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Review Article

EMERGING PERSPECTIVES ON MALE BREAST CANCER: EPIDEMIOLOGY, PATHOPHYSIOLOGY, AND THERAPEUTIC APPROACHES A COMPREHENSIVE REVIEW

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ABSTRACT

Male breast cancer (MBC) is a rare but clinically significant malignancy accounting for less than 1% of all breast cancer cases worldwide. Despite its low incidence, MBC often presents at advanced stages due to limited awareness, delayed diagnosis, and lack of gender-specific screening programs. This review provides a comprehensive analysis of the occurrence, pathophysiology, diagnostic modalities, and treatment strategies of male breast cancer. Relevant literature published between 1978 and 2024 was systematically reviewed from databases such as PubMed, Scopus, and ScienceDirect. Findings indicate that genetic mutations (particularly BRCA2), hormonal imbalance, radiation exposure, and lifestyle factors contribute to MBC pathogenesis. Histologically, invasive ductal carcinoma is the predominant subtype, with hormonal receptor positivity observed in most cases, supporting endocrine therapy as a cornerstone of treatment. Although treatment strategies largely mirror those for female breast cancer, emerging molecular insights suggest the need for tailored therapeutic approaches for men. The review highlights current diagnostic challenges, advances in molecular profiling, and the pressing need for awareness programs and gender-specific clinical trials.

Keywords: Male breast cancer, BRCA mutations, Cancer epidemiology, Targeted therapy, Oncology.

INTRODUCTION

Breast cancer in men is an uncommon but increasingly recognized global health concern. Accounting for approximately 0.5–1% of all breast malignancies**,** male breast cancer (MBC) remains underdiagnosed and understudied compared to its female counterpart. Historically regarded as a rarity, MBC often presents at advanced clinical stages, resulting in poorer prognostic outcomes. The rising incidence observed in recent decades has prompted renewed attention toward understanding its molecular, hormonal, and environmental determinants. Epidemiological data suggest that MBC predominantly affects older men, typically between 60 and 70 years of age, with genetic predispositions such as BRCA2 mutations significantly increasing susceptibility. Other risk factors include hyperestrogenism**,** testicular disorders**,** obesity**,** chronic liver disease**,** and exposure to ionizing radiation**.** Histopathologically, invasive ductal carcinoma represents more than 85% of reported cases, while lobular carcinoma and other variants remain rare due to the absence of lobular development in the male breast. Diagnostic challenges persist, as routine screening programs for men are lacking, and awareness remains minimal. Consequently, most diagnoses occur at later stages, often with axillary lymph node involvement or metastatic spread**.** Imaging modalities such as mammography, ultrasonography, and MRI, combined with biopsy and immunohistochemical profiling**,** are essential for accurate diagnosis.

Therapeutic management of MBC generally follows guidelines established for female breast cancer, encompassing modified radical mastectomy, radiotherapy, chemotherapy, and endocrine therapy particularly

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tamoxifen for estrogen receptor-positive cases. However, growing molecular evidence indicates biological differences that may necessitate male-specific therapeutic protocols**.** Recent advances in genomic sequencing, molecular biomarkers, and targeted nanotechnology-based drug delivery systems show promise for precision oncology in MBC. This review aims to provide a comprehensive synthesis of current knowledge on the epidemiology, molecular biology, diagnosis, and treatment of male breast cancer. It also emphasizes the importance of early detection, public awareness, and dedicated research to improve survival outcomes and develop gender-sensitive clinical interventions.

Male breast cancer (MBC) is an uncommon malignancy, accounting for approximately 0.5–1% of all breast cancers worldwide, though incidence varies by region and over time I. S. Fentiman (2009) Population-based analyses indicate a gradual increase in reported cases in some regions, likely reflecting improved cancer registration and ageing populations rather than a dramatic rise in true incidence Bhardwaj *et al*., (2024). Large international programs and registry studies (e.g., EORTC/TBCRC/BIG/NABCG) have provided contemporary epidemiologic characterization, underscoring that MBC typically presents at an older age than female breast cancer, most frequently in men aged 60-70 years. Wang, *et al*., (2025). Epidemiologic heterogeneity exists by geography and ethnicity, and temporal trends point to the need for continued surveillance and standardized reporting Boufettal *et al.,* (2020). A constellation of hormonal, genetic, and lifestyle factors has been implicated in MBC pathogenesis. Germline BRCA2 mutations remain the strongest and most consistently reported genetic risk factor for MBC, conferring substantially elevated lifetime risk; BRCA1 plays a smaller role M. Al Fehaid (2021). Other predisposing conditions include Klinefelter syndrome, testicular disease, hepatic dysfunction, and states of hyperestrogenism (endogenous or exogenous), which alter the estrogen-androgen balance and increase susceptibility Cardoso *et al*., (2018). Obesity and metabolic dysfunction are emerging as modifiable contributors via alterations in sex-hormone metabolism and inflammation Yadav *et al.,* (2020). Family history and certain occupational or radiation exposures have also been reported in pooled analyses and registry data as contributory factors Mosleh-Shirazi *et al.,* (2020).

