Section: Pathology

Original Research Article

EGFR EXPRESSION IN TRIPLE NEGATIVE BREAST CARCINOMA: A COMPREHENSIVE STUDY

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ABSTRACT

Background: Triple Negative Breast Carcinoma (TNBC) is an aggressive form of breast cancer, defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2/neu expression. The Epidermal Growth Factor Receptor (EGFR), a transmembrane tyrosine kinase receptor, has emerged as a potential therapeutic target and prognostic indicator in Triple negative Breast carcinoma. This study aims to evaluate the immunohistochemical expression of EGFR in triple-negative breast carcinoma and to correlate its relationship with various clinicopathological parameters. **Materials and Methods:** This retrospective study included 60 cases of triple negative breast carcinoma and was conducted in the Department of Pathology, Government Thoothukudi Medical College, over a period of 24 months. Formalin-fixed paraffin-embedded tissue blocks of histologically proven TNBC cases were analyzed. EGFR expression was assessed by immunohistochemistry and scored based on intensity and distribution of membranous staining. Statistical correlation with clinicopathological variables was performed. The results were analysed using the Statistical Package for the Social Sciences (SPSS) version 21.0. **Result:** EGFR expression was observed in 56/60 (93.3%) cases, with strong positivity primarily observed in high-grade tumors. In our study, EGFR expression showed a statistically significant association with increasing histological grade ($p = 0.001$). There was a positive correlation between strong expression of EGFR and both higher histological grade and tumor stage. **Conclusion:** EGFR is frequently overexpressed in Triple negative breast carcinoma and shows a significant correlation with high grade tumors. EGFR may serve as a valuable prognostic marker and therapeutic target in TNBC patients.

INTRODUCTION

Breast cancer is the most common malignancy worldwide among women.[1] Triple Negative Breast Carcinoma (TNBC) accounts for approximately 15–20% of all breast carcinomas, characterized by absence of Estrogen Receptor, Progesterone Receptor and HER2/neu expression.[2] Triple negative breast carcinoma is associated with a younger age at presentation, higher histological grade, and poor survival outcomes.

Unlike hormone receptor–positive or HER2-amplified breast cancers, TNBC lacks established targeted therapies, making management largely dependent on chemotherapy.

Epidermal Growth Factor Receptor (EGFR) is a transmembrane glycoprotein, also known as ErbB1, involved in cell proliferation, angiogenesis, differentiation, and survival. Expression of Epidermal growth factor Receptor has been reported in various epithelial malignancies, including Triple negative breast carcinoma, and is associated with high grade tumour and poor prognosis. This study was conducted to evaluate EGFR expression in TNBC and its clinicopathological significance.

Aims and Objectives

1. To evaluate the immunohistochemical expression of Epidermal growth factor Receptor in Triple Negative Breast Carcinoma.
2. To correlate Epidermal Growth Factor Receptor expression with clinicopathological parameters of patient age, tumor grade, and tumor stage.

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MATERIALS AND METHODS

Study Design: A retrospective study was conducted in the Department of Pathology, Government Thoothukudi Medical College, Thoothukudi.

Study Duration: 24 months (September 2022 to September 2024).

Study Sample: Formalin-fixed paraffin-embedded tissue blocks of breast carcinoma cases reported as Triple Negative Breast Cancer. Sixty cases of triple negative breast carcinoma were selected.

Inclusion Criteria

- Histopathologically confirmed Triple negative Breast carcinoma cases
- Adequate tissue for immunohistochemistry studies

Exclusion Criteria

- Cases with incomplete clinical data
- Inadequate tissue samples

Study Procedure: After obtaining approval from the Institutional Ethics Committee, clinicopathological details including age, tumor grade, and stage were retrieved from pathology records. All cases were confirmed to be negative for Estrogen Receptor, Progesterone Receptor and HER2/neu by immunohistochemistry.

EGFR immunohistochemical staining was performed on representative tumor sections. Slides were independently evaluated by two pathologists blinded to clinical details.

