

Positive Sentinel Lymph Node Biopsy in Breast Cancer Related to Tumor Characteristics - An Experience at Tertiary Care Hospital

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ABSTRACT

Objective: To assess the accuracy of sentinel lymph node biopsy in breast cancer, therefore, reducing the morbidity of axillary clearance in patients having clinically impalpable axillary lymph nodes.

Study Design: A Prospective study

Place and Duration of Study: This study was conducted at the Department of Surgery, Unit II, Chandka Medical College / Hospital, Larkana from January 2014 to December 2016.

Materials and Methods: All cases having histopathologically evidenced breast carcinoma with clinically no palpable axillary lymph nodes were included. In our study patients having clinically palpable lymph nodes, past history of ipsilateral breast operation, stage III& IV disease were excluded.

All patients underwent sentinel lymph node sampling before taking informed and written consent. In operation theatre, under general anesthesia, 2ml of a basic thiazine dye (Methylene Blue) infiltrated around primary breast lesion then applied manual rubbing technique for 2 minutes over the area. Surgical procedure of Simple mastectomy and sentinel lymph node biopsy performed after 30 minutes of infiltrating dye.

Results: Sixty patients after fulfilling the inclusion criteria were enrolled with mean age of 46 years $\pm$ 12 years. Two third of patients had right breast involvement and most of the patients presented with Intra ductal carcinoma (71.1%) and had estrogen receptor +/- progesterone receptor positive disease (55%).

Simple mastectomy with sentinel lymph node axillary sampling was performed. Majority of patients were in early T disease (T1 42%, T2 38%), while most of the patients had well and moderately differentiated gradetumors (88%). Sentinel node sampling revealed 35 cases positive, while 25 cases were negative. It has been observed that patients with sentinel node positivity had higher grades of disease and also more advanced T stage.

Conclusion: Infiltrating a dye is technically simple and reliable to detect a sentinel node in majority of cases. It is observed that this technique is more accurate in high grade and higher T stage tumors in breast cancer.

Key Words: Carcinoma breast, axillary sampling, sentinel node biopsy.

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INTRODUCTION

The detection of metastasis in axillary lymph nodes is a very important prognostic factor in breast cancer because of its impact on subsequent management and overall survival. Various methods are used to detect metastasis in axillary lymph nodes preoperatively.¹

Although some studies have used ultra-sonographic imaging techniques alone, others have used fine-needle aspiration (FNA) cytology with or without ultrasound guidance to improve the detection of metastasis.^{2,3}

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Multi-institutional studies have shown the safety of omitting axillary lymph node dissection (ALND) for women whose sentinel node (SN) is free of metastatic disease⁴. However, the American Society of Clinical Oncology recommend ALND for patients whose SN contains macro metastasis or micrometastasis.⁵ Sentinel node biopsy remained the state of art for staging of the patients with axillary node negative disease and axillary clearance was reserved for patients with clinically palpable nodes or for those who have positive disease on sentinel node biopsy.⁶

Introduction of sentinel lymph node biopsy has emerged as practice changing and currently axillary node dissection is not a practical option for patients with clinically negative nodes. Clinically positive nodes and inflammatory breast cancer are absolute contraindications for SLNB. Axillary lymph node dissection (ALND) is recommended for this group of patients to maximize locoregional control.⁷

The incidence of lymphedema, seroma and ipsilateral arm pain in post operative ALND reported 6 to 30%, which can be minimized with SLN biopsy. Several studies have shown that the risk of arm morbidity, particularly, sensory loss and shoulder abduction deficits, is significantly less in SLNB than ALND.⁸

Different methods for isolating the sentinel node are in clinical practice but methylene blue dye is more used as it is convenient and cheaper, with less skin hypersensitivity reaction as compared to isosulfanblue.⁹ It has been found that in 40 to 70% of breast cancer patients, sentinel nodes are only nodes to be involved with tumor without any additional non sentinel lymph node involvement.¹⁰

Various studies reported that patients having sentinel node positivity could be managed other than aggressive axillary lymph node dissection. SLNB is a reliable technique to assess the axillary nodal status for tumor metastasis.¹¹

The advantages of sentinel lymph node biopsy (SLNB) in breast cancer having histopathologically node negative patients, axillary lymph node dissection (ALND) can be discouraged is well established.¹⁰

