Original Article

TUMOR ASSOCIATED MAST CELLS: CORRELATION WITH CLINICOPATHOLOGICAL PARAMETERS IN BREAST CARCINOMA

Meghana Shree S[1], Rashmi P[1], Bala Veena[1]

[1]Department of Pathology, J.J.M medical college, Davangere, Karnataka, India

Abstract

Background: Mast cells are key component of innate immune system, intact closely with tumor cells and exert both protumorigenic and antitumorigenic effect through their diverse mediators. However, there exact role on invasive breast carcinoma remains ambiguous with study relating to both tumor prognosis and favouring tumor growth. The objective is to asses Mast cell density (MCD) in Inavsive breast carcinoma. To analyze its association of MCD with Clinicopathological prognostic parameters. **Material and Methods:** 34 cases of histopathologically confirmed breast carcinomas, sections from the tumor proper and non neoplastic adjacent breast tissue where stained using Tissue Geimsa and mast cell density (MCD) was assessed. The tumor mast cell density was compared with Clinicopathological parameters such as Age, Tumor size, Tumor type, Histological grade, TILs, Lymph node involvement, LVI and Molecular subtype. **Results:** Of 34 cases, majority of the cases belongs to 4th decade constituting to around 29.4 (10 cases). Mean tumor size is 4.7+_1.7 cm with majority belonging to T2 category of TNM staging. The tumor mast cell density was higher than the mast cell density of non neoplastic breast tissue($p<0.0001$). There were 26 cases of Invasive ductal carcinoma NOS (76.4%). The remaining 8 cases of IDC with mucinous features, one case each of micropapillary, medullary, metaplastic, cribriform and micropapillary variant of mucinous carcinoma. There was no significant difference between mean values of mast cell density in IDC- NOS and breast carcinoma variants. No significant association of mast cell density was seen with other clinicopathological parameters such as tumor size, tumor grade, lymph node metastasis and Tumor infiltrating lymphocytes. However, the higher mast cell density was significantly associated with Lymphovascular invasion (p-0.02). **Conclusion:** Our study favors the hypothesis of Protumorigenic effect of Mast cells in Breast carcinoma. Further studies on mast cell density and breast carcinomas, should be studied to elucidate their role and for development of novel therapeutic and diagnostic strategies.

Keywords: Breast carcinoma, Tumor microenvironment, Mast cell density.

Received: 13 August 2026 **Revised: 17 August 2026** **Accepted: 20 August 2026** **Published: 22 October 2026**

INTRODUCTION

Inflammation is a fundamental component of the body's defense mechanism, acting against both internal and external stimuli and playing a crucial role in maintaining tissue homeostasis.[1,4] The tumor microenvironment, an integral part of the immune system, is known to significantly influence tumor behaviour. Several cancers are associated with infection and chronic inflammation, including gastric, colorectal, cervical, and hepatocellular carcinoma.[3,5] Mast cells are granular, immune cells which constituted by rich content of inflammatory mediators. In this study, we will explore the evidence supporting both protumoral and antitumoral roles of mast cells in the progression of breast cancer.[2] Mast cells contain a wide array of bioactive molecules within their cytoplasmic granules and are recognized for their dual nature of role in either inhibiting or promoting tumor growth. The release of cytokines and proteolytic enzymes by mast cells can induce apoptosis in neoplastic cells. In breast cancer, particularly within fibrotic regions, mast cells may suppress tumor growth by directly inducing tumor cell death through Tumour Necrosing Factor and indirectly via the action of heparin.[6,7] In contrast, mast cells can also enhance tumor proliferation by promoting angiogenesis. This occurs through the release of heparin-like substances and various growth factors, including PDGF, VEGF, stem cell factor, and nerve growth factor present in the ECM.[6] These factors are known to stimulate fibroblast proliferation and neovascularization thereby supporting tumor growth. The dual role of mast cells in both inhibiting and promoting breast carcinoma progression necessitates further study to determine the overall impact of mast cell density on tumors, as well as their potential utility as prognostic markers and targets for therapy.

