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# A RETROSPECTIVE STUDY OF BREAST CARCINOMA CORRELATING STAGE AND GRADE OF TUMOUR WITH CD4 EXPRESSION OF TUMOUR INFILTRATING LYMPHOCYTES

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## ABSTRACT

**Introduction:** Tumour infiltrating lymphocytes (TILs) are an important component of the tumour microenvironment and are known to influence tumour progression, immune regulation, and clinical outcome in breast carcinoma. Among them, CD4-positive T lymphocytes play a major role in modulation of immune response. The present study was undertaken to evaluate CD4 tumour infiltrating lymphocytes and correlate their expression with established clinicopathological prognostic parameters in breast carcinoma.

**Methods:** This retrospective observational study included 23 cases of invasive ductal carcinoma of no special type treated with modified radical mastectomy data retrieved from archival histopathology records for two years in the department of pathology,Saveetha medical college. Immunohistochemical staining for CD4 was performed on formalin-fixed paraffin-embedded tissue sections. $CD4^+$ tumour infiltrating lymphocytes were assessed in both intratumoural and stromal compartments and correlated with clinicopathological variables including tumour size, grade, stage, lymph node status, oestrogen receptor (ER), progesterone receptor (PR), and HER2/neu status. Statistical analysis was performed using Chi-square test, with $p < 0.05$ considered statistically significant.

**Results:** The mean age of patients was 49 ± 9.4 years, and the majority were females. Stromal CD4 tumour infiltrating lymphocytes constituted the predominant component of immune infiltration compared to intratumoural lymphocytes. A statistically significant association was observed between CD4 TILs and tumour size ($p = 0.006$), tumour stage ($p = 0.026$), and lymph node metastasis ($p = 0.007$). Increased $CD4^+$ lymphocytic infiltration was observed in larger tumours, advanced-stage disease, and lymph node-positive cases. No significant association was found between CD4 TILs and tumour grade, lymphovascular invasion, ER, PR, or HER2/neu status.

**Conclusion:** The present study demonstrates that increased CD4 tumour infiltrating lymphocytes are associated with aggressive clinicopathological features in breast carcinoma, suggesting their potential role in tumour progression and prognostication.

**KEYWORDS:** Breast carcinoma; CD4 lymphocytes; Tumour infiltrating lymphocytes; Immunohistochemistry; Tumour microenvironment.

## INTRODUCTION

Breast cancer is one of the most common neoplasms and in India, it is the second most common neoplasm in females. It is considered as a heterogeneous disease comprising a range of clinical patterns, prognostic characteristic, biological behaviour and response to different types of treatment. The field of cancer diagnosis in breast cancer is being evolved tremendously and multiple studies have been conducted to improve the survival rate by early diagnosis of the neoplasm and multiple targeted therapies. However, mortality still persists to be high and metastatic disease remains incurable. The limitations in the current treatment practice have provoked an increased enthusiasm to define new prognostic tools and developing highly targeted therapies [1].

Current studies suggest that human cancer tissue is infiltrated by lymphocytes called tumour infiltrating lymphocytes (TILs) which represent the local immune response directed against the growth of a tumour and its metastasis and are considered as an independent prognostic indicator in many malignant tumours [2]. A malignant tumour is comprised of cancer cells and the tumour microenvironment which is composed of a mixture of malignant tumour cells with a varied group of stromal cells such as endothelial cells, fibroblasts and infiltrating immune cells along with products of these cells such as an extracellular matrix, chemokines, cytokines, growth factors, various enzymes and metabolites all of which alters the progress of cancer cells and there by its clinical outcome. The interaction between tumour to stroma and between stroma to stroma has implicated in regulating tumour growth, metastatic potential, the location of metastasis and also influence the outcome of therapy [3].

The immune system of the affected individual interacts with tumour cells throughout their development and the consequence of these interactions has an implication in cancer therapy [4]. Pathogenesis of breast cancer is multifactorial and the interplay between the host immune system and breast cancer tissue has been pondered upon for over decades. Breast cancer tissue is infiltrated by a mixed group of immune cells such as T cells, B cells, natural killer cells and

