Raised Blood Pressure as a Risk Factor of Post-Operative Seroma Formation in Patients of Modified Radical Mastectomy

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ABSTRACT
Despite seroma is rarely potentially lethal and is typically harmless, it can cause considerable sequelae such as flap necrosis, wound dehiscence, predisposes to infection. The objective of the study was to determine the association of raised blood pressure as a risk factor of development of seroma after MRM in breast cancer patients.

Material Methods: In this case control study, all women of age 30 to 70 years with MRM done for carcinoma of the breast of stage T2 and lymph nodes N2 were enrolled and followed for 3 days after MRM surgery for seroma formation. Out of total 122 patients, 64 patients were cases and 58 controls. Patients with disease upto N2 had level 2 clearances with upfront surgery. Age, history, of essential hypertension, compression bandage applied, serum albumin level, seroma formation and volume of seroma on 3rd post-operative day was documented.

Results: Mean age of the patients was 51.2 ± 9.5 years and 53.5 ± 10.8 years in case and control, respectively. Majority of the patients were of the age group 40 to 50 year’s age group. 56.3% (n=36) cases and 43.8% (n= 28) controls had history of essential hypertension. Seroma formation was seen in cases 51% (n=31) as compare to controls 13% (n= 8) with odd ratio OR 1.48. Drainage volume among two groups was analyzed as in case group, the drainage volume was 148.1 ± 76.4 ml (range 50 to 290) while in control group the drainage volume was 130 ± 56.9 ml (range 60 to 250) and was statistically significant with p-value <0.001.

Conclusion: Although the pathogenesis of seroma remains controversial, hypertension is the most consistent significant risk factor for seroma formation subsequent to modified radical mastectomy for carcinoma breast. Good pre, peri and post-operative blood pressure control can reduce the risk of seroma formation and the associated morbidity.

Keywords: MRM, Seroma, nodal clearance, breast cancer.

INTRODUCTION
Carcinoma of breast has been one of the most feared of human ailments, despite years of theoretical and academic investigation. It is the most frequent tumor in women in the United States and the second most common disease in India (1). It is also the major cause of cancer-related deaths among females worldwide. Positive family history, early menarche, late first pregnancy, nulliparity, and advance age at menopause all enhance the risk (2).

The illness can remain limited to the breast, disseminate to nearby lymph nodes (most usually axillary), or extend to distant body areas (most commonly bones, lungs, pleura and liver) (3). Breast carcinoma management is determined by the state of the emptying regional lymph nodes, the size of the cancer, whether the cancer contains hormone receptors and/or the protein HER2, the female’s age or reproductive status, and the existence of metastases (4). Management options might be localized, such as surgery or radiation (RT), or systemic, such as chemo, hormone treatment, or humanized monoclonal antibodies (5).

Based on the extent of the disease spread and other patient variables, the surgical therapy of choice for these individuals is either modified radical mastectomy (MRM) or breast conservation. ALND is a component of modified radical mastectomy and is the primary therapy for clinically positive or sentinel node biopsy (SNB) positive axillary lymph nodes (6).

Due to late patient diagnosis, surgical methods in popularity, and inconsistent patient check up, MRM is the most often utilized therapy method in Pakistan (7). Seroma development is the most common early consequence of breast carcinoma operations, with estimated rates ranging from 3% to 92 percent (8).

After a breast cancer mastectomy or axillary lymph node removal, a seroma can grow between the chest wall and skin. Unknown is seroma’s pathogenesis. Seroma can be caused by a large surgical field, lymphoid channel separation, a loose axillary skin hollow, and the region’s manoeuvrability and reliance. Seroma often occurs without explanation or paroxysmal indication. Some writers consider seroma as a “necessary evil” that affects a predicted percentage of people. (9).

The presence of malignant nodes in the axilla, past surgical biopsy, and usage of heparin has all been linked to an increased risk of seroma (10). Surgery can cause seroma. It’s more common if the folds are raised with diathermy rather than a surgical blade, and it’s more common in modified radical mastectomy than breast-sparing surgery, axillary lymph node dissection than sentinel lymph node dissection, and modified radical mastectomy without instantaneous reconstruction than with instantaneous reconstruction. (11).

