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EVALUATION OF NIPPLE INVOLVEMENT IN CARCINOMA BREAST AND CORRELATION WITH TUMOR FACTORS.

Pathology

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ABSTRACT

This was a hospital based descriptive study. One hundred and ninety one therapeutic mastectomy specimens were included .Age range of patients was from twenty two to eighty seven years. Twenty specimens out of one hundred and ninety one cases had grossly retracted nipples with thirteen cases (65%) showing neoplastic involvement. Nine out of the remaining one hundred and seventy one grossly unremarkable nipples (5.26%) showed occult neoplastic involvement. Overall neoplastic involvement of nipple was 11.51% (22 out of 191). Location of tumour, nipple tumour distance and lymphovascular invasion showed significant association with nipple involvement. This study indicated a low frequency of neoplastic involvement of nipple in mastectomy specimens thus favouring replacement of conventional mastectomy with nipple sparing mastectomy in selected cases. This study also proposes a unique selection criteria for nipple sparing mastectomy.

KEYWORDS

nipple sparing mastectomy, neoplastic involvement of nipple, tumour

Introduction:

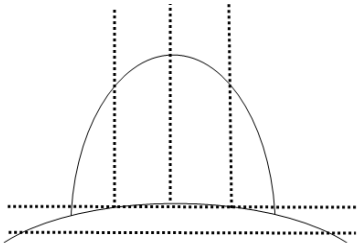
Early detection and subsequent management of breast cancer requires an integrated and multidisciplinary approach. Improvement in general awareness and easy accessibility to screening methods (eg: mammography) help in detection of cancer in an early stage Breast surgery has undergone a revolutionary change from the conventional radical mastectomy to less debilitating breast conservation surgeries. Breast conservation surgeries include subcutaneous mastectomy, skin sparing mastectomy, nipple sparing mastectomy (NSM) etc. Breast conservation surgery is not suitable for individuals with extensive and multifocal or multicentric carcinomas. Individuals who are undergoing mastectomy for cancer in preinvasive stage or risk reduction / prophylactic mastectomies (BRCA1/BRCA2 mutation) are the ideal candidates for breast conservation surgeries1. Reported frequency of occult involvement of grossly unremarkable nipples in therapeutic mastectomy specimens varies from 5.9% to 58%. Studies reported an inverse relation between neoplastic involvement and nipple - tumor distance. "Nipple involvement was reported in an average of 50% cases when the tumour – nipple distance was less than 2.0 cm whereas this decreases to 15-20% when the tumour – nipple distance was greater than 2.0 cm" 2. The aim of the present study is to find out the frequency of occult and overt neoplastic involvement of nipple and to evaluate the tumor factors associated with this involvement

Aim and Objectives:

To evaluate the frequency of neoplastic involvement of nipple, in mastectomy specimens. Association between tumour factors and neoplastic involvement of nipple were also studied.

Materials and Methods:

This was a hospital based descriptive study conducted in Department of Pathology, Amala Institute of Medical Sciences, Thrissur. One hundred and ninety one therapeutic mastectomy specimens received over a period of eighteen months were included. Mastectomy specimens of male patients, post lumpectomy and post neo adjuvant chemotherapy were excluded. A modified grossing protocol was applied for nipple grossing alone. Representative sections were examined following haematoxylin and eosin staining.

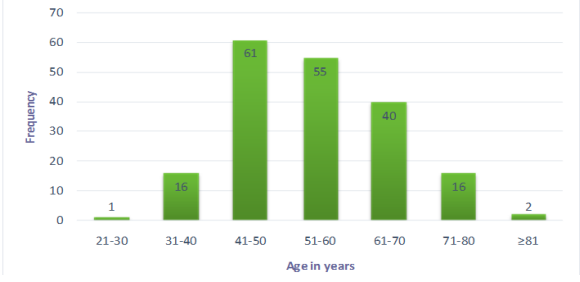


Mean, median and proportion were performed using Microsoft excel and SPSS. Chi – square analysis was to find association between neoplastic involvement of nipple and tumor factors.

Results:

Age range of patients was from twenty two to eighty seven years. Mean age was 54.98 years.

Graph 1: Age and tumor frequency distribution among patients.



Twenty specimens out of one hundred and ninety one cases had grossly retracted nipples with thirteen cases (65%) showing neoplastic involvement. Nine out of the remaining one hundred and seventy one grossly unremarkable nipples (5.26%) showed occult Neoplastic involvement.