macrophages, and the presence of this immune response does not inhibit the progression and spread of breast cancer, thus questioning the role of tumour infiltrating lymphocytes in the tumour microenvironment [5].
The basic role of the immune system is to maintain tissue homeostasis by performing continuous immunosurveillance and initiate inflammatory reactions by coordinated activation of both the innate and adaptive immune cells [6]. The process of immune cells escaping from immune response is best conceptualized by cancer immunoediting theory which defines malignant progression in three phases: elimination, equilibrium and escape [7]. Even at advanced disease stage, immune parameters have been recognized as directly or indirectly influencing survival status of patients [8].
Among the tumour infiltrating lymphocytes present in the tumour microenvironment, CD4 T lymphocytes are a major part of adaptive immunity and include helper T cells and regulatory T cells which play a significant role in modulation of immune response. CD4 antigen is a glycoprotein found on the surface of helper T cells, macrophages and monocytes. The tumour infiltrating lymphocytes are also capable to produce and release vascular endothelial growth factor and basic fibroblastic growth factor which induces angiogenesis and lymphangiogenesis thereby enabling the spread of cancer cells through lymphatics to regional lymph nodes [9].
Several studies addressing tumour immune cell infiltration have demonstrated an association of lymphocyte infiltration with prognosis and response to therapy; however conflicting results exist regarding the exact role of CD4 tumour infiltrating lymphocytes in breast cancer. [10–16] The traditional prognostic markers for breast cancer are clinical stage, tumour grade, lymph node status, estrogen receptor, Progesterone receptor and HER2/neu status [17,18].
However, without knowing the phenotype of the cells contributing to this immune response, further therapeutic developments cannot be possible. Hence, this study is undertaken to evaluate the role of CD4 tumour infiltrating lymphocytes and to correlate their expression with established prognostic parameters to assess the response of disease severity in breast carcinoma.

## METHODS

### *Study design and setting*

This was a retrospective observational study carried out over a period of two years from 2023-2026 at department of pathology Saveetha medical college.. Relevant clinicopathological data including age, tumour size, grade, stage, and lymph node status were retrieved from histopathology records. Ethical clearance was obtained from the Institutional Ethics Committee, and as the study utilized archival material, informed consent was waived.

### *Study participants and study size*

The sample size 23 was calculated based on a similar study by Rajhans AR et al [19]. The expected proportion of CD4 expression as 0.816 with the relative precision of 20%. The level of significance was taken as 5%. The formula used for calculation was

$$n \geq \frac{Z_{1-\frac{\propto}{2}}{}^2 p(1-p)}{(dp)^2}$$

Where p is the expected proportion or prevalence of event of interest for the study

d is the relative precision

$Z_{1-\frac{\propto}{2}}$ is normal deviate at a level of significance

$$n \geq \frac{(1.96)^2\ 0.816(1-0.816)}{(0.20 * 0.816)^2}$$

$$n \geq 23$$

Thus, a total of 26 cases were included in the study based on the availability of eligible archival specimens during the study period. Paraffin-embedded tissue blocks of breast carcinoma cases were retrieved, all of which had undergone modified radical mastectomy and were histologically confirmed as invasive ductal carcinoma of no special type, with no prior treatment. Cases with other histological variants of breast carcinoma, non-epithelial tumours, distant metastasis, prior neoadjuvant chemotherapy, or inadequate tissue material were excluded.

### *Histopathological evaluation*

Formalin-fixed paraffin-embedded tissue sections of 4 μm thickness were prepared and stained with haematoxylin and eosin for histopathological evaluation. Tumours were graded using the Nottingham modification of the Bloom–Richardson system [20] and staged according to the American Joint Committee on Cancer (AJCC) TNM classification [21].

### *Immunohistochemistry (CD4)*

Immunohistochemical analysis was performed using a mouse monoclonal antibody against CD4 (clone 4b12, ready-to-use). Sections were deparaffinized, rehydrated, and subjected to antigen retrieval at 99°C for 40 minutes. Endogenous peroxidase activity was blocked using 3% hydrogen peroxide, followed by protein blocking to prevent non-specific binding. Slides were incubated with primary antibody for 1 hour, followed by secondary antibody using a Novolink polymer detection system. The antigen-antibody complex was visualized using diaminobenzidine and counterstained with haematoxylin. Tonsil tissue was used as a positive control, and omission of primary antibody served as a negative control.

### *Assessment of CD4 tumour infiltrating lymphocytes*

CD4 tumour infiltrating lymphocytes were assessed according to established methods for evaluation of TILs [22]. CD4 positivity was defined as membranous staining of lymphocytes. Slides were evaluated independently by two pathologists

to minimize interobserver variability and re-evaluated after a time interval to reduce intraobserver bias. $CD4^+$ lymphocytes were counted in ten high-power fields (400× magnification) within the tumour area, including both intratumoural and stromal compartments. Intratumoural lymphocytes were defined as cells present within tumour epithelial nests, while stromal lymphocytes were located in the interstitial tumour stroma [23]. The number of positive cells was counted, summed, and expressed as mean counts per high-power field. Digital image analysis using Adobe Photoshop (version 7) was performed to improve accuracy and reproducibility of counting [24].

***Bias***

In order to reduce observer bias, all slides were independently assessed by two pathologists and re-evaluated after a time interval. Digital image analysis was used as an additional method to validate manual counting.

***Variables***

The primary outcome variable was CD4 tumour infiltrating lymphocyte (TIL) expression. The predictor variables included age, tumour size, tumour grade, tumour stage, lymph node status, and immunohistochemical status of oestrogen receptor (ER), progesterone receptor (PR), and HER2/neu.

