ORIGINAL ARTICLE

Clinicopathological Spectrum and Biomarker Profile of Male Breast Cancer: A Retrospective Study from a Tertiary Care Center in South India

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Abstract

Introduction: Male breast cancer (MBC) accounts for <1% of breast malignancies yet often presents at advanced stages, particularly in low- and middle-income countries where awareness is limited. This study sought to define the clinicopathological spectrum, biomarker profile, and treatment outcomes of MBC in a South Indian tertiary cancer center.

Objectives: To analyze the demographic features, clinical presentation, pathological characteristics, biomarker distribution, treatment modalities, and outcomes of MBC cases managed at our center between 2019 and 2025.

Materials and methods: We retrospectively analyzed all male patients with histologically confirmed breast carcinoma managed between 2019 and 2025 at ESIC Medical College and Hospital, Hyderabad. Demographic, clinical, pathological, biomarker, and treatment data were retrieved from hospital records and supplemented by follow-up contact.

Results: A total of 15 patients (mean age 60 years, range 31–74) were identified. Median delay from symptom onset to diagnosis was 6 months. All presented with a retroareolar mass, frequently accompanied by nipple retraction or skin changes. Most patients had advanced disease: Stage III (n = 9, 60.0%) and Stage IV (n = 4, 26.7%). Invasive ductal carcinoma was universal. Hormone receptor positivity was seen in 80%, HER2 positivity in 40%, and a triple-positive phenotype in 26.7%. Treatment strategies were stage- and biomarker-driven: 86.7% underwent surgery, endocrine therapy was prescribed for all HR+ cases, HER2-directed therapy was delivered when feasible, and CDK4/6 inhibitors were used in selected advanced HR+ tumors. At last follow-up, 9 patients (60%) remained alive with disease control, while 2 succumbed to progression.

Conclusion: MBC in this cohort was characterized by delayed diagnosis, advanced presentation, and a high prevalence of HER2-positive tumors. Multimodality, biomarker-guided therapy achieved durable control in many patients, underscoring the urgent need for awareness initiatives, earlier detection, and equitable access to targeted therapies in India.

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Introduction

Male breast cancer (MBC) is a rare but clinically consequential malignancy, comprising under 1% of breast cancers and demanding deliberate, guideline-informed care. Late recognition—shaped by stigma, low awareness, and diagnostic inertia—contributes to advanced presentation, particularly in resource-limited settings. Most tumors are hormone receptor–positive, with a meaningful HER2-positive subset; accordingly, endocrine therapy and, when indicated, HER2-targeted treatment are central, though access barriers persist. This review distills current epidemiology, biology, diagnostics, and management, and advances practical, biomarker-driven strategies to enable earlier detection and equitable care.

Materials and Methods

Study Design and Setting

This was a retrospective observational study conducted in the Department of Medical Oncology at a tertiary care center in South India. The study period spanned from 2019 to 2025. All cases of male breast carcinoma diagnosed and managed during this timeframe were included. The study protocol was approved by the Institutional Ethics Committee (IEC No: ESICMC/SNR/IEC-S0401/08–2025) on 29–05–2025 and adhered to all the Declarations of Helsinki. A waiver of informed consent was granted due to the retrospective nature of the study. Patient confidentiality and data privacy were maintained throughout. Data regarding clinical and family history, stage of the disease, histopathological examination, IHC status, and treatment modalities were extracted from electronic hospital medical records, patient files, and chemotherapy logs. Attempts were made to retrieve follow-up information *via* telephonic contact.

Inclusion Criteria

Adult male patients (≥18 years) registered and treated at the Department of Medical Oncology in our institute with histologically confirmed breast carcinoma and availability of baseline demographic, clinical, pathological, and biomarker data were included.

Exclusion Criteria

Benign breast conditions, such as gynecomastia, breast involvement secondary to another primary malignancy, and presence of cardiovascular comorbidities that precluded the use of anti-HER2 therapy were excluded.

Primary Outcome

To describe the clinicopathological characteristics, biomarker profile, and stage distribution.