Table 1: Gross appearance of nipple areola complex.

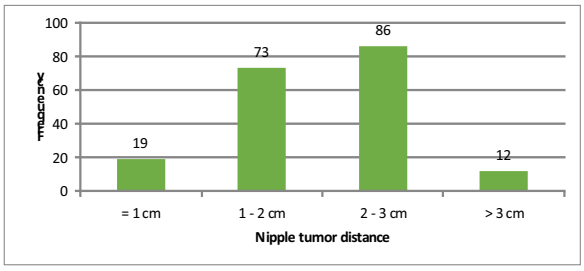
Appearance Of Nipple Areola Complex	Frequency	Percent
Normal	171	89.5
Retracted	20	10.5
Total	191	100.0

Overall neoplastic involvement of nipple was 11.51% (22 out of 191). Out of twenty two, nineteen cases showed direct extension of underlying malignancy and three cases were of Paget's disease. Location of tumour, nipple tumour distance and lymphovascular invasion showed significant association with nipple involvement In the 191 cases, 22 cases (11. 51 %) showed neoplastic involvement of nipple.

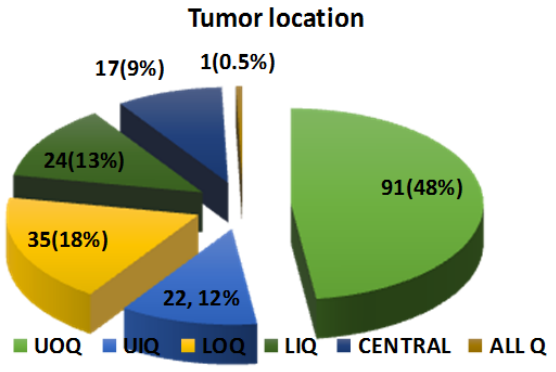
Table 2: Neoplastic involvement of nipple and frequency.

NEOPLASTIC INVOLVEMENT OF NAC	Frequency	Percent
ABSENT	169	88.48
PRESENT	22	11.51
Total	191	100.0

Graph 2: Nipple tumor distance and tumor distribution



Graph 3: Distribution of tumor among quadrants

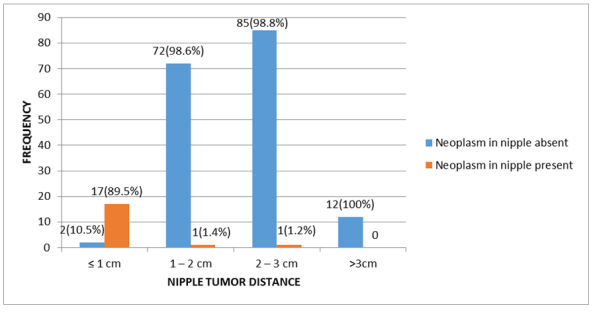


26 cases showed lymphovascular invasion in adjacent breast tissue

Table 3: Frequency distribution of lymphovascular invasion in adjacent breast tissue.

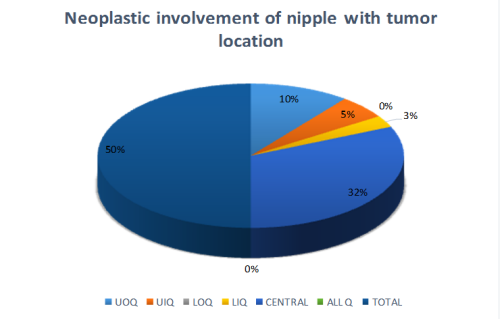
Lymphovascular invasion	Frequency	Percent
Absent	164	86.4
Present	26	13.6
Total	190	100

Graph 4: Association between nipple tumor distance and neoplastic involvement of nipple.

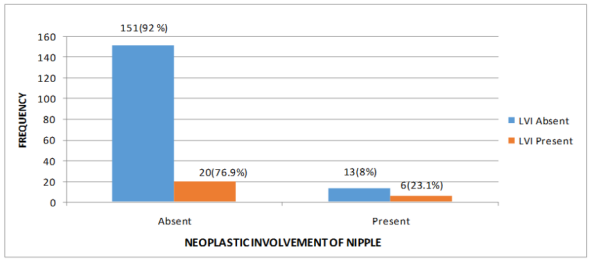


Correlation with neoplastic involvement of nipple and nipple tumor distance gave a p value of 0.0001, shows significant association between these two factors. Out of 19 cases, 17 cases were showed nipple tumor distance ≤ 1 cm.