***Quantitative variables and statistical analysis***

CD4 tumour infiltrating lymphocytes were expressed as mean counts per high-power field and categorized based on their localization into intratumoural and stromal compartments. Statistical analysis was performed using SPSS version 22.0 software. Categorical variables were expressed as frequencies and percentages, and associations between CD4 tumour infiltrating lymphocytes and clinicopathological parameters were analysed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

***Statistical analysis***

CD4 tumour infiltrating lymphocytes were expressed as mean counts per high-power field and categorized based on their localization into intratumoural and stromal compartments. Statistical analysis was performed using SPSS version 22.0 software. Categorical variables were expressed as frequencies and percentages, and associations between CD4 tumour infiltrating lymphocytes and clinicopathological parameters were analysed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

**RESULTS**

**Table 1:** Demographic and Clinicopathological Characteristics of Study Participants (N = 23)

| **Variables** | | **Frequency N=23** | **Percentage (%)** |
|---|---|---|---|
| Age (in years) | | 49 ± 9.4 | |
| Gender | Male | 1 | 4.3 |
| | Female | 22 | 95.7 |
| Laterality | Right | 8 | 34.8 |
| | Left | 15 | 65.2 |
| Quadrant | Upper outer | 12 | 52.2 |
| | Upper inner | 5 | 21.7 |
| | Central | 3 | 13.0 |
| | Lower inner | 2 | 8.7 |
| | Lower outer | 1 | 4.3 |
| Size of the tumours (cm) | | 4.22 ± 1.94 | |
| Grade of the tumour | 1 | 8 | 34.8 |
| | 2 | 10 | 43.5 |
| | 3 | 5 | 21.7 |
| Stage of tumour | II | 15 | 65.2 |
| | III | 8 | 34.8 |
| Lymph node status | Positive | 11 | 47.8 |
| | Negative | 12 | 52.2 |
| Lymphovascular status | Positive | 11 | 48.0 |
| | Negative | 12 | 52.0 |
| ER Status | Absent | 16 | 69.6 |
| | Present | 7 | 30.4 |
| PR Status | Absent | 13 | 56.5 |
| | Present | 10 | 43.5 |
| HER2/neu | Negative | 16 | 70.0 |
| | Equivocal | 3 | 13.0 |
| | Positive | 4 | 17.0 |

The table 1 presents the clinicopathological profile of the study participants (N = 23), with a mean age of 49 ± 9.4 years. The majority of participants were female (22, 95.7%), with only one male (1, 4.3%). Left-sided involvement (15, 65.2%) was more common than right-sided (8, 34.8%). The most frequently affected quadrant was the upper outer quadrant (12, 52.2%), followed by the upper inner quadrant (5, 21.7%), while central (3, 13.0%), lower inner (2, 8.7%), and lower outer (1, 4.3%) quadrants were less commonly involved. The mean tumour size was 4.22 ± 1.94 cm. Regarding tumour grade, most participants had grade 2 tumours (10, 43.5%), followed by grade 1 (8, 34.8%) and grade 3 (5, 21.7%). A higher proportion of cases were in stage II (15, 65.2%) compared to stage III (8, 34.8%). Lymph node status was nearly equally distributed, with 11 (47.8%) positive and 12 (52.2%) negative cases. Similarly, lymphovascular invasion was present in 11 (48.0%) participants and absent in 12 (52.0%). Hormone receptor analysis showed that oestrogen receptor (ER) was absent in the majority (16, 69.6%), while progesterone receptor (PR) was absent in 13 (56.5%) participants. HER2/neu expression was negative in most cases (16, 70.0%), with smaller proportions showing equivocal (3, 13.0%) and positive (4, 17.0%) status.

