



PROSPECTIVE OBSERVATIONAL STUDY OF WOUND COMPLICATIONS AFTER BREAST SURGERY FOLLOWING NEOADJUVANT CHEMOTHERAPY IN A TERTIARY CARE CENTER FROM SOUTHERN INDIA.

Breast Surgery

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ABSTRACT

Introduction: Breast cancer is the most common cancer. One in 29 women in India develop breast cancer during their lifetime. Even though surgery is definitive treatment, Neoadjuvant chemotherapy improves survival and facilitates local therapy. Given the immunosuppressive nature of the drug, concern about increased risk of wound complications are always present. With this background we conducted a prospective observational study of the incidence of wound complications in patients who received neoadjuvant chemotherapy and underwent surgery.

Method: Prospective observational study was done on the patients attending our Institute with history of breast lump and histologically proven malignancy. Data was collected from patients after obtaining their consent. All wound complications were recorded and following results were formulated.

Results: The study involved 52 patients. At the time of presentation, the average age was 48.17 +/- 10.25 years. Overall, 25% of patients had wound complications, with wound infection accounting for 11.53 percent, seroma for 5.76 percent, and flap necrosis accounting for 13.46 percent. On days 1, 5, and 8, the average drain output was 190.3mL, 57.8mL, and 9.7mL respectively. The total number of days spent in the hospital was 7.92 +/- 2.57 days. The incidence of complications were 50% when associated with comorbidities which was significantly higher at p=0.04 when compared to patients who had no comorbidities. When compared to other research, the rates of complications were similar.

Conclusion: We believe that adding Neoadjuvant chemotherapy to a patient's treatment plan does not enhance the likelihood of wound complications.

KEYWORDS

Breast Cancer, Neoadjuvant Chemotherapy, Wound Complications, Wound infections, Seroma, Flap Necrosis

INTRODUCTION

Breast cancer is the most frequent malignancy in women and the primary cause of cancer death. In India, one out of every 29 women gets diagnosed with breast cancer at some point in their lives (Mathur et al., 2020). The incidence of breast carcinoma in India is 25.8 per 100,000 Women and mortality of 12.7 per 100,000 women (Malvia et al., 2017). Complete removal of the tumor is a definitive therapy. In these patients, preoperative or neoadjuvant chemotherapy (NACT) is a treatment with the dual goals of enhancing survival and making local therapies easier (Thompson & Moulder-Thompson, 2012).

Down staging results with a small increase (7 to 12%) in breast conservation rates in predominantly operable tumors, and NACT may convert a previously unresectable, locally progressed breast cancer to an operable tumor (De Lena et al., 1981; Schott & Hayes, 2012). Therapy provides for direct and early monitoring of a patient's response to therapy, which could lead to treatment plan revisions in the event of a poor response. Any patient who is expected to require systemic treatment should investigate NACT as a treatment option. Given that neutropenia is the most prevalent chemotherapeutic side effect, there has been worry about the increased risk of postoperative problems (Kumar et al., 2018).

With the advent of NACT, the treatment of breast carcinoma has been revolutionized. There is a shift from a radical approach to a more conservative approach in treatment of breast cancers. More and more breast cancers are being treated with breast conservative surgeries. NACT is a tool used to down stage the disease and also allow us to conserve the breast. Apart from breast conservation, it also helps in addressing the microscopic systemic metastasis in locally advanced breast carcinomas (Mieog & van de Velde, 2009; Specht & Galow, 2009).

Use of NACT, however, alters the physiological status of the patient. Thus can lead to impaired wound healing, decreased immune status, susceptible to infections (Wargo et al., 2015). These alterations can increase the risk of wound complications when a patient is subjected to surgery, which formed the objective of our study.

MATERIALS AND METHODS

Study Design

This is a prospective observational study of the patients attending our institute for the treatment of breast carcinoma during the period of November 2013 to November 2015. Study was presented in the

Institutional Ethical Committee and approval was obtained (No/VIMS/PG/IEC/12/2013-14).

INCLUSION CRITERIA

Any female patient with a history of swelling in the breast and pathological evidence of breast carcinoma, requiring systemic therapy. Patients willing to participate in the study.

EXCLUSION CRITERIA

The following patients were excluded from our study- Inoperable stages of breast carcinoma, Patient who has taken previous chemotherapy/radiotherapy, Patient with residual or recurrent disease following any form of treatment.

Data Collection

All patients intended to be included in our study was explained regarding the same. After obtaining written informed consent from each individual, patients were subjected to NACT followed by surgery. Data was collected in the proforma which consisted of, Demographic details including name, age, sex, address, In-Patient registration number of our hospital. Disease details including symptoms and its duration, significant past history, clinical and pathological diagnosis, clinical staging of the disease. Details of chemotherapy received: Drug and its dosage, number of cycles of chemotherapy received. Details of surgery performed. Number of days of hospital Stay. Details of the complications occurred.

Wound infection was studied using ASEPSIS Criteria (Wilson et al., 1986). Seroma was graded as no seroma, asymptomatic, symptomatic with single aspiration, symptomatic requiring multiple aspirations, symptomatic requiring biopsy or excision (Watkins et al., 2008). Hematoma is also graded similar to seroma. Flap Necrosis (Nykiel et al., 2014) was classified as minor or major, <30% or >30% respectively. Further intervention required is also considered. Intervention was categorized as moisturizing gel application, regular dressings, antibiotic ointment application, secondary suturing or debridement and split skin graft closure. Drain output in the form of amount and type of drainage was noted on day 1, day 5 and day 8.

STATISTICAL ANALYSIS

All the data collected were tabulated. Quantitative data were expressed in the form of percentage and qualitative data expressed in the form of mean. Chi-square test was used to identify statistical significance for quantitative data.