Seroma is seldom dangerous and usually innocuous, but it can cause flap necrosis, wound dehiscence, infection, a long healing time, lymphedema, and repeated health checks. It can also postpone adjuvant treatment. (12). Seromas cause psychological pain in addition to financial costs and delayed healing. This can embarrass the surgeon, whose experience has little bearing on seroma after mastectomy. (13).

Several techniques have been used to reduce seroma. Most aim to reduce dead space behind skin flaps and drain collections. These include using bovine thrombin, fibrin glue, and sealant, suturing flaps to deeper tissues or fascia, and using tubes to remove buildup. (14).

MATERIAL AND METHODS
This case control study was conducted, after approval from ethical and research committee of hospital from 25/04/2020 to 24/10/20. All women of age 30 to 70 years with MRM done for carcinoma of the breast of stage T2 and lymph nodes N2 were enrolled and followed for 3 days after surgery for seroma formation.

Out of total 120 patients, 64 patients were enrolled in the case group and 58 patients in the control group. Cases were those women who underwent MRM for carcinoma breast with no documented raised blood pressure in post-operative period.
Seroma formation was noted in the post-operative period (initial 72 hours).

Any patient with drainage volume of more than 150 ml on 3rd post-operative day was labeled as having seroma formation. All the patients underwent level II axillary clearance. Patients with disease up to N2 were taken and only those with upfront surgery were included.

The purpose and goals of this research were given to all participants, and signed consent permission was acquired after stressing the use of the research and the importance of anonymity. Among both cases and controls, detailed history was taken along with careful scrutiny of past medical and surgical records. This was done to avoid confounders and possible bias in the study results.

All the observations, diagnosis of seroma and clinical assessments were conducted under supervision of a team of expert general surgeons. Patients having history of bleeding disorder, fungating carcinoma, intake of antithrombotic or antiplatelet drugs and Body Mass Index of > 25 were excluded because they act as confounders and will make the study results biased. Extreme care was exercised in the selection of cases and controls to avoid selection bias. Age, history of essential hypertension, compression bandage applied, serum albumin level, seroma formation and volume of seroma on 3rd post-operative day was demoted.

Data was analyzed using SPSS and chi square test was applied to compare the categorical variables to determine the statistical significance of difference between the two groups. Similarly, t-test was applied to compare continuous variables like age and seroma volume. p value calculated using these tests was taken significant below 0.05.

RESULTS

This study was conducted at Surgical Unit Mayo Hospital Lahore in which 120 cases were observed to determine the association of raised blood pressure with seroma formation in post-operative patients of modified radical mastectomy for carcinoma breast.

Mean age of the patients was 51.2 ± 9.5 years and 53.5 ± 10.8 years in case and control, respectively. Majority of the patients were of the age group 40 to 50 year’s age group. 56.3% (n=36) cases and 43.8% (n= 28) controls had history of essential hypertension. In our study, seroma formation was seen in cases 51% (n=31) patients as compare to controls 13% (n= 8) with odd ratio OR 1.488. Drainage volume among two groups was analyzed because they act as confounders and will make the study results biased. Extreme care was exercised in the selection of cases and controls to avoid selection bias. Age, history of essential hypertension, compression bandage applied, serum albumin level, seroma formation and volume of seroma on 3rd post-operative day was demoted.

Data of incidence of seroma formation was stratified for the data of history of essential hypertension, compression bandage done after surgery, and low level of serum albumin in all the patients was compared between the two groups, and post-stratification chi square was applied. Analysis showed that p value was significant for history of essential hypertension, and low serum albumin level.

Seroma formation was stratified among various age groups in both case and controls, but was not significant. Similarly, application of compression bandage for seroma formation was also not significant. t-test was applied for mean volume of seroma between the two groups, difference was statistically significant, p value <0.0001.