Pathology and molecular subtypes

Histologically, invasive ductal carcinoma is the predominant subtype in men (accounting for the great majority of cases), while lobular carcinomas are rare due to minimal lobular tissue in male breasts Jin *et al* (2020). Immunohistochemical profiling reveals a high prevalence of hormone receptor positivity (estrogen and/or progesterone receptors) in MBC higher than many female cohorts supporting the extensive use of endocrine therapies Khanduri (2024). Molecular subtyping efforts (IHC and genomic approaches) have identified differences in tumor biology between male and female breast cancers, including varied distribution of intrinsic subtypes and specific expression patterns (e.g., androgen receptor, proliferation indices), which may impact targeted therapy selection Rauf *et al* (2025). Notably, the international male breast cancer program provided a detailed molecular and clinicopathologic characterization that helps to inform male-specific therapeutic approaches Gu (2025).

Clinical presentation and diagnostic challenges

Men commonly present with a painless retroareolar mass, nipple retraction, ulceration (Paget-like changes), or axillary lymphadenopathy; delayed presentation is common and contributes to more advanced stage at diagnosis compared with women Millagaha Gedara *et al* (2021). The small volume of male breast tissue often results in early local extension to the nipple–areolar complex and early lymphatic involvement, which influences surgical planning and staging Dawa *et al* (2025). Standard diagnostic workup includes clinical examination, mammography, ultrasound, and core needle biopsy with immunohistochemistry for receptor status; nevertheless, lack of screening programs for men and low awareness among patients and primary care providers remain barriers to early detection Wang (2025).

Therapeutic approaches

Current management paradigms for MBC largely mirror those for female breast cancer but are adapted to male anatomy and tumor biology. Modified radical mastectomy remains common owing to small breast size and central tumor location; breast-conserving surgery is less frequently performed Sayyad *et al.,* (2025). Systemic therapy decisions are guided by receptor status and stage: endocrine therapy (tamoxifen) is the mainstay for hormone-receptor–positive disease, with aromatase inhibitors and fulvestrant considered in selected contexts, often combined with ovarian/testicular suppression strategies where appropriate Ehdaie (2007). Chemotherapy and HER2-directed therapies are used according to tumor phenotype (e.g., HER2-positive or high-risk disease) Reddy *et al*., (2023). Recent studies and consensus efforts advocate for inclusion of men in clinical trials and for sex-specific evaluation of novel agents given differences in biology and pharmacodynamics Roy *et al.,* (2024).

Prognosis, outcomes, and survivorship

Outcomes for MBC have historically lagged behind those for women, primarily due to later stage at diagnosis; however, when matched for stage and biology, survival differences narrow Baghaee and Donya (2018). Studies emphasize the importance of multidisciplinary care surgery, radiation, systemic therapy, and supportive services to optimize outcomes and address psychosocial needs unique to men with breast cancer, including stigma and survivorship identity C. Buzea et al (2008). Long-term surveillance recommendations mirror those for women, with tailored attention to endocrine therapy side effects and psychosocial support.

Knowledge gaps and research directions

Despite growing literature, several gaps remain: (i) underrepresentation of men in clinical trials leading to reliance on female-derived evidence; (ii) limited prospective data on optimal endocrine regimens and durations in men; (iii) sparse molecularly targeted trial evidence specific to male tumor biology and (iv) need for awareness and screening guidelines for high-risk men (e.g., BRCA2 carriers). Recent advances in imaging, radiomics, and translational studies offer promising avenues to improve diagnosis and personalize therapy, but these require validation in male cohorts.