**Figure 1:** Descriptive analysis for CD4 TILs, CD4iTILs, and CD4 sTILs

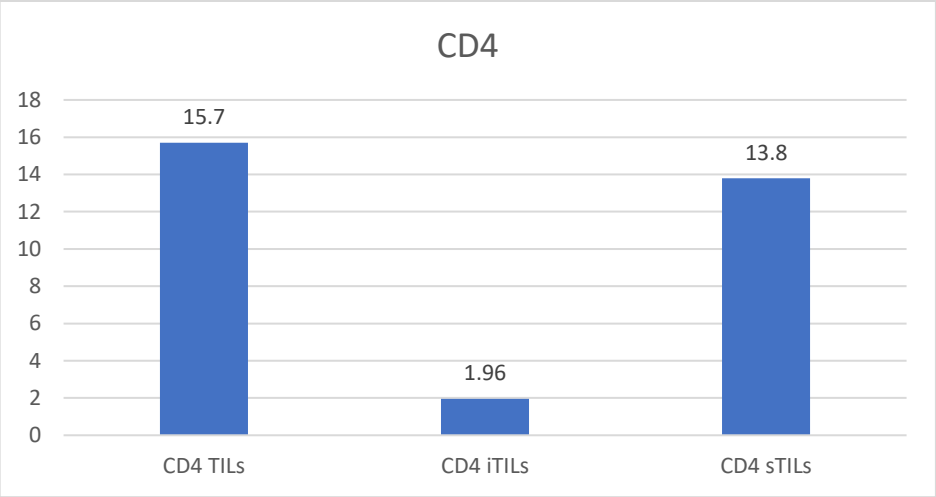



Figure 1 shows that the mean CD4 TILs was 15.78 ± 7.24, with moderate variability (95% CI: 12.65–18.91). CD4 iTILs had a low mean of 1.96 ± 2.69 and a median of 0.00, indicating minimal intratumoral infiltration in many cases (95% CI: 0.79–3.12). In contrast, CD4 sTILs had a higher mean of 13.83 ± 5.87 (95% CI: 11.29–16.37), suggesting that stromal infiltration constitutes the major component of total CD4 TILs.

**Table 2:** Association of age, tumour Size, and Grade with CD4 TILs and CD4 sTILs (N= 23)

| Variable | Category | CD4 TILs Low (<15) | CD4 TILs High (≥15) | P-value | CD4 sTILs Low (<12) | CD4 sTILs High (≥12) | P-value |
|---|---|---|---|---|---|---|---|
| **Age (years)** | <51 | 9 (70%) | 3 (30%) | 0.062 | 8 (67%) | 4 (33%) | 0.305 |
| | ≥51 | 4 (30.77%) | 7 (70%) | | 5 (45%) | 6 (55%) | |
| **Tumour Size (cm)** | <4.2 | 12 (75%) | 4 (25%) | 0.006* | 9 (56%) | 7 (44%) | 0.061 |
| | ≥4.2 | 1 (14%) | 6 (86%) | | 1 (14%) | 6 (86%) | |
| **Tumour Grade** | 1 | 6 (75%) | 2 (25%) | 0.399 | 6 (75%) | 2 (25%) | 0.399 |
| | 2 | 5 (50%) | 5 (50%) | | 5 (50%) | 5 (50%) | |
| | 3 | 2 (40%) | 3 (60%) | | 2 (40%) | 3 (60%) | |

Table 2 depicts the association of age, tumour size, and tumour grade with CD4 TILs and CD4 sTILs. A statistically significant association was observed between tumour size and CD4 TIL count ($p = 0.006$), indicating that larger tumours were associated with higher CD4 TIL levels. However, no statistically significant association was observed between age or tumour grade and CD4 TILs or CD4 sTILs ($p > 0.05$). CD4 sTILs demonstrated a borderline association with tumour size ($p = 0.061$), although this did not reach statistical significance. Grade I tumours demonstrated mild pleomorphism with low stromal CD4-positive lymphocytic infiltration [Figure 2A, B], whereas Grade III tumours showed increased stromal $CD4^+$ lymphocytic infiltration [Figure 2C, D].