Graph 5: Neoplastic involvement of nipple with tumor location.



Graph 6: Association between lymphovascular invasion and neoplastic involvement of nipple



Association between lymphovascular invasion and neoplastic involvement of nipple gave a p value of 0.03 (< 0.05), shows significant association between these two factors.

Discussion:

Operable breast cancers can be managed either by wide local excision or by mastectomy. Efficacy of each surgery to obtain local control and prolonged survival still requires further follow up studies. Nowadays as cosmetic and psychological consideration gain importance the trend for conservative surgery like nipple sparing mastectomy is increasing. Our study included 191 samples of mastectomy specimens. We could find out 11.51% (22 out of 191) neoplastic involvement of nipple comprising both overt and occult involvement. Considering occult involvement alone, it was found in 5.26 % (9 out of 171 cases) of cases with grossly unremarkable nipples. This value well matches with the recent publication by Reynolds et al 2011[3]. Even after including clinically retracted nipples, our study showed a lower range of neoplastic involvement (11.51 %). Reason for this may be because majority of our cases were small volume disease with lower stage at presentation which indirectly reveals efficacy of screening modalities and increased awareness about breast cancer among people

Weakness of this study is that the percentage of occult neoplastic proliferation is less than sufficient to come to a strong conclusion which can be applicable to the entire cohort of patients with breast cancer. This study is also subject to selection bias because tumors requiring such debilitating surgery could be more advanced than that requiring nipple preservation mastectomy Overall frequency of occult involvement in our series was 5.26 % (9 out of 171). If this value is further stratified, 8 out of 9 cases showed direct extension of underlying malignancy and one was a Paget disease. Microscopic extension of underlying malignancy was occurred in 4.6 % (8 out of 171). This value is more in keep with current statistics of breast cancer and so this frequency should be considered in patients contemplating nipple preservation for therapeutic mastectomy Our study also correlates neoplastic involvement of nipple and many tumor characteristics like nipple tumor distance, location of tumor,. Nipple tumor distance and central location of tumor proved significant association with nipple involvement. Of these nipple tumors distance was the most important one. Studies have shown an inverse relationship between nipple involvement and nipple tumor distance. Preoperatively it can be assessed by mammography. When this distance is less than 2.0 cm, neoplastic involvement of nipple is reported in 50% of cases. This value decreases to 15 – 20 % when nipple tumor distance is greater than 2.0 cm[2]. In our case mean nipple tumor distance of involved cases was 0.95 cm. Laronga et al [4] study on 286 mastectomy specimen revealed an association of nipple involvement with location of tumor (subareolar and multicentric). Simmons et al [5]showed an association only with central or retroareolar location of tumor. Size of tumor and nipple tumor distance show association with neoplastic involvement in Rusby et al [6] study. Brachtel et al [7] study on 232 mastectomy specimens revealed parameters like tumor size, nipple tumor distance, growth pattern of carcinoma, histological grade, show significant association with nipple involvement. Our study show significant association with central quadrant or subareolar location of tumor and with decreasing nipple tumor distance. In our study majority of invasive carcinoma with neoplastic involvement in nipple showed ductal carcinoma in situ component. Chi square test gave a significant p value of less than 0.05. This finding well correlate with study done by Brachet et al. [7]

Conclusion:

This study indicated a low frequency of neoplastic involvement of nipple in mastectomy specimens thus favouring replacement of

conventional mastectomy with nipple sparing mastectomy. This study and results reported in reviewed literature conclude that nipple preservation is oncologicaly safe in patients with defined selection criteria.

We are proposing a selection criterion for nipple sparing mastectomy based on this study:

This includes:
1. Grossly unremarkable nipple
2. Nipple tumor distance of more than 1 cm
3. Location other than central or retroareolar
4. No lymphovascular invasion or neoplastic involvement in retroareolar frozen section

Nipple – tumor distance is assessed clinically if possible. It can be assessed by mammography with ultrasound or MRI to obtain a precise distance. Retroareolar tissue from base of nipple should be removed and assessed by frozen section for the presence of lymphovascular invasion or neoplastic involvement. If this section is positive for either of these, nipple should not be preserved

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