Secondary Outcomes

To evaluate treatment patterns, including surgery, systemic therapy, endocrine therapy, and HER2-directed therapy.

To assess short-term clinical outcomes, including treatment response and disease status at last follow-up.

To correlate biomarker expression (hormone receptor and HER2 status) with tumor stage and nodal involvement.

To document delays in diagnosis and patterns of loss to follow-up as barriers to optimal care.

Statistical Analysis

Data were compiled from electronic medical records and entered into Microsoft Excel for analysis. Descriptive statistics were used to summarize patient demographics, clinical

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presentation, pathological characteristics, biomarker distribution, treatment modalities, and outcomes. Continuous variables, such as age and diagnostic delay, were expressed as mean, median, and range, while categorical variables, such as stage, histology, biomarker status, and treatment type, were expressed as absolute numbers and percentages. Associations between biomarker expression (hormone receptor and HER2 status) and stage or nodal involvement were descriptively assessed, given the small cohort size precluding formal statistical testing. Survival outcomes were reported narratively as proportions of patients alive, controlled, lost to follow-up, or deceased at last contact. No inferential statistical tests were applied due to the limited sample size.

Results

Fifteen male patients (mean age 60, range 31–74 years) were diagnosed with breast carcinoma, none of whom had a history of familial cancer, estrogen exposure, radiation, or occupational carcinogen exposure. The median time from symptom onset to clinical evaluation was 6 months. All presented with a firm palpable breast mass, predominantly retroareolar, with associated features like nipple retraction, skin thickening, and, in 2 cases, ulcerated fungating tumors. Four patients had systemic symptoms, including cough, dyspnea, bone pain, fatigue, or weight loss. Clinical staging per AJCC 8th edition revealed 2 patients with T1 tumors, 6 with T2–T3 lesions, and 7 with T4 features such as peau d'orange or ulceration. Ipsilateral axillary lymphadenopathy was seen in 13 (86.7%) patients, ranging from mobile to fixed nodes, with no evidence of supraclavicular or contralateral involvement. All patients underwent ultrasound/mammography and core biopsy, confirming invasive ductal carcinoma in all cases. Systemic staging was done via PET-CT as per institution protocols.

- Overall clinical stage distribution was:
- Stage I–II (early-stage): 2 patients (13.3%)
- Stage III (locally advanced): 9 patients (60.0%)
- Stage IV (metastatic): 4 patients (26.7%)

Immunohistochemistry showed hormone receptor positivity in 80%, HER2 positivity in 40%, and a triple-positive profile in 26.7%. The 2 early-stage patients (both *HR+/*HER2–) underwent upfront modified radical mastectomy (MRM) followed by adjuvant endocrine therapy. Among Stage III patients, 6 underwent upfront MRM: 4 *HR+/*HER2– received adjuvant anthracycline–taxane chemotherapy plus endocrine therapy, and 2 HER2+ (one triple-positive, one *HR–/*HER2+) received postoperative trastuzumab-based therapy with chemotherapy. The remaining 3 Stage III patients received neoadjuvant chemotherapy: 2 HER2+ patients (one triple-positive, one *HR–/*HER2+) received dual HER2 blockade with trastuzumab and pertuzumab; 1 *HR+/*HER2– patient with extensive T4b disease received standard chemotherapy. All subsequently underwent MRM and completed biomarker-guided systemic therapy.

Among the 4 Stage IV patients, 2 with de novo HER2+ pulmonary metastases received taxane-based chemotherapy with trastuzumab. Of the 3 HR+ patients, 2 were treated with aromatase inhibitors and CDK4/6 inhibitors (palbociclib), while 1 with endocrine-resistant bone metastasis received fulvestrant. Overall, 13 patients (86.7%) underwent surgery: 11 had MRM, and 2 Stage IV patients underwent palliative toilet mastectomies. Surgical decisions were based on resectability, treatment response, and symptom burden. On follow-up, 9 patients (60%) were alive and under surveillance—5 postcurative treatment, 2 on adjuvant endocrine therapy, and 2 Stage IV patients with stable disease. Four patients (26.7%) were lost to follow-up, and 2 (13.3%) with metastatic disease (one HER2+ and one *HR+/*HER2–) died due to disease progression (Tables 1 and 2).