**Figure 2: Association of CD4 Tumour-Infiltrating Lymphocytes with Tumour Grade**

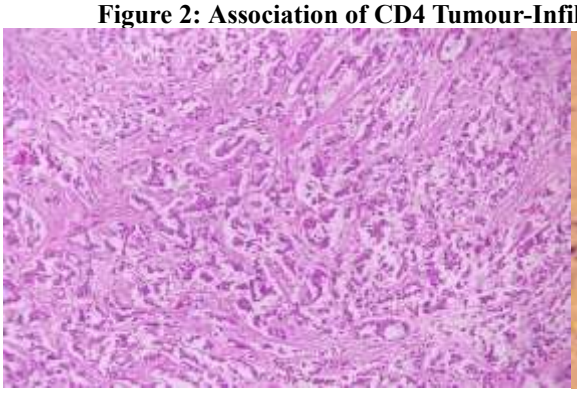


**Fig 2A (H&E, Grade I, 100X)**

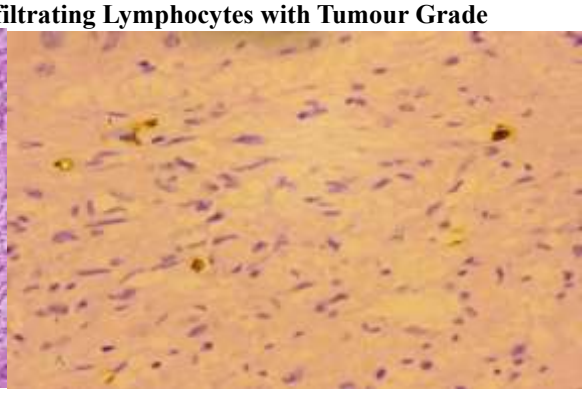


**Fig2B (IHC, Grade I, 400X)**

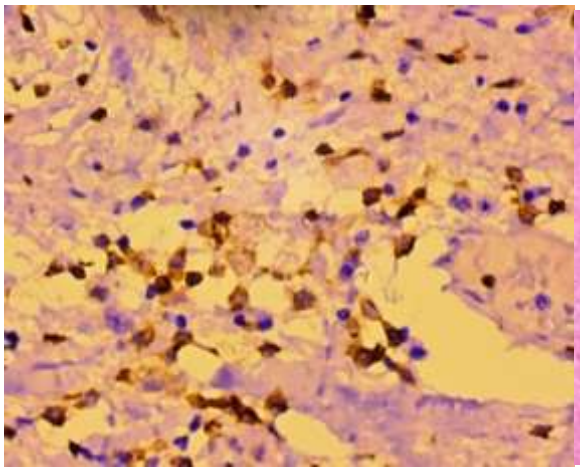


**Figure 2C (H&E, Grade III, 100X)**

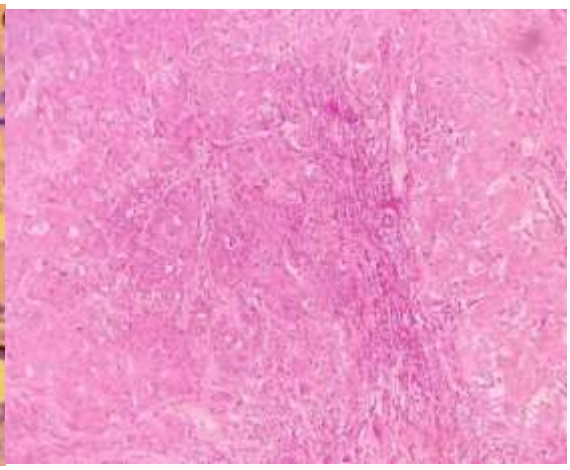


**Figure 2D (IHC, Grade III, 400X)**

**(A)** H&E stained section (100X) showing Grade I invasive ductal carcinoma with malignant cells arranged predominantly in glandular pattern and exhibiting mild pleomorphism.
**(B)** Immunohistochemistry for CD4 (400X) showing low stromal $CD4^+$ lymphocytic infiltration in Grade I tumour.
**(C)** H&E stained section (100X) showing Grade III invasive ductal carcinoma composed of pleomorphic malignant cells arranged in sheets with mononuclear inflammatory cell infiltrate.
**(D)** Immunohistochemistry for CD4 (400X) demonstrating high stromal $CD4^+$ tumour infiltrating lymphocytes in the stromal component of Grade III tumour.

**Table 3:** Association of Histopathological Variables with CD4 TILs and CD4 sTILs (N= 23)

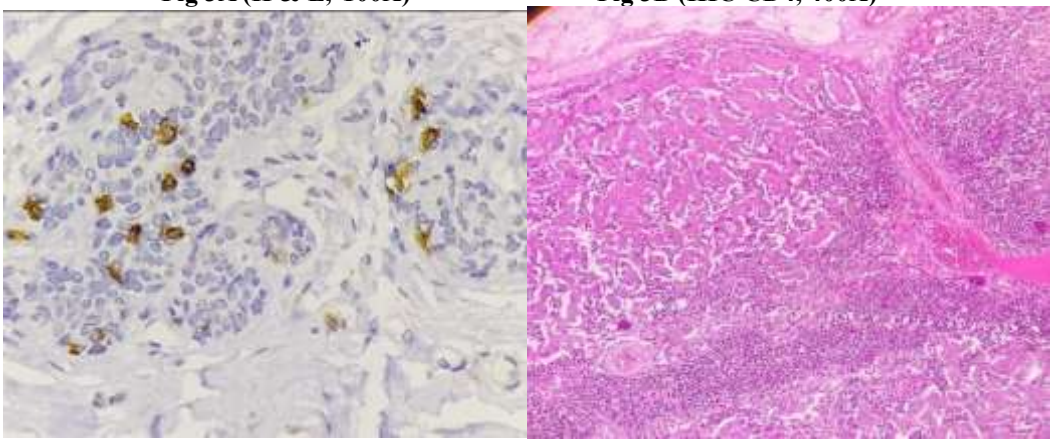
| Histopathological variable | Category | CD4 TILs Low (<15) | CD4 TILs High (≥15) | P-value | CD4 sTILs Low (<12) | CD4 sTILs High (≥12) | P-value |
|---|---|---|---|---|---|---|---|
| **Tumour stage** | II | 11 (73%) | 4 (27%) | 0.026* | 11 (73%) | 4 (27%) | 0.026* |
| | III | 2 (25%) | 6 (75%) | | 2 (25%) | 6 (75%) | |
| **Lymph node status** | Negative | 10 (83%) | 2 (17%) | 0.007* | 10 (80%) | 2 (20%) | 0.007* |
| | Positive | 3 (23%) | 8 (80%) | | 3 (23%) | 8 (80%) | |
| **Lymphovascular Status** | Negative | 6 (50%) | 6 (50%) | 0.827 | 3 (27%) | 8 (73%) | 0.375 |
| | Positive | 5 (45%) | 6 (55%) | | 5 (45%) | 6 (55%) | |
| **ER Status** | Absent | 7 (44%) | 9 (56%) | 0.062 | 7 (44%) | 9 (56%) | 0.062 |
| | Present | 6 (86%) | 1 (14%) | | 6 (86%) | 1 (14%) | |
| **PR Status** | Absent | 7 (54%) | 6 (46%) | 0.768 | 4 (31%) | 9 (69%) | 0.16 |
| | Present | 6 (60%) | 4 (40%) | | 6 (60%) | 4 (40%) | |
| **HER2/neu Status** | Negative | 7 (44%) | 9 (56%) | 0.462 | 6 (38%) | 10 (63%) | 0.372 |
| | Equivocal | 1 (33%) | 2 (67%) | | 1 (33%) | 2 (67%) | |
| | Positive | 3 (75%) | 1 (25%) | | 3 (75%) | 1 (25%) | |