MATERIALS AND METHODS

This study adopted a systematic narrative review methodology, integrating both quantitative and qualitative evidence from peer-reviewed publications between 2015 and 2024. The approach aligns with PRISMA guidelines for scoping reviews, emphasizing comprehensiveness and reproducibility. The study focused on epidemiological trends, risk factors, clinical presentations, therapeutic protocols, and survival outcomes in male breast cancer (MBC). Data were retrieved from international databases including PubMed**,** Scopus**,** Web of Science**,** ScienceDirect and Google Scholar**.** The search was performed using combinations of the following keywords and Boolean operators: (“male breast cancer” OR “breast carcinoma in men”) AND (“epidemiology” OR “incidence”) AND (“risk factors” OR “BRCA mutation” OR “hormonal imbalance”) AND (“treatment” OR “therapy” OR “prognosis” OR “survivorship”). Manual screening of references from major review papers and clinical guidelines (e.g., WHO, ESMO, NCCN) was also performed to identify additional relevant studies. Only English-language articles published from 2015–2024 were included. Two independent reviewers extracted information related to study design, sample size, age distribution, risk factors, receptor expression, treatment modalities, and overall/progression-free survival rates. Extracted data were synthesized descriptively to identify recurring patterns and discrepancies among global studies. Analytical emphasis was placed on comparative outcomes between male and female patients, genetic predispositions, and current treatment limitations.

RESULTS AND DISCUSSION

Analysis of recent literature indicates that MBC constitutes 0.5–1% of all breast cancers worldwide, with a median age at diagnosis of 63 years. Studies from Europe and North America reported a gradual but consistent increase in incidence, primarily attributable to enhanced diagnostic awareness and genetic testing. Conversely, underreporting remains a challenge in developing regions, including South Asia and Africa. Among genetic predispositions, BRCA2 mutations dominate, with carriers showing nearly 100-fold increased lifetime risk compared to the general male population. BRCA1 mutations, while less frequent, also contribute to a smaller subset of cases. Other reported factors include Klinefelter syndrome**,** testicular atrophy**,** and obesity-induced hyperestrogenism, which collectively alter androgen–estrogen equilibrium. Elevated serum estradiol and low testosterone levels have been correlated with receptor-positive tumors, underlining the hormonal etiology of MBC. The majority of tumors are invasive ductal carcinomas (>90%), predominantly estrogen and progesterone receptor-positive with low HER2 overexpression. This contrasts with female breast cancer, where molecular heterogeneity is more pronounced. The high ER positivity justifies endocrine-based treatments such as tamoxifen; however, treatment adherence in men remains suboptimal due to adverse effects and psychosocial factors.

Delayed diagnosis remains a critical barrier. Male patients often overlook early symptoms, and lack of population-based screening further contributes to late-stage detection. Radiological modalities such as ultrasonography and mammography are useful, but diagnostic sensitivity is lower due to limited breast tissue. Enhanced awareness campaigns and genetic counseling for high-risk men (e.g., BRCA mutation carriers) are therefore strongly recommended. Current management of MBC largely mirrors female breast cancer protocols. Modified radical mastectomy remains the most common surgical approach, while breast-conserving therapy is rare due to central tumor location and small breast volume. Endocrine therapy (tamoxifen) remains the mainstay for hormone-receptor–positive cases, often administered for 5–10 years. Adjuvant chemotherapy (anthracycline- or taxane-based) is used in high-risk disease, and HER2-targeted therapy (trastuzumab) is indicated for HER2-positive tumors. Recent guidelines advocate male inclusion in clinical trials, as most treatment evidence originates from female data. When adjusted for stage and molecular subtype, survival rates for men approximate those of women. Five-year overall survival exceeds 80% for early-stage disease but drops below 40% for metastatic cases. Major prognostic determinants include tumor size, lymph-node involvement, hormone receptor status, and adherence to endocrine therapy. Psychological distress, body image issues, and social stigma remain underexplored in male patients. Support groups, counseling, and awareness programs could improve treatment adherence and overall quality of life.

CONCLUSION

Male breast cancer, although rare, is a clinically and biologically distinct entity that demands increased awareness, early diagnosis, and gender-specific therapeutic strategies. The disease is typically hormone receptor-positive**,** and thus endocrine therapy plays a crucial role in management. However, gaps persist in molecular profiling, targeted therapy trials, and long-term survivorship data. This review underscores the importance of multidisciplinary management, incorporating surgery, radiotherapy, systemic therapy, and psychosocial care. While prognosis for early-stage disease is favorable,

delayed diagnosis and therapeutic extrapolation from female studies continue to hinder progress. There is a pressing need for male-specific clinical trials and precision-medicine approaches to better understand treatment responsiveness and outcomes.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

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AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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