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Triple-Negative Breast Cancer in Indian Women: A Review

Bandana Kumari Soni
Assistant Professor (Zoology), Jai Prakash University, Chapra, Bihar

Abstract

Triple-negative breast cancer (TNBC), defined by the absence of estrogen receptor (ER), progesterone receptor (PR) and HER2 expression, is an aggressive breast cancer subtype with limited targeted treatment options. Compared with Western populations, Indian cohorts demonstrate a markedly higher proportion of TNBC, younger median age at diagnosis, and more frequent presentation at advanced stage. Molecular profiling of Indian TNBC series reveals distinctive features, including elevated rates of germline BRCA1/2 mutations, frequent TP53 alterations, high EGFR expression in many cohorts, and variable androgen receptor (AR) and PD-L1 expression. Systemic therapy remains anchored in anthracycline- and taxane-based chemotherapy; however, immune checkpoint blockade and PARP inhibitors are emerging in selected patients. Structural barriers — late detection, constrained access to molecular diagnostics, and limited availability and affordability of novel agents - diminish the potential clinical impact of these advances. This review synthesizes published Indian data on epidemiology, molecular characteristics, treatment patterns, and outcomes of TNBC, identifies research and policy gaps, and proposes priorities to improve care and generate regionally relevant evidence.

Keywords

Triple-negative breast cancer; TNBC; India; epidemiology; BRCA; molecular profiling; immunotherapy; PARP inhibitors; outcomes.

Introduction

Breast cancer incidence in India is increasing and the median age at diagnosis is lower than in many high-income countries. TNBC represents a biologically heterogeneous subgroup that lacks ER, PR and HER2 expression and therefore is not amenable to endocrine or HER2-directed therapies. Globally, TNBC accounts for approximately 10–15% of breast cancers; multiple Indian series and meta-analyses report substantially higher proportions (25–31%) among Indian patients. Given the aggressive clinical course and limited targeted options for TNBC, a comprehensive

understanding of its epidemiology, molecular landscape, and treatment outcomes within the Indian context is necessary to inform clinical practice and health policy.

Methods

Search strategy and selection criteria: Studies reporting primary data on Indian women with TNBC, or meta-analyses summarizing Indian cohorts, were considered. Eligible study designs included retrospective and prospective observational studies, clinical trials, systematic reviews and meta-analyses. Excluded were single case reports, editorials without original data, and abstracts lacking full peer-reviewed text.

Data extraction and quality assessment: Two independent reviewers extracted data on study design, sample size, TNBC prevalence, age distribution, stage at presentation, molecular and genetic findings (BRCA, EGFR, TP53, AR, PD-L1), treatment modalities, pathologic complete response (pCR) to neoadjuvant therapy, and survival outcomes. Observational studies were appraised using the Newcastle–Ottawa Scale, randomized trials with the Cochrane Risk of Bias tool, and systematic reviews with the AMSTAR checklist. Where possible, pooled values reported in published meta-analyses were used to provide summary prevalence estimates.

Results

Epidemiology and clinical presentation

Indian studies consistently report a higher prevalence of TNBC compared with Western cohorts, with pooled estimates in meta-analyses ranging from 25% to 31%. Indian patients with TNBC are typically younger, with median ages in clinical series clustered in the early to mid-40s versus the mid-50s reported in many Western registries. A substantial proportion of
Indian patients present with locally advanced or metastatic disease (stage III/IV), contributing to inferior survival metrics compared with Western series.

• Prevalence: TNBC comprises **25–31%** of Indian breast cancers, compared with 10–15% in Western cohorts [1,2,8].
• Median age: early to mid-40s; more premenopausal cases [3,12].
• Stage at diagnosis: high proportion present with Stage III/IV disease [3,12].

Table 1. Comparative features of TNBC in Indian vs. Western women

Feature	Indian women	Western women	References
Prevalence	25–31%	10–15%	[1,2,8]
Median age	42–46 years	53–57 years	[3,12]
Stage at presentation	More Stage III/IV	More Stage I/II	[3,12]
BRCA mutation rate	20–30%	10–15%	[5,9,10]
Molecular features	Frequent TP53, high EGFR (~60%), AR in subset	TP53, lower EGFR, AR more consistent	[4,9,11,13]

Feature	Indian women	Western women	References
Outcomes	Lower OS, pCR ~25–35%	Better OS, pCR >40% with NACT + IO	[3,7,12]

Genetic & Molecular Feature

Several Indian cohorts report elevated frequencies of germline BRCA1/2 mutations among TNBC patients, with rates of 20–30% in selected tested populations. Somatic TP53 alterations are common, concordant with global TNBC biology. A number of single-center and multi-center series have described high EGFR expression (reports around 60% in some series), variable AR positivity (reported in subsets, often ~20–30%), and heterogeneous PD-L1 expression that complicates direct extrapolation of immunotherapy benefit without local trial data.

• BRCA1/2 mutations: **20–30%** of Indian TNBC patients tested, higher than global rates [5,9,10].
• Molecular markers: frequent TP53 mutations, **EGFR positivity ~60–65%**, androgen receptor positivity in a subset, variable PD-L1 expression [4,9,11,13].