MATERIALS AND METHODS

It is a Retrospective study conducted over the duration of 2 years from June 2023 to June 2025, which included 34 cases of histopathologically confirmed breast carcinomas. The sections from the tumor proper and non neoplastic adjacent breast tissue

Address for correspondence: Dr. Meghana Shree S, Department of Pathology, J.J.M medical college, Davangere, Karnataka, India.
E-mail: meghana1200374@gmail.com

DOI:
10.21276/amit.2026.v13.i3.1135

How to cite this article: Shree SM, Rashmi P, Veena B. Tumor Associated Mast Cells: Correlation with Clinicopathological Parameters in Breast Carcinoma. Acta Med Int. 2026;13(3):724-728.

where stained using Tissue Geimsa and Mast cell density was assessed by selecting hotspot in low power (20x) and then such 10 fields were taken. In 400x the mast cells were counted in those selected 10 fields. Then the mean of 10 fields was taken as MCD. Thus, MCD of peritumoral and intratumoral was obtained. The tumor MCD was compared with Clinicopathological parameters such as age, tumor size, tumor type, histological grade, TILs, lymph node involvement, LVI and molecular subtype.

Table 1: Intratumor MCD Vs Non-Neoplastic Breast MCD

MCD	MEAN	SD	RANGE
Intratumoral MCD	5.67	3.12	1-15
Non-neoplastic breast mcd	1.64	1.09	0-4
T-test	P = <0.0001		

Table 2: Age Distribution

Age groups	No. Of patients	Percentage
31-40	6	17.6
41-50	10	29.4
51-60	7	20.6
61-70	5	14.7
71-80	4	11.8
81-90	2	5.9
Total	34	100

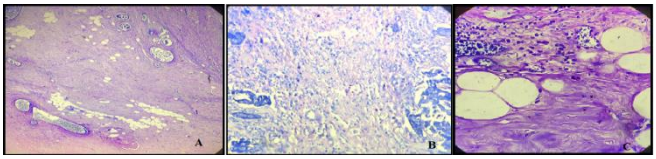


Figure 1: A and B- showing hotspots. C – Showing mast cells in 40x

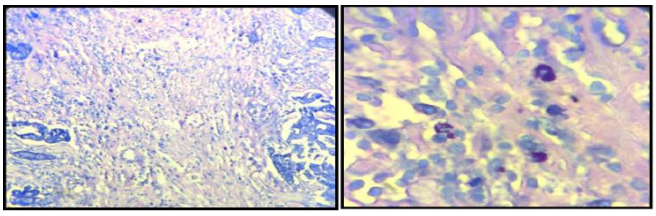


Figure 2: Intratumoral mast cells in 10x and 40x

Results

Mast cell density (MCD) was assessed in both the tumor proper and the adjacent tissue, and the values were compared. Individual clinicopathological parameters were then correlated with intratumoral MCD. The mast cell density within the tumor was significantly higher than that in non-neoplastic breast tissue (p<0.0001), as demonstrated in [Table 1 and Figure 2 and 3].

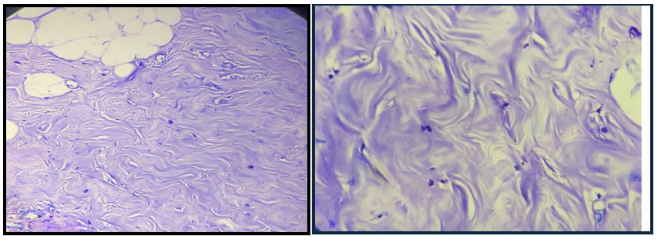
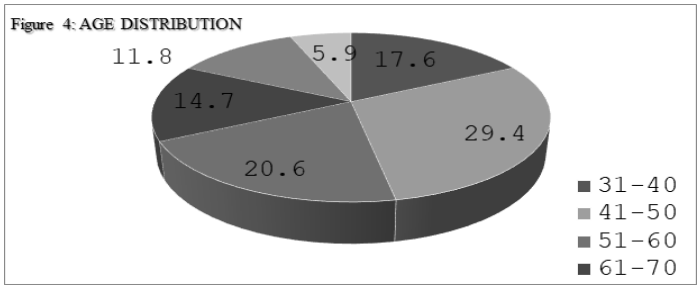