Table 3 shows the association of histopathological variables with CD4 TILs and CD4 sTILs. A statistically significant association was observed between tumour stage and lymph node status with both CD4 TILs and CD4 sTILs ($p < 0.05$). Cases with lymph node metastasis demonstrated increased intratumoural and stromal CD4-positive lymphocytic infiltration [Figure 3A–C]. However, no significant association was found with lymphovascular invasion, ER, PR, or HER2/neu status ($p > 0.05$). ER-positive tumours demonstrated low stromal CD4-positive lymphocytic infiltration [Figure 4A, B]. PR-positive tumours showed low stromal and intratumoural CD4-positive lymphocytic infiltration [Figure 5A,

B]. Similarly, HER2/neu-positive tumours demonstrated low stromal CD4-positive lymphocytic infiltration [Figure 6A, B].

**Figure 3: Association of CD4 tumour infiltrating lymphocytes with lymph node metastasis**

**Fig 3A (H & E, 100X)** **Fig 3B (IHC CD4, 400X)**



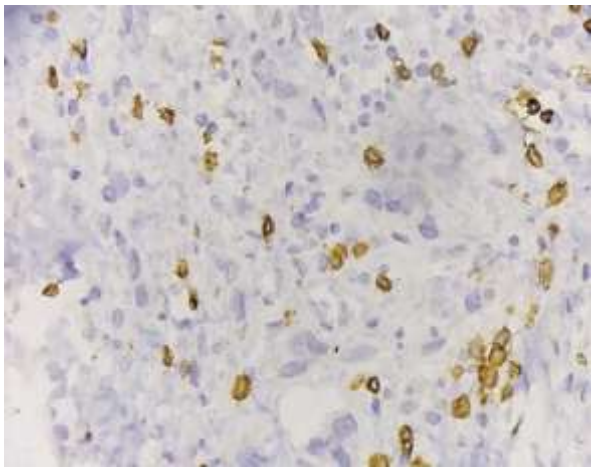


**Fig 3C (IHC CD4, 400X )**

**(A)** H&E stained section (100X) showing lymph node with malignant cells infiltrating the subcapsular region.
**(B)** Immunohistochemistry for CD4 (400X) demonstrating increased intratumoural CD4-positive lymphocytic infiltration.
**(C)** Immunohistochemistry for CD4 (400X) demonstrating increased stromal CD4-positive lymphocytic infiltration.