RESULTS

Total of 52 females were studied during the specified period. Mean age of presentation was 48.17 +/- 10.25 years. Among them three patients had diabetes, two patients had hypertension, two patients had obesity, two patients had hypothyroidism and one patient had nephropathy (Table 1).

Table 1: Demographic Details

Characteristics	Number of patients	Percentage
Age in years		
Mean	48	
SD	10.25	
Comorbidity	10	19.23
Diabetes	3	5.7
Hypertension	2	3.8
Obesity	2	3.8
Hypothyroidism	2	3.8
Nephropathy	1	1.9

Among the 52 patients, 49 patients received Adriamycin and Cyclophosphamide. One patient having nephropathy received four cycles of Taxanes and another patient received three cycles of Adriamycin and Cyclophosphamide followed by two cycles of Taxanes. All the drug doses were calculated according to the patient's body surface area. All patients subjected to NACT underwent surgery. 41 patients underwent Modified Radical Mastectomy (78.85%), 10 patients underwent Breast Conservative Surgery (19.23%). One patient had bilateral breast carcinoma, for which Breast conservative surgery for one side and Modified Radical Mastectomy for another side was done.

Number of patients who had complications was 13 (25%). Six (11.53%) patients developed wound infections, five patients had only erythema while one patient developed serous discharge which was treated with regular dressings. Incidence of seroma was in three (5.76%) patients, one patient was treated with single aspiration and two patients were treated with multiple aspirations. None of the patients developed hematoma. Seven (13.46%) patients developed flap necrosis, six patients were treated with regular dressings and one patient required debridement of flap which healed by secondary intention. Average drain output on day one, five and eight was 190.28 +/- 81.76mL, 57.78 +/- 57.78mL, 9.71 +/- 13.07mL respectively. The average number of days of stay in hospital was 7.92 +/- 2.57 days (Table 2).

Table 2: Complications Observed

Complications	Number	Percentage
Overall Complications	13	25
Wound Infections	6	11.53
Seroma Formation	3	5.76
Flap Necrosis	7	13.46
Mean Drain output in mL		
Day 1	190.28	
Day 5	57.78	
Day 8	9.71	
Hospital stay in Days	Mean	7.92
	SD	2.57

Among the 10 patients with comorbidities, five patients (50%) developed wound complications. While only eight patients (19.04%) without comorbidities developed complications. This difference reached statistical significance with $p=0.04$ (Table 3).

Table 3: Comorbidity and Complications

Comorbidity in Patients	Number of patients with complications		P Value
	Present	Absent	
Present	5	5	0.042
Absent	8	34	

DISCUSSION

This was a prospective study done in our institute to know the incidence of the wound complications that would occur after breast surgery following NACT. Several studies have been done on a larger scale in different parts of the world; a few of them have been described below and compared with our results. Overall, incidence of wound complications in our study was 25%. This was comparable to the wound complications occurring in other studies. Warren Peled et al described wound complication rate of 23% following NACT and

surgery (Warren Peled et al., 2010). Wound problems (3.4% vs. 3.1%, $p=0.4$) were uncommon with or without Neoadjuvant chemotherapy, according to Decker et al (Decker et al., 2012).

The incidence of wound infection in our study was 11.53%. Hoefler et al retrospectively showed a wound infection rate of 8.9% following mastectomy (Hoefler et al., 1990). Chen et al reviewed cases of Mastectomy and lumpectomy and concluded wound infection of 2.6–11.1% (Chen et al., 1991). Vinton et al reviewed 560 cases underwent Mastectomy, lumpectomy, Axillary dissection and showed wound infection of 13–15% (Vinton et al., 1991). The incidence of seroma formation in our study was 5.76%. This incidence was comparable with several studies. Pogson et al reported that seroma aspiration is necessary in 10% to 80% of mastectomy and axillary lymph node dissection cases (Pogson et al., 2003). Classe et al. reported satisfactory use of axillary padding in place of catheter drains in patients with breast cancer having Axillary dissection, with seroma development occurring in 22.2 percent of the cases (*Axillary Padding as an Alternative to Closed Suction Drain for Ambulatory Axillary Lymphadenectomy: A Prospective Cohort of 207 Patients With Early Breast Cancer* | *Breast Cancer* | *JAMA Surgery* | *JAMA Network*, 2021). The incidence of flap necrosis was 13.46%. Broadwater et al described flap necrosis in 11% vs 6%; $p=0.29$ (Broadwater et al., 1991). In a study of nearly 200 locally advanced breast cancer patients treated with mastectomy, about half of whom received prior chemotherapy, comparable operational morbidity was demonstrated; neoadjuvant patients actually had a decreased rate of postoperative seroma formation (Broadwater et al., 1991). Preoperative chemotherapy has little effect on surgical complication rates or delays postoperative treatment, according to Danforth et al (Danforth et al., 1990).

Our study shows that administering Neoadjuvant Chemotherapy does not increase the risk of wound complications following surgery. These results have been consistent across various studies. However our study showed that incidence of complications increased in patients with comorbidities.

The major drawback of this study is that it was not a randomized study, sample size not sufficient to consider significance achieved in presence of comorbidities, there was no comparative arm to give conclusive results.

CONCLUSION

Breast cancer being the most common cancer across the world, neoadjuvant chemotherapy has revolutionized the outcome not only by targeting micrometastasis but also downstaging the disease. Concerns about increased risk of wound complications owing to immunosuppressive nature of the drugs are always present. Our study has shown no increased incidence of wound complications in patients subjected to neoadjuvant chemotherapy. Hence, Neoadjuvant Chemotherapy can be used safely without any increase in the incidence of wound complications. However Randomized trials would give conclusive results.

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