Table 2. Selected Indian studies on TNBC

Author / Year	Sample size (n)	TNBC prevalence	Median age	Key findings	Reference
Kulkarni et al., 2020	9,302 (pooled)	~27% (11–47%)	~45 yrs	First Indian TNBC meta-analysis; higher prevalence vs global	[1]
Sandhu et al., 2022	10,589 (pooled)	~31%	42–46 yrs	Regional heterogeneity noted	[2]
Kumar et al., 2021	201	27%	43 yrs	High EGFR (~60%), AR (~30%), TP53 frequent	[4]
Chikkala et al., 2024	1,000+ tested	29% BRCA mutations	40 yrs	High germline BRCA mutation rates	[5]
Raina et al., 2018	303	25%	45 yrs	5-yr OS lower vs non-TNBC; pCR predictive	[3]
Arora et al., 2025	180 (PhaseII RCT)	TNBC-specific	41 yrs	Low-dose pembrolizumab + NACT improved pCR	[6]

Treatment Patterns and Clinical Outcomes

Standard systemic therapy in India remains conventional cytotoxic chemotherapy, typically anthracycline- and taxane-based regimens in the neoadjuvant and adjuvant settings. International trials such as KEYNOTE-522

demonstrated that the addition of pembrolizumab to neoadjuvant chemotherapy increases pCR and event-free survival in early TNBC; Indian investigational efforts (e.g., PLANeT) have evaluated modified or low-dose immune checkpoint inhibitor strategies in resource-constrained settings with preliminary signals of pCR enhancement. PARP inhibitors are appropriate for patients with deleterious germline BRCA mutations but their routine use in India is limited by cost and access issues.

Pathologic complete response rates to neoadjuvant chemotherapy in Indian cohorts are reported broadly in the 25–35% range; overall survival is generally inferior to outcomes reported in many Western series, driven by later stage at diagnosis and restricted access to advanced therapies and molecular diagnostics.

• Chemotherapy (anthracycline + taxane) remains the backbone [3,12]. • Immunotherapy: Global trial (KEYNOTE-522) established pembrolizumab + chemotherapy [7]; Indian PLANeT trial explored low-dose IO approaches [6]. • PARP inhibitors: Considered in BRCA-mutated TNBC, but access limited in India [5,9,14].

• pCR rates to neoadjuvant chemotherapy: ~25–35% in Indian cohorts [3,12]. • Survival: generally worse than in Western cohorts due to advanced stage at diagnosis and limited access to novel therapies [3,12,14].

Figure 1. TNBC care pathway in India

Discussion

Interpretation and clinical implications

The body of Indian evidence indicates that TNBC in India disproportionately affects younger women and constitutes a larger fraction of breast cancers than in many Western populations. The observed high prevalence and younger age at onset have important implications for population screening strategies, genetic testing criteria, and resource allocation for oncology services in India. Elevated germline BRCA mutation prevalence in selected series argues for reconsideration of genetic testing thresholds and broader access to germline testing in TNBC patients, particularly those diagnosed at young ages or with family histories suggestive of hereditary predisposition.

Molecular heterogeneity — frequent TP53 alterations, high EGFR expression in some cohorts, and variable AR and PD-L1 expression — suggests potential for tailored therapeutic strategies, but translation requires confirmatory, adequately powered studies and local biomarker standardization. While immunotherapy and PARP inhibitors represent important therapeutic advances, their population-level benefit in India will depend on equitable access, cost containment, and context-adapted implementation strategies.

Research Gaps and Future Directions

Despite advances in TNBC research globally, significant gaps remain in the Indian context that impact diagnosis, treatment, and survival outcomes.

Current Gaps: Late presentation due to absent screening, limited nationwide epidemiological data, high cost and low accessibility of genetic/molecular testing, restricted availability of novel therapies, sparse outcome data, and lack of TNBC-specific guidelines [1–6,9–14].

Future Directions:

• Establish **population-based TNBC registries** with integrated molecular profiling. • Promote **awareness and early detection** through community-based initiatives. • Develop **affordable molecular testing** platforms for BRCA, PD-L1, EGFR, and AR. • Expand **access to immunotherapy and PARP inhibitors** via cost negotiations, generics, and government schemes.
• Support **multi-center genomic research** to identify Indian-specific biomarkers. • Introduce **TNBC-focused national guidelines** and strengthen rural cancer care infrastructure.

Limitations of evidence base and this review

Available Indian data are heterogeneous and dominated by retrospective, single-center studies that vary in case definition, assay methodology (IHC thresholds, PD-L1 platforms), and completeness of follow-up. Nationally representative, prospective datasets are sparse. The present review is limited by reliance on published studies and meta-analyses of variable quality; potential publication bias and interstudy heterogeneity limit precision of pooled estimates and external validity. Additionally, differences in diagnostic and reporting standards over time may confound comparisons.

Conclusion

TNBC in Indian women represents a significant clinical and public health challenge characterized by higher prevalence, younger age at diagnosis, and advanced stage at presentation relative to many Western populations. Molecular features observed in Indian cohorts — including elevated germline BRCA mutation rates and distinct expression patterns of EGFR, AR and PD-L1 in subsets — underscore the need for regionally relevant translational research and adaptive clinical strategies. To translate molecular and therapeutic advances into improved population outcomes, India must prioritize registry development, equitable access to affordable diagnostics and targeted therapies, and prospective multi-center research that informs context-specific guidelines and implementation pathways.

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