The recent trend of management for staging the axilla is sentinel LN biopsy (SLNB), while patients having LNs positivity for metastasis need radiotherapy to the axilla, therefore, avoiding complications after ALND.¹² Non-surgical axillary treatment is beneficial, leading to reduced arm stiffness, pain, paraesthesia, and risk of lymphedema.¹³

The trend of sentinel lymph node biopsy is beneficial and rapidly rising as an innovative standard of care.¹⁴ Some studies suggested that by the use of two techniques in combination of methylene blue dye and radioisotope, very high accuracy rate may be achieved and fewer SLN may be missed as compared to single technique mapping.¹⁵ Combination of both the techniques increases the yield of SLN identification from 0% to 18% when compared to blue dye alone.¹⁶

The purpose of our study was to assess the accuracy of sentinel lymph node sampling, therefore, reducing the morbidity of aggressive axillary clearance in patients having negative axillary lymph nodes clinically, and to identify the factors associated with likely positive sentinel node biopsy.

MATERIALS AND METHODS

A prospective study conducted at Department of Surgery, Surgical Unit II, Chandka Medical College Hospital, Larkana, from January 2014 to December 2016.

Only female patients were included in our study. All patients were diagnosed cases of breast cancer with clinically negative lymph nodes in the axillae. Ultrasound axilla was done to evaluate the evidence of lymph nodes. Patients having stage III and IV disease, palpable axillary nodes, bleeding diathesis, were

excluded.

After obtaining written and informed consent and approval from institutional Ethical Review Committee, all patients were entered in specified proforma.

Information regarding name, age, sex, tumor grading, T stage/size of tumor according to TNM classification, site of breast involved, nodal involvement with sentinel node sampling noted. Information of patients like histological type, site of breast involved and hormone receptor status were also documented.

In operation theatre, all patients underwent sentinel lymph node mapping. Two ml of a basic thiazine dye (blue dye) was infiltrated around the tumor than applied the technique of manual rubbing the area for 2 minutes. Surgical procedure of simple mastectomy and sentinel lymph node sampling (dye stained lymph node), was performed after 30 minutes of infiltration of dye, and specimen sent for histopathology marked and labeled accordingly, as there was no facility available for frozen section in our institution.

Data was analyzed by using computer software program SPSS version 19. The correlation between two variables were evaluated by using chi-square, and student t-test. P-value < 0.05 was considered as significant.

RESULTS

Sixty patients with diagnosis of breast cancer were included in our study. All patients were female and mean age of patients was 46 years $\pm$ 12 years. All patients underwent simple mastectomy and ipsilateral axillary node sampling after injecting blue dye.

Majority of the patients were having Intra ductal carcinoma (IDC) on histopathology (Table 1). 43 patients (71.7%) were having IDC and 13 patients (21.7%) with Intralobular carcinoma and four patients had both IDC and ILC (6.7%). Most of the cases were in T Stage according to TNM stage, T1 stage 25 patients (41.7%) as compared to T2 stage in 23 patients (38.3%). While in advanced disease, T3 stage was found in 8 patients (13.3%) and T4 in 4 patients (6.7%). In Tumour Grading, in Grade 1, 29 patients (48.3%), in Grade II, 24 patients (40%) and in Grade III, only 7 patients (11.6%) (Table 1). Out of 60 patients, predominant Right breast was involved in 40 patients (66.7%) (Table 2). The hormone receptor positive disease was found in 45 patients, while 15 patients had the triple negative disease. Axillary node sampling detected in 35 cases with tumor involvement, while 25 patients were having no tumor involvement. Nodal disease was more detectable in patients with advanced grade and advanced T stage (Table 2), however no statistical significant results were found according to type of histopathology. All the sentinel lymph node positive patients after confirmation by histopathology were referred to oncologist for axillary radiotherapy.