Figure 3: showing mast cells in Peritumoral stroma showing mast cells in 10x and 40 x respectively



Among the 34 cases, the majority were in the fourth decade, accounting for approximately 29.4% (10 cases). The mean age was 55.38 years, with a range of 32–90 years, as shown in [Table 2 and Figure 4]. Tumors larger than 5 cm showed relatively higher MCD, with greater values observed in the T2 category compared to other categories; however, the t value was 0.09 [Figure 5]. The mean tumor size was 4.7±1.7 cm, with most cases belonging to the T2 category of TNM staging, and its comparison with MCD is presented in [Table 3 and 4].

Histopathological variants was classified and compared separately. There were 26 cases of Invasive ductal carcinoma NOS (76.4%). The remaining 8 cases of IDC with Mucinous features, one case each of Micropapillary, Medullary, Metaplastic, Cribriform and Micropapillary variant of Mucinous carcinoma. The histological type like metaplastic, cribriform and papillary and medullary had more MCD than the IDC-NOS. However, no significant difference between mean values of mast cell density in IDC- NOS and breast carcinoma variants was acheived. [Table 5 and Figure 5]. No significant association of MCD was seen with other clinicopathological parameters such as tumor size, tumor grade, lymph node metastasis and tumor infiltrating lymphocytes. [Table 6-10]. But the higher mast cell density was significantly associated with lymphovascular invasion (p-0.02) as shown in [Table 9].

Table 3: Tumor size

Tumor size	No. Of cases	Percentage
<2	1	2.9

2-5	23	67.6
>5	10	29.4
TOTAL	34	100

Table 4: Tumor Size VS MCD

TUMOR SIZE (T STAGE)	MCD		N
	MEAN	SD	
<2 (T1)	4.0	0.0	1
2-5 (T2)	5.0	2.8	23
>5 (T3)	7.3	3.6	10
T1&T2 VS T3	0.09		

Table 5: Histological Type

Histological type	Factor	n	Median	Average rank
IDC-NOS	1	26	4.5	17.23
MICROPAPILLARY CARCINOMA	2	2	5	15
MUCINOUS CARCINOMA	3	2	3.5	8.5
MEDULLARY	4	1	5	18.5
CRIBRIFORM CARCINOMA	5	1	6	22.5
METAPLASTIC CARCINOMA	6	1	12	33
PAPILLARY CARCINOMA	7	1	7	26
KRUSKAL WALLIS TEST	P = 0.499			

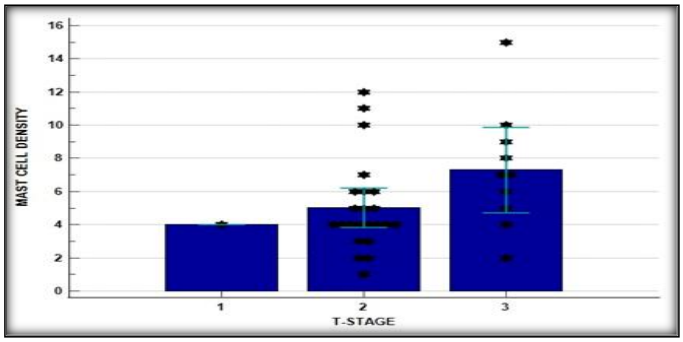


Figure 5: Graph Representing Stage of Tumor Compared with MCD.

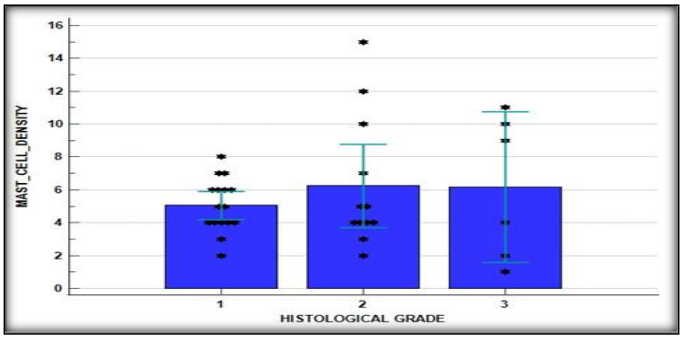


Figure 6: Graph Representing Histological Grade of Tumor Compared with MCD.