Evaluation of EGFR Staining

EGFR expression was assessed based on membranous staining of tumor cells:

Intensity Scoring

- 0 – No staining
- 1+ – Weak staining
- 2+ – Moderate staining
- 3+ – Strong staining

Distribution Scoring

- 0 – Negative
- 1 – <25% tumor cells
- 2 – 25–50% tumor cells
- 3 – >50% tumor cells

Total Score = Intensity × Distribution

- Score <3: Weakly positive
- Score ≥3: Strongly positive

Statistical analysis

The data obtained from our study was compiled and tabulated on Microsoft Excel worksheet and master tables were prepared accordingly. Suitable charts and diagrams were made for better presentation to analyze the data and conclusions were drawn accordingly. Data were analyzed using IBM SPSS statistics version 21.0. Chi-square test was used to assess association between categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

EGFR expression was detected in a large number of Triple Negative breast carcinoma cases.

Table 1: Age wise distribution of TNBC patients

Age Range (years)	Number of cases	Percentage (%)
≤30	0	0
31- 40	6	10
41-50	29	48.3
51-60	18	30
>60	7	11.6
Total	60	100

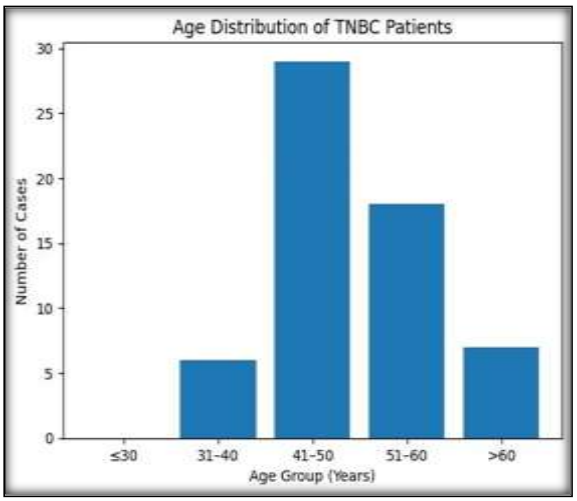

Chart 1: Age wise Distribution of TNBC patients

Observation and Interpretation:

This study included total of 60 patients with Triple-Negative Breast Carcinoma Age at diagnosis ranged from 31 to more than 60 years. Patients were grouped into five age groups for this analysis.

The 41–50 years age group was the largest proportion of cases (29/60; 48.3%), followed by the 51–60 years group (18/60; 30%). Patients aged 31–40 years constituted 10% (6/60), while 11.6% (7/60) were more than 60 years. No cases were noted in patients aged ≤30 years.

This distribution demonstrates that TNBC predominantly involved middle-aged women, with a peak incidence in the fourth to fifth decade of life. There is no statistically significant association between age group and EGFR expression in triple-negative breast carcinoma patients ($p > 0.05$).

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Table 2: Distribution of histological grade in TNBC

Histological Grade	Number of cases	Percentage (%)
Grade I	12	20
Grade II	21	35
Grade III	27	45
Total	60	100

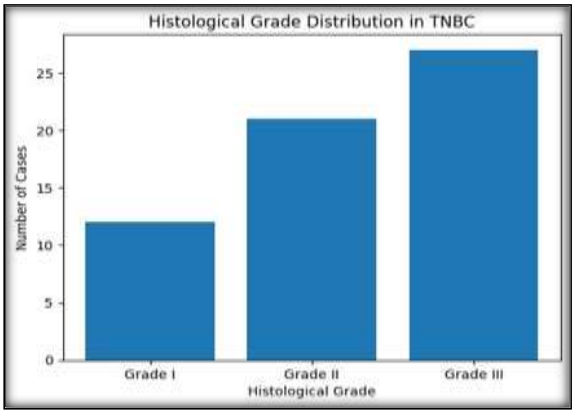

Chart 2: Distribution of histological grade TNBC

Observation and Interpretation: A high prevalence of high-grade tumors (Grades II and III) was observed, correlating with the aggressive behaviour of TNBC.

[Chart 2] demonstrates the distribution of TNBC according to histological grade. The most common Grade III tumors (45%), followed by Grade II (35%), whereas Grade I tumors accounted for 20% of cases. The predominance of high-grade tumors reflects the aggressive biological behavior of TNBC.

