	25.95	3.49	25.47	26.41
Duration of disease (months)	9.03	1.67	8.81	9.26

Table II: Frequency of seroma formation in patients undergoing modified radical mastectomy With neo – adjuvant therapy By age groups

Age Groups (Years)	Seroma Formation		Total	P-Value
	Yes	No		
≤40	23(46%)	27(54%)	50	0.877
41-50	41(41%)	59(59%)	100	
51-60	21(42%)	29(58%)	50	
>60	8(35.3%)	11(64.7%)	17	

Chi-Square=0.683

Table III: Frequency of seroma formation in patients undergoing modified radical mastectomy with neo – adjuvant therapy By BMI and stage of disease

BMI	Seroma Formation		Total	P-Value	Chi-Square
	Yes	No			
≤25	31(34.4%)	59(65.6%)	90	0.092	4.77
25.1-29.9	49(50%)	48(50%)	96		
≥30	12(38.7%)	19(61.3%)	31		
Stage					
Stage I	1(14.3%)	6(85.7%)	7	0.003	11.90
Stage II	71(38.8%)	112(61.2%)	183		
Stage III	19(70.4%)	8(29.6%)	27		

Discussion

Breast cancer is the second leading cause of cancer death among women.¹⁻⁵ Depending upon primary stage of tumor, surgical treatment includes mastectomy, modified radical mastectomy or breast conservation. Though the trends toward breast-conserving therapy is developing, as many as 70% of women diagnosed with breast cancer undergo mastectomy as primary surgical treatment.⁷ Mastectomy is associated with few

significant complications. Wound seroma is the most common early complication, with a reported rate of 3% to 60%.⁹⁻¹⁰ It has been assumed that all patients develop seromas after a mastectomy.¹³ Most patients after mastectomy develop it and is now increasingly being considered as a side effect of surgery rather than a complication. However, all patients are not clinically symptomatic¹⁰. Though seroma is not a life threatening complication, it is associated with the significant morbidity (e.g. flap necrosis, wound dehiscence, predisposition to sepsis, prolonged recovery period, multiple physician visits and may delay adjuvant treatments. In this study we determined the frequency of seroma formation in patients undergoing Modified Radical Mastectomy who received neo – adjuvant therapy, a total of 217 histopathologically proven breast cancer patients ranging from 15-65 years of age were selected.

In our study, frequency of seroma formation was found in 41.94% (91/217). A study by Bhatti et al, conducted in 2004 to study complications after modified radical mastectomy, reported seroma formation in 20% cases.¹⁴ Another local study conducted in 2004, to identify the early complications of modified radical mastectomy concluded wound infection as the commonest complication occurring in 16.6% patients and Seroma formation occurred in 17 patients (14%).¹⁵ In a retrospective study, early complications as noted from history and medical records, reported seroma formation 20%, wound infection 18% and skin flap necrosis in 02% patients¹⁶. Others have reported seroma formation in 100%¹², incidence rate of wound infection ranging from 6-14%¹³ and necrosis in 8-60%¹⁶ of cases. A study conducted in 2003 by Gonzalez et al found overall seroma rate of 15.8%. Procedure specific seroma frequency was 19.9% following MRM and in 9.2% after breast-conserving surgery (p=0.01).¹⁷ Seromas are usually painless, but discomfort may be associated with these and have been linked to wound infection, problems with wound healing, and lymphedema. Its occurrence also may delay the start of adjuvant therapy.¹²⁻¹³ Most seromas are usually treated with the repeated aspirations. Chilson et al reported an average of three extra office visits for treatment of seromas.¹⁸ Tadych and Donegan noted that almost one fourth of the seromas in their study persisted for over 6 weeks, and in some cases, required open drainage for complete resolution. Thus, the cost of care for breast cancer patients may be increased as a result of wound

seroma formation.¹⁹ Many factors have been evaluated for the cause of this problem, including age of the patient, obesity, type and extent of mastectomy, experience of the operator, and type of wound drain.²⁰ In our study the age ranged from 15-65 years while the average age of the women was 47.29±8.38 years. A direct correlation has been shown to exist between the age of the patient and the development of seroma.²¹ Surprisingly, our study did not find any association between age and frequency of seroma formation. As shown in table III there was no effect of BMI on seroma formation in our study, whereas seroma formation was most frequently observed in stage II and stage III. Few studies had found a positive correlation between body weight and seroma formation,²²⁻²³ In contrast no association was observed with respect to nodal status or positivity of LNs,²³⁻²⁴ and stage.²¹ Similarly, one study found a significant association with other factors such as grade, histological type, and pathological tumor size¹⁷⁻¹⁹ Our study did not include long term complications and other short term complications such as pain, strength and range of arm exercises, bleeding and lymphedema, which might have contributed to or be sequel to seroma formation and thus remains the major limitation of our study. Moreover, our study provides institute specific overall seroma formation rates Modified radical mastectomy (MRM) associated with preceding neo-adjuvant chemotherapy and does not compare this cohort with frequency of seroma formation when surgical procedures are performed upfront.

Conclusion

The results of our study suggest that seroma formation in patients undergoing Modified Radical Mastectomy with neo-adjuvant therapy is 42% which is independent of patient age, weight, height and BMI. In conclusion, the prediction of seroma formation following Modified Radical Mastectomy with neo – adjuvant therapy remains challenging. We identified no potential risk factors other than the pathological status of tumor which is uncontrollable factors. The high frequency of seroma formation observed in our study warrants active interventions to decrease this complication rate. Future studies comparing seroma formation when surgical procedures are performed upfront without prior neo adjuvant chemotherapy should be encouraged to validate

the contradictory evidence available regarding incidence of seroma with neoadjuvant chemotherapy.

Authors Contribution: **UR:** Conception of work, Acquisition and analysis of data and drafting. **AS:** Design of work Interpretation of data and revising. **SF:** Conception of work, Design of work and drafting. **MS:** Acquisition and analysis of data drafting.

All authors critically revised and approve its final version.

Conflict of Interest: Authors has declared no conflict of interest.

Sources of Funding: The source of funding was self.

Disclaimer: None

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