Table 6: Histological grade

Histological grade	MEAN	SD	N
GRADE 1	5.1	1.6	16
GRADE 2	6.3	4.0	12
GRADE 3	6.2	4.4	6
GRADE 1 VS GRADE 2			P = 0.35
GRADE 1 VS GRADE 3			P = 0.57
GRADE 2 VS GRADE 3			P = 0.97

Table 7: Lymph node metastasis

LN METASTASIS	Mast Cell Density		N
	Mean	SD	
PRESENT	5.9	3.5	13
ABSENT	5.5	2.9	21
CHI-SQUARE TEST	0.73		

Table 8: Molecular subtype VS MCD

Molecular subtype	No. of cases	Mean	SD
LUMINAL A	7	5.7	2.06
LUMINAL B	9	4.4	1.24
HER2 ENRICHED	9	7.0	4.10
TNBC	9	5.6	3.87
LUMINAL VS HER2 ENRICHED			P = 0.70
LUMINAL VS TNBC			P = 0.17
HER2 ENRICHED VS TNBC			P = 0.45

Table 9: Lymphovascular invasion

LVI	Mast Cell Density		N
	Mean	SD	

PRESENT	7.36	4.07	14
ABSENT	4.50	1.43	20
Chi-square test	P = 0.023		

Table 10: Til VS MCD

Til	Mast Cell Density				N
	Mean	Sd	Median	Average Rank	
1+	5.67	3.7	4	16.63	15
2+	5.80	2.9	5	18.43	15
3+	5.25	2.1	5	17.25	4
KRUSKAL WALLIS TEST	P = 0.88				

Discussion

Mast cells, first described in tumors by Paul Ehrlich, are increasingly recognized as important components of the tumor microenvironment across numerous solid malignancies including thyroid, gastric, bladder, breast cancer pancreatic, and Merkel cell carcinoma and also few hematologic tumors such as Hodgkin and non-Hodgkin lymphomas and plasmacytoma. Their presence within tumors is influenced by microenvironmental factors such as hypoxia, low pH, accumulation of lactic acid, adenosine, IFN-γ, and PGE2, as well as chemotactic signals including VEGFs and Ang1 produced by tumor cells.[1,3]

In this study, MCD was significantly higher in IBC in adjacent non-neoplastic breast tissue. This finding is consistent with Aaltomaa et al,[2] suggesting a possible biological relationship for mast cell recruitment and tumor progression.

Mast Cell Localization - Mast cells can be distributed as peritumoral or intratumoral,[10] and this localization influences their biological activity. In our study, intratumoral mast cell density was higher than peritumoral, similar to findings by Rajabi et al. in malignant melanoma.[13]

Some studies, such as those by Glajcar et al,[12] highlight mast cell heterogeneity using tryptase and chymase immunohistochemistry to demonstrate functional subtypes. This supports the need for molecular subtyping to better understand their distinct roles in breast tumors.[13]

Correlation with Clinicopathological Features -Although HER2-enriched and triple-negative tumors in our study showed a higher MCD, we did not find statistically significant associations between MCD and ER/PR/HER2 status, tumor grade, necrosis, lymph node metastasis, or tumor-infiltrating lymphocytes (TILs). Similar conclusions were reported by Dabiri et al., Meyer et al., and Kermani et al., all suggesting that MCD alone does not.[16,17]

When multivariate analysis was expanded to include tumor grade, ER status, HER2 status, tumor size, and nodal status, the presence of stromal mast cells approached significance as an independent prognostic variable, as previously noted by Dabiri et al.[16]

Some studies have even shown opposite trends: Dabiri et al,[16] and Elpek et al,[24] reported that higher mast cell infiltration, particularly intratumoral, was associated with better prognosis, highlighting the dual and context-dependent role of mast cells in breast cancer biology.