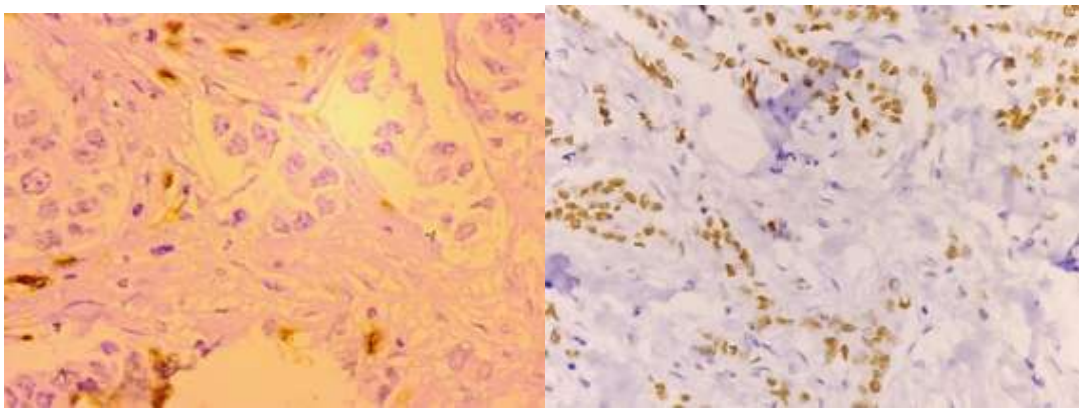
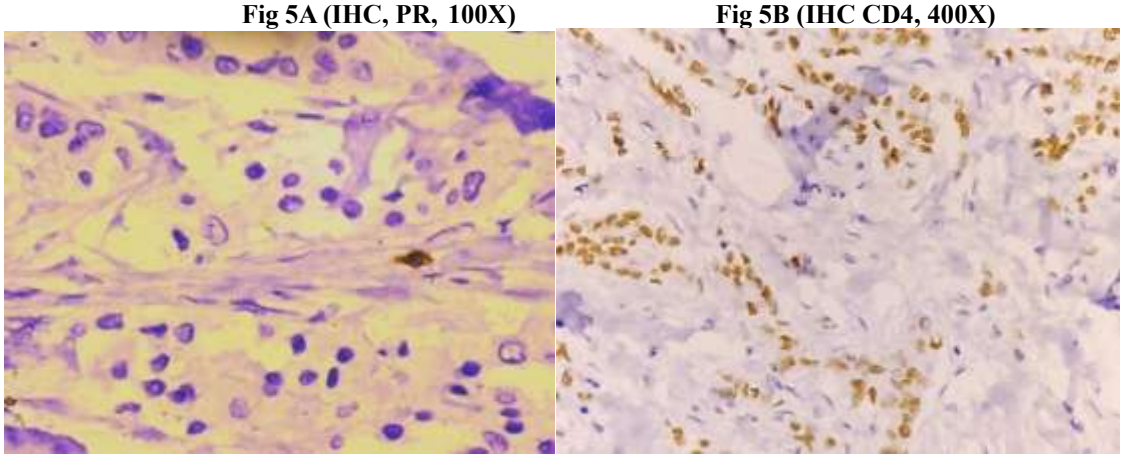


**Figure 4: Association of CD4 tumour infiltrating lymphocytes with ER status**

**Fig 4A (IHC, 100X)** **Fig 4B (IHC CD4, 400X)**

**(A)** Immunohistochemistry for ER (100X) showing nuclear positivity in tumour cells.
**(B)** Immunohistochemistry for CD4 (400X) demonstrating low stromal CD4-positive lymphocytic infiltration in ER-positive tumour.

**Figure 5: Association of CD4 tumour infiltrating lymphocytes with PR status**
**Fig 5A (IHC, PR, 100X) Fig 5B (IHC CD4, 400X)**



\(A) Immunohistochemistry for PR (100X) showing strong nuclear positivity in tumour cells.
(B) Immunohistochemistry for CD4 (400X) demonstrating low stromal and intratumoural CD4-positive lymphocytic infiltration in PR-positive tumour**.**

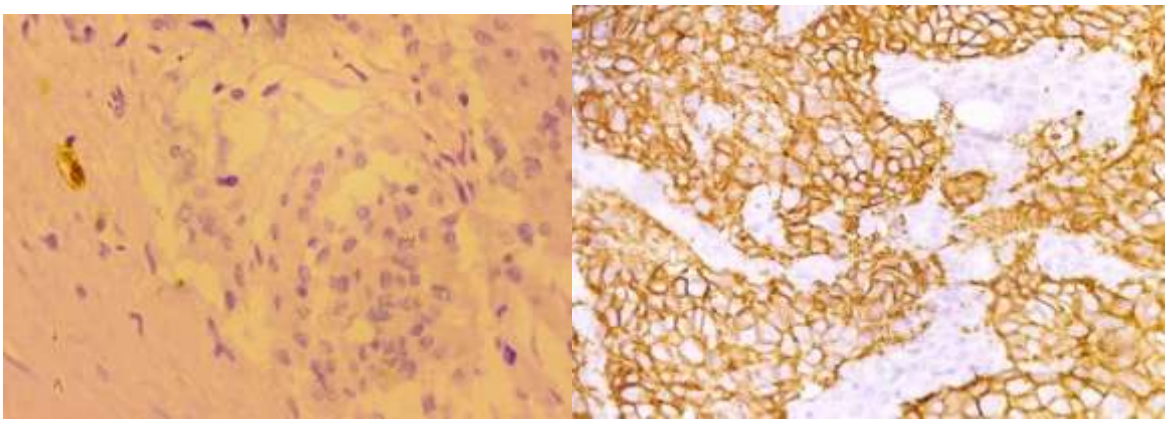


**Figure 6: Association of CD4 tumour infiltrating lymphocytes with HER2/neu status Fig 6A (IHC HER2/neu, 100X) Fig 6B (IHC CD4, 400X)**

**(**A) Immunohistochemistry for HER2/neu (100X) showing complete intense membranous staining (3+) in tumour cells.
(B) Immunohistochemistry for CD4 (400X) demonstrating low stromal $CD4^+$ lymphocytic infiltration in HER2/neu-positive tumour.
In the text: HER2/neu-positive tumours demonstrated low stromal CD4-positive lymphocytic infiltration [Figure 6A, B].