Table No.1: Patient characteristics

Total number of patients	60
Mean age	46 years±12 years
Types of breast cancer	Intra Ductal Carcinoma (IDC) 43(71.7%) Intra Lobular Carcinoma (ILC) and 13(21.7%) IDC + ILC 4 (6.7%)
T stage according to TNM staging	T1 25 (41.7%) T2 23 (38.3%). T3 8 (13.3%) T4 4 (6.7%)
Tumor grading	Grade I—29 (48.3%) Grade II—24 (40%) Grade III—7 (11.6%)

Table No.2: Tumor Characteristics

Site of breast Involved		Right 40 Left 20	
Hormone receptor status		ER+, PR- 4 (6.7%) ER-, PR+ 6 (10%) ER+, PR+ 23 (38.3%) ER+, PR+, HER2Neu + 8(13.3%) Triple negative 15 (25%) ER-, PR-, Her2Neu+ 4(6.7%)	
Sentinel node involvement		Yes 35 No 25	
Sentinel node involved according to Grade		Sentinel node positive	Sentinel node negative
	Grade I	9	20
			05
	Grade II	19	p=<0.00
	Grade III	7	0
Sentinel node involved according to T Stage		Sentinel node positive	Sentinel node negative
	T1	9	16
	T2	14	09
	T3	08	00
	T4	04	P0.003
Sentinel node involved according to histopathology		Sentinel node positive	Sentinel node negative
	IDC	27	16
	ILC	6	7
	IDC+ILC	2	P=<0.53
			2

DISCUSSION

The incidence of cancer related deaths worldwide is highest among patients having carcinoma breast.¹⁷ The occurrence of carcinoma breast in our country is 24.4%, considered as the most common cancer in developing countries.¹⁸

Recently the carcinoma of breast is diagnosed earlier because of implementation of screening methods in advanced countries, therefore the involvement of axillary lymphnode metastasis is declining.¹⁹

In some studies sentinel lymphnode in the axilla is the most specific lymphnode positive for metastasis in 40% to 60% of cases after SLND. In other studies the technique of sentinel lymphnode biopsy without further axillary dissection is positive in clinically node-negative breast cancer patients.²⁰

Despite the increasing knowledge that many women will not have additional nodal metastasis at completion ALND, the management of the patient with clinically negative, histologically positive lymph nodes has not changed, and ALND remains the gold standard.

In axillary nodes the tumor involvement in both cases of which no S L N was detected correlates that there were poor selection of patients, and failure of the S L N to take up the blue dye, rather than failure of technique.²¹

Worldwide increased awareness in females, recent screening techniques for early detection of cancer, and introduction of breast conservative surgery technique, has reduced the incidence of breast cancer in developed countries.²²

In last 20 years, various reports on SLNB technique suggested the benefits of the retrieval node biopsy as an accurate method of detecting axillary LN metastasis in patients having breast cancer.^{23, 24}

It is considered that an alternative technique to axillary lymph node dissection in early breast cancer. Therefore, this technique is more appropriate and minimal invasive method for staging the tumor, leading to reduce the morbidity by discouraging aggressive axillary lymph node clearance.²⁵

However, sentinel node biopsy has emerged as an alternate to axillary surgery in breast cancer. The false negative rates are variable in various studies from 0% to 19%. Some studies reported that size of tumor has directly effects on node positive cases despite tumor type and behaviour.^{26, 27}

In our study despite clinically negative axillary nodes and smaller tumor size, sentinel lymph nodes reports were positive for metastasis and negative for large tumor size. This shows association of different factors rather than tumor size in our study.

Other studies revealed that the size, site, the grade of tumor, and lymph nodes in the axilla remained as independent variables of nodal metastasis.²⁸

However, the number of lymph nodes or tumor factors predicts high false negative results. Therefore, patients having T1 and T2 tumors may be appropriate for SLNB. Thorough clinical examination of the axilla should be undertaken to palpate the axillary lymph nodes so that these should not be missed. This technique worldwide accepted for T1 and T2 lesions, and in larger tumors remain controversial.²⁹

In our study 4 patients with locally advanced cancer (T4), clinical and ultrasonological examination revealed axillary lymph node negative, while in all these four patients sentinel lymph node removed were found positive for tumor metastasis, later referred to oncologist for radiotherapy to the axilla, therefore axillary dissection/clearance was avoided.

CONCLUSION

Our study revealed that patients with sentinel node positivity had higher grades of disease and also more advanced T stage, while sentinel node positivity does not differ on the basis of histopathological type of breast cancer.

Author's Contribution:

Concept & Design of Study:	Muhammad Saleem Shaikh
Drafting:	Muharram Ali
Data Analysis:	Muharram Ali & Muhammad Saleem Shaikh
Revisiting Critically:	Muharram Ali & Kheo Ram Dholia
Final Approval of version:	Muhammad Saleem Shaikh & Kheo Ram Dholia

Conflict of Interest: The study has no conflict of interest to declare by any author.

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