Association with Lymphovascular Invasion- A key finding in our study was the significant association between higher MCD and lymphovascular invasion (LVI). This is similar with the observations of Keser et al,[16] who reported a strong correlation between mast cells and lymphatic vessel density using D2-40 IHC, supporting the protumorigenic role of mast cells in promoting lymphangiogenesis. Similarly, Silva et al,[19] demonstrated that perivascular mast cell infiltration correlates with LVI in breast carcinoma.

Mast cells are known to release mediators such as tryptase, chymase, VEGF, TNF-α, IL-8, and MMPs, which enhance endothelial permeability, stromal remodeling, angiogenesis, and vasculogenesis Ribatti et al. (06) demonstrated tryptase in mast cell which strongly correlates with microvascular density, facilitating tumor invasion and metastatic potential. These mechanisms support our studies observation, that mast cells likely contribute to tumor spread via lymphovascular channels.

Pro-tumorigenic vs Anti-tumorigenic Role- The literature reveals conflicting roles for mast cells as tumor progression and in few as immune survelliance against tumor

Pro-tumorigenic Evidence

- Takanami et al,[14] and Ariel et al,[22] linked higher MCD with poor prognosis, increased angiogenesis, and aggressive tumor behavior.
- Meta-analyses by Montovani et al,[15] and Aponte-López et al,[1] describe mast cells as "microenvironment remodelers" promoting invasion, metastasis, and vascular remodeling.

Anti-tumorigenic Evidence

- Dabiri et al,[16] identified stromal mast cells as markers of favorable prognosis.
- Elpek et al,[24] showed intratumoral mast cells correlate with better survival.
- Sullivan et al,[18] suggested that intratumoral mast cells may exert tumor-suppressive cytokine effects.

These discrepancies underscore that mast cell localization (intratumoral vs peritumoral), microenvironmental cues, and functional heterogeneity likely determine their behavior. Glajcar et al,[10] further emphasized this by distinguishing mast cell subtypes using tryptase and chymase.

Therapeutic Relevance- Recent studies suggest mast cells may serve as therapeutic targets

- In bladder cancer, mast cells promote proliferation via estrogen receptor-β, and ERβ antagonists suppressed tumor growth
- In vivo colon cancer models showed induction of mast cell apoptosis showed corresponding reduction in tumor development.[11]
- Mast cells and also dendritic cells have been proposed as cellular immune checkpoints in solid tumor immunotherapy.[11,26]

However, as there is no usage of specific mast cell markers for tumor-associated mast cell subtyping, this categorization complicates therapeutic targeting.

Conclusion

MCD is significantly increased in invasive breast carcinoma compared to adjacent non-neoplastic tissue.

Higher MCD has got significant association with lymphovascular invasion, supporting a role in tumor dissemination and early metastatic processes.

Whereas, no significant associations were observed with tumor grade, ER/PR/HER2 status, lymph node metastasis, tumor size, or TILs, reflecting the complex and context-dependent biology of mast cells.

Overall, our findings support a predominantly pro-tumorigenic role of mast cells in breast cancer, particularly in facilitating vascular invasion.