**DISCUSSION**

Tumour infiltrating lymphocytes (TILs) represent the host immune response within the tumour microenvironment and play an important role in influencing tumour behaviour and progression. The interaction between tumour cells and immune cells is complex, involving both tumour suppressive and tumour -promoting mechanisms.

In the present study, the mean age of patients was 49 ± 9.4 years, with a considerable proportion of cases occurring below 50 years of age. This finding suggests a trend toward earlier onset of breast carcinoma, which has been increasingly reported in recent literature [25]. The majority of patients were female, consistent with the known epidemiology of breast cancer. The upper outer quadrant was the most commonly involved site, which correlates with the higher density of breast tissue in this region and is in agreement with previous studies [26].

A key finding of this study was that CD4 tumour infiltrating lymphocytes were predominantly localized in the stromal compartment rather than within the tumour cell nests. This indicates that stromal lymphocytes constitute the major component of immune infiltration in breast carcinoma. Similar observations have been reported in earlier studies, supporting the concept that the stromal microenvironment is the primary site of immune interaction [27-29]. The relatively low intratumoural CD4 infiltration observed may reflect limited direct immune-tumour cell interaction.

Similar findings have also been reported by Divyapriya C et al., who observed predominant stromal and tumour-interface $CD4^+$ lymphocytic infiltration compared to intratumoural infiltration in invasive breast carcinoma [30]. Furthermore, Rustamadji P et al similarly demonstrated stromal predominance of $CD4^+$ tumour infiltrating lymphocytes and reported significant associations with tumour size, HER2 status, and lymph node metastasis, supporting the role of $CD4^+$ lymphocytes in tumour progression
n and modulation of the tumour microenvironment [31].

No significant association was found between CD4 TILs and patient age or tumour grade, which is consistent with findings from previous studies [5,25,32]. However, a significant association was observed between CD4 TILs and tumour size,

with higher CD4 counts noted in larger tumours. This may indicate that increasing tumour burden stimulates a greater immune response, possibly due to enhanced antigen exposure.

A statistically significant association was also observed between CD4 TILs and tumour stage, with higher CD4 infiltration in advanced stages of disease. This suggests that CD4 lymphocytes may play a role in tumour progression rather than tumour suppression in later stages. It is possible that as the tumour evolves, CD4 T cells shift toward regulatory or pro-tumour phenotypes, contributing to immune evasion and tumour growth.

Furthermore, a significant association was noted between CD4 TILs and lymph node metastasis. Increased CD4 infiltration in node-positive cases may reflect an active but ineffective immune response or may indicate a tumour -promoting microenvironment. CD4 T cells are known to secrete cytokines and growth factors that can facilitate angiogenesis and tumour spread.

No significant association was observed between CD4 TILs and HER2/neu or hormone receptor status, highlighting the complex and heterogeneous nature of immune interactions in breast cancer. This variability may be influenced by differences in tumour biology and immune regulation.

Although the present study is limited by a relatively small sample size, the findings are consistent with several previous reports. Overall, the study suggests that increased CD4 tumour -infiltrating lymphocytes are associated with features of tumour progression, including larger tumour size, advanced stage, and lymph node metastasis. These findings highlight the importance of the tumour microenvironment and suggest that CD4 TILs may serve as a potential marker for disease progression in breast carcinoma.

## CONCLUSION

The present study demonstrates that increased CD4 tumour infiltrating lymphocytes are significantly associated with aggressive clinicopathological features in breast carcinoma. Higher CD4 TIL levels showed a strong correlation with tumour size, pathological stage, and lymph node metastasis, suggesting a potential role in tumour progression and disease severity. These findings highlight the importance of the tumour immune microenvironment in influencing tumour behaviour.

However, the assessment of tumour -infiltrating lymphocytes using histopathology and immunohistochemistry may be influenced by methodological variability, and quantitative evaluation alone may not fully capture the complex functional dynamics of immune cells within the tumour microenvironment.

Further studies with larger sample sizes, extended follow-up, inclusion of diverse histological subtypes, and integration of molecular and cytokine profiling are warranted to better elucidate the role of CD4 tumour -infiltrating lymphocytes and their potential as prognostic biomarkers and therapeutic targets in breast carcinoma.

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