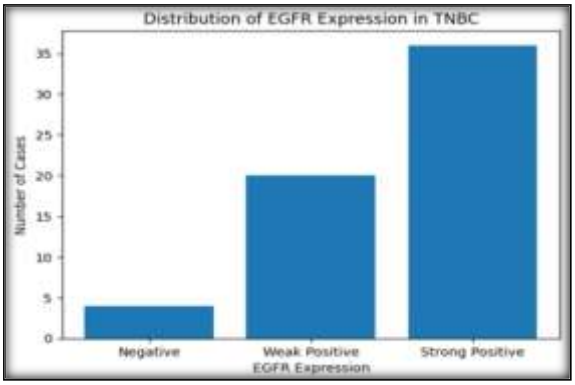

Chart 3: Distribution of EGFR expression in TNBC

Observation and Interpretation: EGFR expression was observed in a significant proportion of TNBC cases, with strong positivity.

[Chart 3] demonstrates EGFR expression patterns in TNBC. Strong EGFR positivity was observed in 60% of cases, [Figure 5], and weak positivity was seen in 33.3%, [Figure 4] and only 6.6% of cases were EGFR negative. [Figure 3]

This indicates an increased prevalence of Epidermal growth factor Receptor expression in Triple negative Breast carcinoma.

Table 3: Expression of EGFR in TNBC

EGFR Expression	Number of cases	Percentage (%)
Negative	4	6.6
Weak Positive	20	33.3
Strong Positive	36	60
Total	60	100

Table 4: Correlation between EGFR expression and histological Grade

Histological grade	EGFR Negative	EGFR weak Positive	EGFR strong Positive
Grade I	3	9	0
Grade II	1	8	12
Grade III	0	3	24

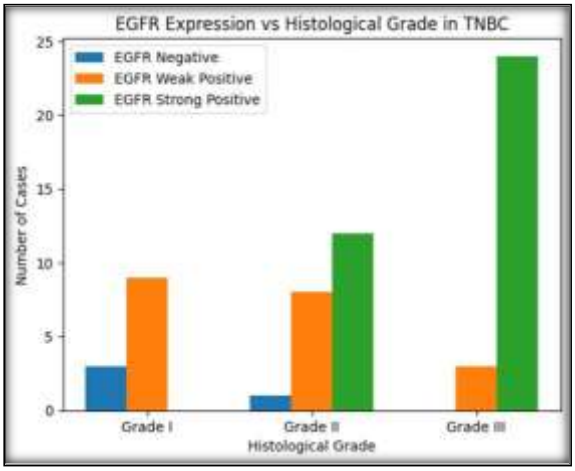

Chart 4: Correlation Between EGFR expression and histological grade

Observation and Interpretation: Strong EGFR expression was observed in Grade III tumors, suggesting a significant association between EGFR overexpression and tumor aggressive behavior.

Grade I tumors predominantly showed weak EGFR positivity (9 cases), with a small proportion showed EGFR negative (3 cases) and none showing strong positivity.

In Grade II tumors, predominantly showed strong EGFR expression (12 cases), and weak positivity observed less proportion (8 cases), and EGFR-negative cases were observed rare (1 case).

Grade III tumors demonstrated increased EGFR expression, with the increased number of cases

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showing strong EGFR positivity (24 cases) and no EGFR-negative cases observed.

Overall, strong EGFR expression showed a significant positive correlation with higher histological grade, indicating its association with higher tumor aggressiveness.

Association between histological grade and EGFR expression was assessed using the Chi-square test. A statistically significant association was observed ($\chi^2 = 18.72$, df = 4, p = 0.001).

Table 5: Correlation between EGFR expression and tumour stage

Tumour Stage	EGFR Negative	EGFR weak Positive	EGFR Strong Positive
Stage I	3	1	0
Stage II	0	12	13
Stage III	1	7	23

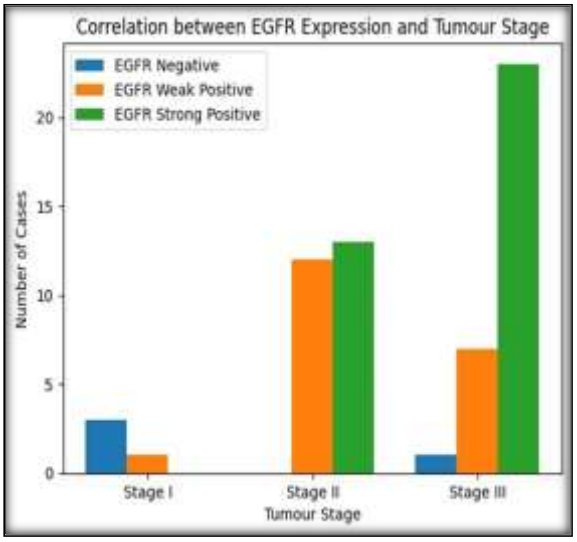

Chart 5: Correlation between EGFR expression and tumour stage

Observation and Interpretation: EGFR positivity increased with advancing tumor stage, with indicating a role in progression of disease