Table 1: showing the details of seroma formation with respect to age, essential hypertension, low serum albumin and compression bandage application. (n=120)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Prev. H/o Essential Hypertension</th>
<th>Seroma formation</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>Yes</td>
<td>30</td>
<td>5</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>Yes</td>
<td>8</td>
<td>29</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: One-Sample Statistics: Seroma Quantity

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>95% Confidence Interval of the Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>64</td>
<td>50</td>
<td>290</td>
<td>148.1</td>
<td>76.4</td>
<td>9.6</td>
<td>Lower: 116.29 Upper: 179.81</td>
</tr>
<tr>
<td>Control</td>
<td>58</td>
<td>60</td>
<td>250</td>
<td>130.0</td>
<td>56.9</td>
<td>7.5</td>
<td>Lower: 115.0 Upper: 145.0</td>
</tr>
</tbody>
</table>

DISCUSSION

Similar results were also observed in another study done by Akinci M et al 106 in which hypertension were found to be more likely to develop, 50% among the cases while 11% in controls. In another study done by Soomro SA et al 107 an incidence of seroma in 61% in hypertensive patients as compare to 5% in normotensive patients with relative risk of 12.72% (16) Given that age is generally associated with high blood pressure due to vascular sclerosis and nephropathy, our finding that hypertension was related to seroma production in the univariate rather than multivariate analysis is not surprising and is backed up by numerous other studies. (17, 18). Seromas can be created by inflammatory exudation or lymphogenous effusion, hence it is thought that increased blood pressure leads to seroma formation, most likely through extended contact area secretion. (19, 20).

There are disagreements on the effect of neoadjuvant chemotherapy on seroma development (21). We found no significant difference in seroma production among patients who had induction chemotherapy and those who did not (22). As a result, more research with a bigger sample size is needed to explain this issue. We found that low levels of total protein and albumin in serum were linked to a higher likelihood of seroma development, even when both median levels were all within normal limits. Seroma is a component of acute healing process that is dependent on proper feeding (23). According to this concept, assessing overall nutritional status, particularly total protein and albumin levels in serum, may be critical in predicting the incidence of postoperative seroma development (24,25). The daily drainage volume was substantially prognostic of eventual seroma development. (26).

Around four investigations on axillary lymph node dissection have uniformly found that the amount of LNs excised has no effect.
on seroma development (9, 10, 27, 28). Likewise, one researcher found that the degree of axillary lymph node dissection had no effect on seroma production (10). In Purushotham et al RCT in contrast, found that sentinel LN biopsy (SLNB) is linked with much less seroma development than standard axillary lymph node dissection (29).

In terms of chem radio, Say et al. found that pre- or postoperative radiotherapy had no effect on seroma production in individuals who underwent modified radical mastectomy (30). Additionally, in an RCT comparing neoadjuvant chemotherapy to upfront MRI, preoperative chemotherapy had no effect on seroma development (30).

Compression bandage of wound is a typical treatment used by many clinicians to limit seroma incidence (31). A research found that wearing a pressure clothing to minimise postoperative discharge after the axillary clearance for breast cancer is unnecessary (32). Nevertheless, we believe that wearing a compression garment and restricting arm movement for an extended period of time not only minimises seroma formation but also increases the likelihood of seroma formation following drain retrieval and may potentially induce shoulder pain.

Seroma formation after breast cancer surgery persists despite surgical improvements. Due to the controversial process of seroma production, it is unknown if/how successful it is to filter out persons who will get seroma, restricting prophylactic and therapeutic efforts. This study and others have looked for seroma risk factors as a strategy to compensate for the lack. To reduce seroma risk, limit discharge quantity and duration with local pressure, injections of exudate reduction and healing medicines, and increased blood total albumin levels.

CONCLUSION

Although the pathogenesis of seroma remains controversial, hypertension is the most consistent significant risk factor for seroma formation subsequent to modified radical mastectomy for carcinoma breast. Good pre, peri and post-operative blood pressure control can reduce the risk of seroma formation and the morbidity that is caused by this. However small sample size is the limiting factor to this study. More research must be undertaken to confirm this association.

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