



ANALYSIS OF PREDICTIVE FACTORS OF AXILLARY LYMPH NODE METASTASIS IN BREAST CANCER PATIENTS

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ABSTRACT**Aim:** To evaluate the predictive factors for axillary lymph node metastasis in breast cancer patients.**Materials and methods:** Patients diagnosed with invasive breast carcinoma and underwent modified radical mastectomy were included in the study. Parameters like histological grade, ER, PR and HER2 status were analyzed.**Results:** 25% of grade 1 cases showed positive nodal metastasis. Grade 2 and 3 tumors showed 36% and 50% nodal positivity respectively. 48% of ER positive tumors showed nodal metastasis whereas 50% of ER negative cases had positive nodes. Out of the 25 cases that showed PR positivity, nodal metastasis was seen in 52% of cases. Positive lymph node metastasis was seen in 76% of cases with HER2 positivity and only 37% of cases with HER2 negativity.**Conclusion :** Higher grade and HER2 positivity were associated with increased lymph node metastasis.**KEYWORDS :** Axillary lymph node metastasis, histological grade, ER, PR and HER2 status**INTRODUCTION**

Breast cancer is the second most common form of cancer^{1,2} and the most common cancer type in women³. Axillary lymph node status is an important factor in determining the staging, prognosis and treatment of breast cancer patients⁴. The widely accepted standard treatment in patients with invasive breast cancer includes axillary lymph node dissection. This helps in the accurate assessment of lymph node status. But only 33.2% to 39% of patients show axillary lymph node metastasis^{5,6,7} and approximately 60-70% of patients underwent unnecessary invasive axillary dissection. Several predictive factors of lymph node metastasis have been described. This study was done to analyze the correlation of certain predictive factors described in other studies with axillary metastasis so that it can be used as a guide for axillary management decisions.

MATERIALS AND METHOD

55 patients with invasive breast carcinoma who underwent modified radical mastectomy were included in the study. Parameters like histological grade, ER, PR and HER2 status were analyzed. Nottingham's index was followed to assess grade of the tumor. Aldred's scoring system was used to assess ER, PR and HER2 status. Number of cases with positive and negative nodal metastasis was determined and correlated with those parameters.

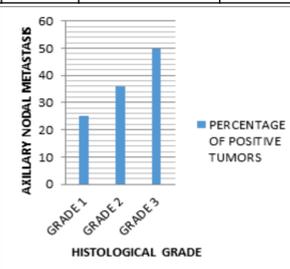
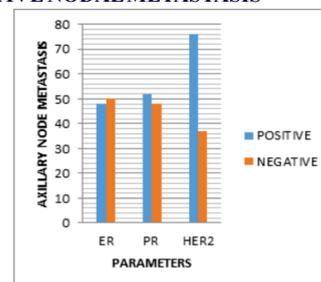
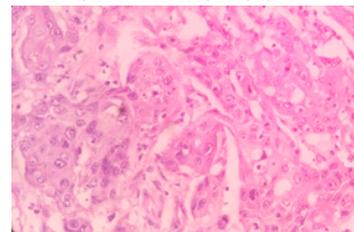
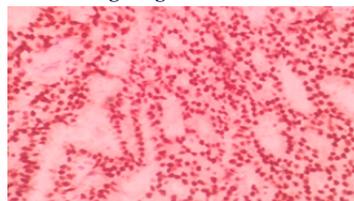
RESULTS

A total of 55 cases were included in the study. Out of 55 cases 4 cases showed histological grade 1, 25 cases showed grade 2 and 26 cases were grade 3. 25% of grade 1 cases showed positive nodal metastasis. Grade 2 and 3 tumors showed 36% and 50% nodal positivity respectively. 25 cases were ER positive and the rest were negative. About 48% of ER positive tumors showed nodal metastasis whereas 50% of ER negative cases had positive nodes. Out of the 25 cases that showed PR positivity, nodal metastasis was seen in 52% of cases. In PR negative tumors, about 46% cases had positive nodes. Positive lymph node metastasis was seen in 76% of cases with HER2 positivity and only 37% of cases with HER2 negativity.