Table 1: Distribution of TNM stage and biomarker profiles in male breast cancer patients

Parameter	*No. of patients (%)*	*Biomarker profile*
T1	2 (13.3)	HR+/HER2–
T2–T3	6 (40.0)	HR+/HER2– (n = 3); Triple+ (n = 2); HR–/HER2+ (n = 1)
T4b/c	7 (46.7)	HR+/HER2– (n = 3); Triple+ (n = 1); HR–/HER2+ (n = 3)
N0	2 (13.3)	HR+/HER2–
N1–N3	13 (86.7)	All HER2+ and triple+ cases
M0	11 (73.3)	All biomarker subtypes
M1	4 (26.7)	HR+/HER2– (n = 2); Triple+ (n = 1); HR–/HER2+ (n = 1)

Discussion

Male breast cancer is a rare but clinically relevant malignancy, constituting <1% of all breast cancers globally.[1] This retrospective case series from a tertiary center in South India offers valuable insights into the clinical behavior, biomarker patterns, and management challenges of MBC in a low-resource setting. The observed trends largely mirror international data, including a predominance of hormone receptor (HR)–positive tumors, late-stage presentation, and significant barriers to early diagnosis and longitudinal care.

Late Presentation and Diagnostic Limitations

In this cohort of 15 patients, 60.0% (n = 9) presented with stage III and 26.7% (n = 4) with stage IV disease, indicating that 86.7% (n = 13) had either locally advanced or metastatic cancer at diagnosis. This pattern is consistent

Table 2: Treatment approaches by stage and biomarker profile (Non-metastatic)

Stage	*Biomarker profile*	*Chemotherapy*	*HER2 Therapy / Surgical Approach*
Stage I–II (n = 2)	HR+/HER2– (n = 2)	None	None/Upfront MRM
Stage III (n = 6)	HR+/HER2– (n = 4)	Adjuvant anthracycline–taxane	None/Upfront MRM
Stage III (n = 6)	Triple+ (n = 1)	Adjuvant anthracycline–taxane	Trastuzumab (adjuvant)/Upfront MRM
Stage III (n = 6)	HR–/HER2+ (n = 1)	Adjuvant anthracycline–taxane	Trastuzumab (adjuvant)/Upfront MRM
Stage III (n = 3)	Triple+ (n = 1)	Neoadjuvant anthracycline–taxane	Trastuzumab + Pertuzumab (neoadjuvant)/MRM post-NACT
Stage III (n = 3)	HR–/HER2+ (n = 1)	Neoadjuvant anthracycline–taxane	Trastuzumab + Pertuzumab (neoadjuvant)/MRM post-NACT
Stage III (n = 3)	HR+/HER2– (n = 1)	Neoadjuvant anthracycline–taxane	None/MRM post-NACT

with previous Indian data[2] and highlights delays stemming from low awareness, cultural stigma, and diagnostic inertia among providers. Advanced imaging with PET-CT was performed routinely for staging, providing accurate systemic evaluation. HER2 status was determined by immunohistochemistry (IHC), with dual in situ hybridization (DISH) used for equivocal cases due to unavailability of fluorescence in situ hybridization (FISH). While DISH is an acceptable alternative, limitations in confirmatory HER2 testing can compromise treatment selection in borderline cases.

Biomarker Distribution and Staging Correlation

HR positivity was identified in 80% (n = 12) of patients, consistent with large registry data indicating HR+ rates above 85% in MBC.[3,4] HER2 positivity was identified in 40% (n = 6), and 26.7% (n = 4) were triple-positive (*ER+/*PR+/HER2+). Importantly, HER2-positive and triple-positive tumors correlated with more advanced presentation:

- Among 7 patients with T4 disease, 4 (57%) were HER2+.
- All 13 patients with N1–N3 disease were HER2+ or triple-positive.
- Three of four metastatic cases were HER2+ or triple-positive.