The chart 5 illustrated Epidermal growth factor Receptor expression in relation to tumor stage. Stage II and Stage III tumors showed an increase number in EGFR positivity, with the increased expression showed in Stage III disease. This indicates that Epidermal growth factor Receptor expression increased with advanced tumor stage, supporting its potential role in tumor progression and in TNBC.

A statistically significant association was observed between EGFR expression and tumor stage. EGFR positivity showed in advancing stage, with the highest expression in Stage III tumors. ($\chi^2 = 36.71$, df = 4, $p < 0.001$).

Figure 1: Gross specimen of modified radical mastectomy

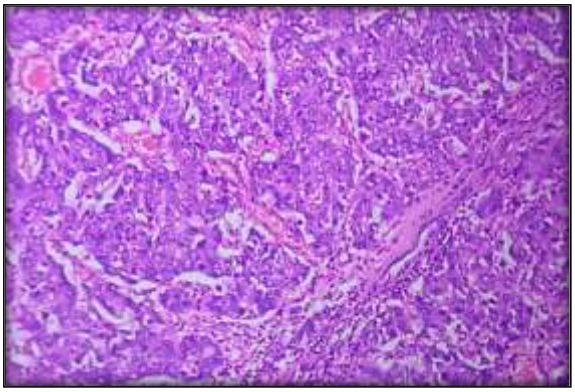

Figure 2: Histopathology of Triple Negative Breast Carcinoma.

Hematoxylin and Eosin stain (40x) showing malignant epithelial cells arranged in sheets and nests with marked nuclear pleomorphism, high nuclear-cytoplasmic ratio, prominent nucleoli, and brisk mitotic activity.

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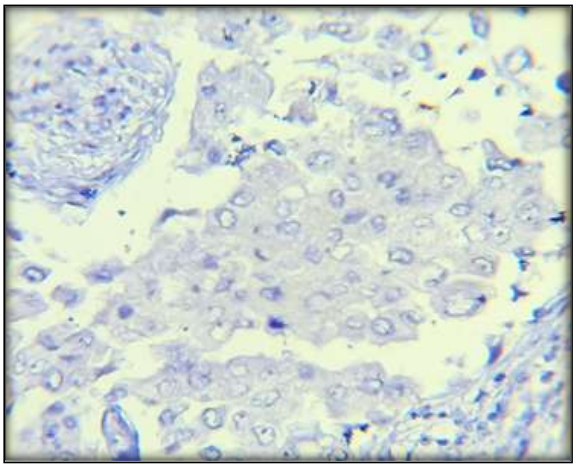

Figure 3: Negative EGFR Expression in TNBC

Immunohistochemistry for EGFR (40x) showing absence of membranous staining in tumor cells.

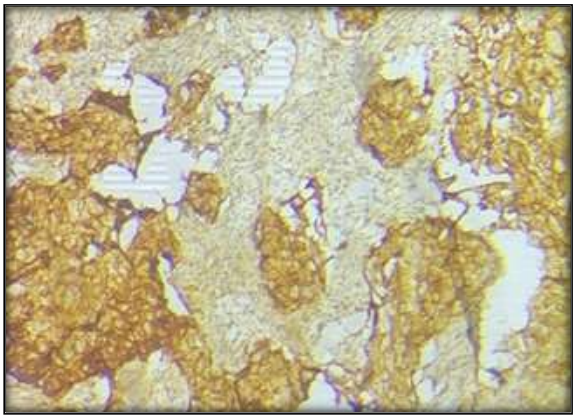

Figure 4: Weak EGFR Expression in TNBC

Immunohistochemistry for EGFR (40x) demonstrating faint membranous staining in less than 25% of tumor cells (Score 1+).