Table 1: RELATIONSHIP OF FACTORS WITH LYMPH NODE METASTASIS

PARAMETERS	TOTAL CASES	POSITIVE AXILLARY LYMPH NODE METASTASIS	NEGATIVE AXILLARY LYMPH NODE METASTASIS	PERCENTAGE OF NODAL POSITIVITY (%)
Grade 1	4	1	3	25
Grade 2	25	9	16	36
Grade 3	26	13	13	50
ER Positive	25	12	13	48
ER Negative	30	15	15	50
PR Positive	25	13	12	52

PR Negative	30	14	16	48
HER2 Positive	17	13	4	76
HER2 Negative	37	14	23	37

**CHART NO. 1: ASSOCIATION OF HISTOLOGICAL GRADE WITH POSITIVE NODAL METASTASIS****CHART NO.2: ASSOCIATION OF HORMONE RECEPTORS WITH POSITIVE NODAL METASTASIS****Fig.1 Tumor with histological grade 3****Fig.2 Tumor with ER nuclear positivity**

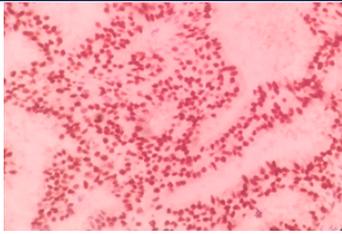


Fig.3 Tumor with PR nuclear positivity

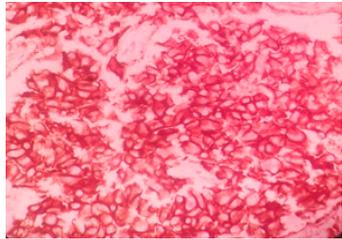


Fig.4 Tumor with HER2 membrane positivity

DISCUSSION

Axillary lymph node metastasis is commonly the earliest detectable clinical manifestation of metastatic breast cancer⁸. As nodal status determines the staging, prognosis and treatment of breast cancer patients, the understanding of predictive factors of nodal metastasis helps in better treatment options for patients.

In our study histological grade had a significant role in axillary lymph node metastasis. Grade 3 tumors had a higher percentage of metastasis compared to lower grade tumors. A study by Ding J. et al⁹ has concluded that combination of patient's age, tumor size and grade could effectively predict metastasis. Histological grade was also considered as the third predictor of metastasis in the studies conducted by Yenidunya S. et al¹⁰ and Tseng H S. et al¹¹. Even though grade of tumor is an important predictor of nodal metastasis it cannot be considered as an independent predictor.

Regarding the relationship between ER status and lymph node metastasis, out of 25 ER positive cases, 12 cases showed nodal metastasis and out of 30 ER negative cases, 15 cases showed nodal positivity. According to Majid S. et al¹² possibility of metastasis with negative ER status has not been established clearly compared with receptor positive tumors. This correlated with our study because the difference of percentage between ER positive and negative tumors with metastasis was not very significant.

Progesterone negative tumors were associated with lower risk of lymph node metastasis compared to PR positive tumors in our study. Viale G. et al¹³ showed a similar result in their study and PR negativity was associated with a 27% lower risk.

In our study the association between hormone receptor status and lymph node metastasis was not very significant. Many recent studies^{3,9,14} have also reported similar lack of association between hormone receptor status and lymph node metastasis.

The association between HER2 expression and axillary lymph node metastasis was very significant in our study. The nodal positivity was 76% in HER2 positive cases and it was only 37% in HER2 negative cases. Tong Z J. et al¹⁵ also showed that HER2 overexpression promoted nodal metastasis. Wolff et al¹⁶ and Duran et al¹⁷ also suggested that HER2 expression was related to worse prognosis and rising possibility of lymph node metastasis. Cabioglu et al¹⁸ also pointed out that HER2 expression might be a biological signature in predicting lymph node metastasis. VEGF-C is a key factor that promotes lymph node metastasis of tumor cells by increasing lymphangiogenesis¹⁹. HER2 over expression was proved to be correlated with increased expression of VEGF-C in breast cancer²⁰.

CONCLUSION

To conclude higher grade and HER2 positivity were associated with increased lymph node metastasis. There was no significant association between hormone status and nodal metastasis. Our findings may play a role in guiding axillary treatment considerations if further confirmed in larger sample sized studies.

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