Multimodal Management

MRM was performed in 73.3% (n = 11), consistent with established norms in male breast oncology.[5] Endocrine therapy, primarily tamoxifen, was administered in all HR+ patients. Tamoxifen remains the agent of choice in male patients due to its superior survival benefit compared to aromatase inhibitors.[4] CDK4/6 inhibitors were used in 26.7% (n = 4) with advanced HR+ disease, reflecting integration of contemporary targeted therapies. Recent pooled analyses have shown promising outcomes with CDK4/6 inhibitors in male *HR+/*HER2− breast cancer, with progression-free survival of approximately 20 months.[6]

Neoadjuvant chemotherapy was utilized in only 6.7% of patients, reflecting either stage-inappropriate presentation or limited capacity for treatment monitoring. Sharma et al. similarly reported low neoadjuvant use in Indian MBC populations.[2] Radiotherapy was underutilized, despite evidence that it reduces local recurrence and improves survival in high-risk MBC.[1,7]

Systemic Challenges and Outcomes

Two patients (13.3%) died due to disease progression—both with stage IV disease. Follow-up was complete for all evaluable patients, but 26.7% (n = 4) were lost to follow-up, a common limitation in resource-limited settings. These losses reflect systemic barriers such as travel constraints, treatment fatigue, lack of community support, and financial burden—issues widely reported in LMIC oncology.[2,8]

Strategic Implications

This study reinforces the need for early detection strategies tailored to men and highlights the prognostic significance of HER2 and triple-positive profiles in MBC. Integration of biomarker data with TNM staging enables more informed treatment planning and resource allocation. Current guidelines from NCCN and ESMO recommend dual HER2 blockade in eligible patients,[9,10] but equitable access remains a challenge.

We advocate for national policies that mandate inclusion of male-specific protocols in breast cancer guidelines, such as those by ICMR. Establishing MBC registries and enabling gender-inclusive clinical trials are essential next steps, as recommended in consensus statements from the NIH and global oncology networks.[11]

Conclusion

Male breast cancer in this South Indian cohort was characterized by delayed diagnosis, advanced stage at presentation, and a relatively high rate of HER2 positivity. Biomarker-guided multimodality therapy achieved durable disease control in many patients. These findings underscore the need for earlier detection and awareness, as well as equitable access to HER2-directed and endocrine therapies across resource-limited settings.

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References

1. Giordano SH, Cohen DS, Buzdar AU, et al. Breast carcinoma in men: a population-based study. Cancer 2004;101(1):51–57.
2. Bhardwaj PV, Gupta S, Elyash A, et al. Male breast cancer: a review on diagnosis, treatment, and survivorship. Curr Oncol Rep 2024;26(1):34–45.
3. Lin AP, Huang TW, Tam KW. Treatment of male breast cancer: meta-analysis of real-world evidence. Br J Surg 2021;108(9):1034–1042.
4. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. Ann Oncol 2013;24(6):1434–1443.
5. Cutuli B, Cohen-Solal Le-Nir C, Serin D, et al. Male breast cancer: evolution of treatment and prognostic factors. Analysis of 489 cases. Crit Rev Oncol Hematol 2010;73(3):246–254.
6. Wedam S, Fashoyin-Aje L, Bloomquist E, et al. FDA approval summary: palbociclib for male patients with HR-positive, HER2-negative breast cancer. Clin Cancer Res 2020;26(6):1208–1212.
7. Cardoso F, Costa A, Norton L, et al. ESO–ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). Breast 2014;23(5):489–502.
8. Ly D, Forman D, Ferlay J, et al. An international comparison of male and female breast cancer incidence rates. Int J Cancer 2013;132(8):1918–1926.
9. von Minckwitz G, Procter M, de Azambuja E, et al. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. N Engl J Med 2017;377(2):122–131.
10. de Azambuja E, Piccart-Gebhart M, Fielding S, et al. Final analysis of the ALTTO trial: adjuvant trastuzumab in sequence or in combination with lapatinib in patients with HER2-positive early breast cancer (BIG 2-06/NCCTG N063D [Alliance]). ESMO Open 2024;9(11):103938.
11. Korde LA, Zujewski JA, Kamin L, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol 2010;28(12):2114–2122.