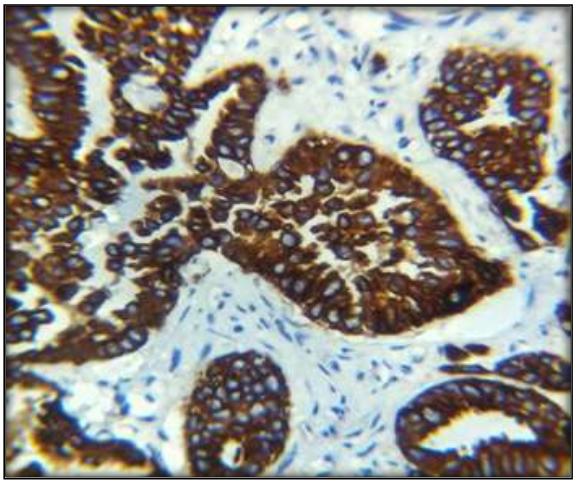

Figure 5: Strong EGFR Expression in TNBC

Immunohistochemistry for EGFR (40x) showing strong, complete membranous staining in more than 50% of tumor cells (Score 3+).

DISCUSSION

Triple Negative Breast Carcinoma (TNBC) is a biologically aggressive subtype of breast carcinoma with limited therapeutic options due to the absence of estrogen receptor, progesterone receptor, and HER2/neu expression.[3] This study assessed the EGFR expression in TNBC and correlated its relationship with clinicopathological parameters emphasizing its potential prognostic and therapeutic significance.

In the present study, a large number of TNBC cases were observed in the fourth and fifth decades of life, indicating a younger age at presentation. This finding is consistent with previous studies which show that TNBC mostly affects younger women with poorer outcomes compared to other molecular subtypes of breast carcinoma.[4,5]

Our study demonstrates EGFR expression was observed on histopathological evaluation with a predominance of high-grade tumors (Grade II and III). This observation is consistent with previous literature, which consistently reports that TNBCs are poorly differentiated and exhibit high histological grades, contributing to their aggressive behavior and unfavorable prognosis.[6,7] Similar findings have been reported by Changavi AA et al., who demonstrated frequent EGFR overexpression in TNBC and basal-like breast carcinomas.[7]

When compared with previously published studies, our findings are largely concordant with the existing literature. EGFR expression was mostly reported in high grade tumors by Changavi AA et al.[7] In our study EGFR expression showed a statistically significant association with increasing histological grade ($p = 0.001$). EGFR overexpression is related to the promoting tumor cell proliferation, invasion, angiogenesis, and resistance to apoptosis, thereby contributing to aggressive tumour behavior.[8,9]

In this study, EGFR expression was associated with tumor dedifferentiation and aggressive biological behavior. Several studies have reported a similar association between EGFR expression and higher tumor grade in TNBC.[10,11]

Advanced stages of carcinoma demonstrated increased EGFR expression, indicating a role for EGFR in tumor progression. EGFR expression was significantly higher in advanced tumour stages, with the highest expression in Stage III tumors ($p < 0.001$). Comparable results have been reported in earlier studies, where EGFR positivity was associated with advanced stage disease and poorer clinical outcomes.[12]

No significant association was observed between EGFR expression and patient age, indicating that EGFR overexpression is more closely related to intrinsic tumor biology rather than patient demographics. This observation is in concordance with prior studies that found no age-related variation in EGFR expression among TNBC patients.[13]

The clinical implications of EGFR overexpression in TNBC are significant. Although anti-EGFR targeted

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therapies have not yet become part of routine TNBC treatment modalities, early clinical trials and experimental studies suggest potential benefit in selected EGFR-positive TNBC cases.[14,15] Routine evaluation of EGFR by immunohistochemistry may therefore aid in identifying patients who could benefit from future targeted therapies.

Limitations

- A relatively small sample size.
- Being a single-center study, multicenter studies are required for validation.
- Lack of molecular confirmation.

CONCLUSION

In conclusion, our study demonstrates that EGFR is frequently expressed in Triple negative Breast carcinoma and is significantly associated with higher tumor grade and advanced stage. EGFR assessment in the routine pathological evaluation of TNBC may contribute to prognostication and personalized therapeutic strategies.

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