Further studies are required for assessing mast cell subtypes, functional states, and spatial distribution for better understanding their prognostic value and therapeutic potential.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Aponte-López A, Muñoz-Cruz S. Mast cells in breast cancer: from biology to clinical relevance. Cancers (Basel). 2021;13:260-6
2. Aaltomaa S, Lipponen P, Papinaho S, Kosma VM. Mast cells in breast cancer. Anticancer Res. 1993;13:785–8.
3. Vendramini-Costa D. B. and Carvalho J. E., Molecular link mechanisms between inflammation and cancer, Current Pharmaceutical Design. (2012) .26, 3831–52
4. Virchow R. Cellular Pathology as Based Upon Physiological and Pathological Histology. Philadelphia: J. B. Lippincott & Co.; 1863.
5. Eiro N, Vizoso FJ. Inflammation and cancer. World J Gastrointest Surg. 2012;4:62–72.
6. Ribatti D, Annese T, Tamma R. Controversial role of mast cells in breast cancer tumor progression and angiogenesis. Clin Breast Cancer. 2021;21:486–91.
7. Amini RM, Aaltonen K, Nevanlinna H, Carvalho R, Salonen L, Heikkilä P, et al. Mast cells and eosinophils in invasive breast carcinoma. BMC Cancer. 2007;7:165.
8. Ju MJ, Qiu SJ, Gao Q, Fan J, Cai MY, Li YW, Tang ZY. Combination of peritumoral mast cells and T-regulatory cells predicts prognosis of hepatocellular carcinoma. Cancer Sci. 2009 Jul;100:1267–74.
9. Hussain SP, Harris CC. Inflammation and cancer: an ancient link with novel potentials. Int J Cancer. 2007;121:2373–80.
10. Zhang S, Yi S, Zhang D, Gong M, Cai Y, Zou L. Intratumoral and peritumoral lymphatic vessel density both correlate with lymph node metastasis in breast cancer. Sci Rep. 2017;7:40
11. Meira LB, Bugni JM, Green SL, Lee CW, Pang B, Borenshtein D, et al. DNA damage induced by chronic inflammation contributes to colon carcinogenesis in mice. J Clin Invest. 2008;118:2516–25.
12. Glajcar A, Szpor J, Hodorowicz-Zaniewska D, Tyrak KE, Okoń K. The composition of T cell infiltrates varies in primary invasive breast cancer of different molecular subtypes as well as according to tumor size and nodal status. Virchows Arch. 2019;475:13–23.
13. Rajabi P, Bagheri A, Hani M. Intratumoral and peritumoral mast cells in malignant melanoma: an immunohistochemical study. Adv Biomed Res. 2017;6:39.
14. Takanami I, Takeuchi K, Naruke M. Mast cell density is associated with angiogenesis and prognosis in invasive breast carcinoma. Cancer. 2000;88:2685–9.
15. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature. 2008;454:436–44.
16. Dabiri S, Huntsman D, Makretsov N, Chia S, Gelmon K, Hayes M, et al. The presence of stromal mast cells identifies a subset of invasive breast cancers with a favorable prognosis. Hum Pathol. 2004;35:569–75.
17. Kermani IA, et al. Mast cell infiltration in breast cancer and its relationship with clinicopathological parameters. Iran J Pathol. 2017;12:345–52.
18. Sullivan M, et al. Intratumoral mast cells and tumor suppression in breast carcinoma. Breast J. 2011;17(3):258–64
19. Silva I, Branco M, Ramos R, Silva S, Catarino R. Perivascular mast cells and lymphovascular invasion in breast carcinoma. Pathol Res Pract. 2020;216:15
20. Montovani A, Allavena P, Sica A, Balkwill F. Tumour-associated macrophages and mast cells in tumour progression. Nat Rev Cancer. 2017;17:451–65.
21. Varricchi G, Galdiero MR, Loffredo S, Marone G, Rivellese F, Granata F. Mast cells and cancer: ambiguous roles. Clin Rev Allergy Immunol. 2017;52:304–16.
22. Ariel A, et al. Breast cancer stromal mast cells: association with clinicopathological features. Hum Pathol. 2018;73:23–30.
23. Meyer S, et al. Mast cells in breast carcinoma: lack of correlation with hormone receptors and HER2. Pathol Oncol Res. 2012;18:215–20
24. Elpek GO, Gelen T, Aksoy NH, Erdogan A, Dertsiz L, Demircan A, et al. The prognostic relevance of mast cell infiltration in breast cancer. Pathol Res Pract. 2001;197:269–75.
25. Samoszuk M, et al. Association of mast cells with angiogenesis in breast carcinoma. Am J Pathol. 2005;166:505–13.
26. Kalkusova K, Smite S, Darras E, Taborska P, Stakheev D, Vannucci L, Bartunkova J, Smrz D. Mast cells and dendritic cells as cellular immune checkpoints in solid tumor immunotherapy. Front Immunol. 2017;8:424.
27. Keser SH, Kandemir NO, Ece D, Gecmen GG, Gul AE, Barisik NO, Sensu S, Buyukuysal C, Barut F. Relationship of mast cell density with lymphangiogenesis and prognostic parameters in breast carcinoma. Kaohsiung J Med Sci. 2017 Apr;33:171–80.