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Triple Negative Breast Cancer: A Comprehensive Review of Epidemiology, Biology, and Management

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ABSTRACT

Background: *Triple Negative Breast Cancer (TNBC) is a biologically aggressive subtype of breast cancer characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) expression. It accounts for 15–20% of breast cancers globally but is disproportionately prevalent in younger women, women of African descent, and patients in low- and middle-income countries (LMICs). TNBC is associated with rapid progression, early recurrence, and limited targeted treatment options.*

Objective: *To provide a comprehensive review of TNBC, focusing on epidemiology, molecular biology, clinicopathological features, diagnostic approaches, management strategies, recent therapeutic advances, and regional disparities.*

Methods: *A narrative review was conducted using PubMed, Scopus, Web of Science, and African Journals Online (2013–2025). Eligible studies addressing TNBC incidence, biology, clinical presentation, diagnostics, treatment, and emerging therapies were included, with emphasis on comparative global and Sub-Saharan African data.*

Results: *TNBC exhibits marked geographic and ethnic variation, with prevalence rates of 12–15% in Western populations and up to 46% in West Africa. Molecular profiling reveals heterogeneity across basal-like, mesenchymal, immunomodulatory, and luminal androgen receptor (LAR) subtypes. Standard treatment remains chemotherapy, particularly in the neoadjuvant setting, where pathologic complete response predicts improved outcomes. Recent advances include PARP inhibitors in BRCA-mutated TNBC, immune checkpoint inhibitors for PD-L1–positive disease, and antibody-drug conjugates such as sacituzumab govitecan, which have demonstrated survival benefit. However, in LMICs, late presentation, limited access to immunohistochemistry, and high treatment costs remain major barriers.*

Conclusion: *TNBC continues to represent a global oncological challenge. While novel therapies are improving outcomes in high-resource settings, substantial gaps in diagnosis and treatment persist in LMICs. Future efforts should prioritize equitable access to molecular diagnostics, affordable targeted therapies, and global collaborations to reduce disparities in TNBC outcomes.*

Keywords: *Antibody-Drug Conjugates, Breast epidemiology, Breast therapy, Liquid biopsy, Molecular Biology, Poly(ADP-ribose) Polymerase Inhibitors, Precision Medicine, Sub-Saharan Africa, Triple Negative Breast Neoplasms.*

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Introduction

Breast cancer is the most commonly diagnosed malignancy in women worldwide and a leading cause of cancer mortality. Triple-negative breast cancer (TNBC)—defined by the absence of estrogen receptor, progesterone receptor, and HER2—accounts for roughly 15–20% of breast cancers globally and is associated with aggressive biology, early relapse, and poorer survival compared with other subtypes [1]. Molecular profiling underscores TNBC's heterogeneity, with transcriptomic classes (e.g., basal-like, mesenchymal, immunomodulatory, and luminal-androgen-receptor) that differ in pathobiology and therapeutic vulnerabilities [7,8].

The epidemiology of TNBC shows striking geographic and ethnic disparities. Meta-analytic estimates across Africa suggest a pooled TNBC frequency around 27%, with the highest burden in West Africa (~46%), far exceeding proportions typically reported in Europe and North America [2,3]. Converging evidence attributes this gradient to interwoven factors,population genetics, reproductive patterns, access to early detection, and health-system constraints [2,3,6].

Sub-Saharan Africa faces disproportionate mortality from breast cancer, driven by late presentation and limited access to timely multimodality care. Recent region-wide analyses report 5-year survival near 40%, with substantial urban–rural gaps [6,9]. These structural challenges are particularly consequential for TNBC, where chemotherapy has historically been the mainstay and delays markedly compromise outcomes [6,9].

In Nigeria, hospital-based series highlight both the prominence and clinical severity of TNBC. Reports from tertiary centers document wide TNBC frequency ranges (≈13–53%), frequent high-grade histology, younger age at diagnosis, and frequent advanced stage at presentation features that compound the inherent aggressiveness of the disease [4,5]. Such patterns underscore the urgency of strengthening diagnostic capacity (receptor/IHC fidelity, feasible subtype surrogates), expanding access to contemporary therapies, and embedding region-specific strategies within national cancer control efforts [4,6].

Methods

This structured narrative review followed best practices for scholarly synthesis. Literature was searched in PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and AJOL for publications from January 2013 to July 2025, supplemented by institutional repositories. Search terms included "triple-negative breast cancer," "TNBC," "basal-like breast cancer," "epidemiology," "molecular biology," "management," "therapy," "Sub-Saharan Africa," and "Nigeria," with Boolean operators applied.

Eligible sources were peer-reviewed original studies (epidemiological, clinical, molecular, or therapeutic), systematic reviews, meta-analyses, guidelines, and regional reports. Excluded were case reports, conference abstracts without full text, commentaries, and non-English publications without an abstract.

Data extracted included study characteristics, methodology, findings, and relevance to TNBC epidemiology, biology, or management, with emphasis on global, Sub-Saharan African, and Nigerian contexts. Evidence was synthesized thematically (epidemiology, biology, clinical characteristics, management, emerging directions).

Studies were appraised for quality, representativeness, and relevance, prioritizing systematic reviews and meta-analyses.

Epidemiology of TNBC

Globally, Breast cancer is the most frequently diagnosed cancerworldwide, with over 2.3 million new cases and 685,000 deaths in 2020 [10]. TNBC accounts for approximately 10–20% of all breast cancers, disproportionately affecting younger women, African ancestry populations, and those of lower socioeconomic status [11]. In the United States, TNBC represents about 15% of breast cancers, with a higher incidence in African-American women compared to Caucasian women [12] (Table 1).

In Sub-Saharan Africa (SSA), TNBC constitutes a larger proportion of breast cancer cases compared to global averages, ranging from 20–30% of diagnoses [13-15]. Studies in East, West, and Southern Africa consistently show a predominance of high-grade, advanced-stage TNBC at diagnosis, with worse survival outcomes compared to hormone receptor–positive cancers [16]. This elevated prevalence has been partly attributed to genetic predisposition, younger age distribution, late presentation, and limited access to molecular diagnostics [17].

In Nigeria, TNBC prevalence is particularly high, accounting for 25–30% of all breast cancer cases [18-21. Studies from Lagos, Ibadan, and Zaria reveal that TNBC is often associated with younger age at presentation (mean 40–45 years), aggressive histology, and late-stage disease [19]. A multicenter Nigerian study reported that up to one-third of all breast cancers lacked ER, PR, and HER2 expression, reinforcing the regional burden [20]. Limited availability of immunohistochemistry (IHC. Services and delayed cancer care further exacerbate TNBC outcomes in the country [21] (Table 1, and Figure 1).

Table 1: Global vs Sub-Saharan vs Nigerian TNBC Burden

Region	Breast Cancer Burden (2020)	TNBC Proportion	Typical Age Group	Distinctive Features
Global	2.3M cases, 685k deaths[1]	10–20% [10-12]	45–60 yrs	More common in younger, African ancestry, and low-SES women
Sub-Saharan Africa	~186k cases, ~85k deaths[4]	20–30% [14,15]	35–50 yrs	High-grade, late stage, poor access to diagnostics
Nigeria	~28k cases, ~15k deaths[9]	25–30%[18-21]	35–45 yrs	Aggressive, younger women, poor survival outcomes

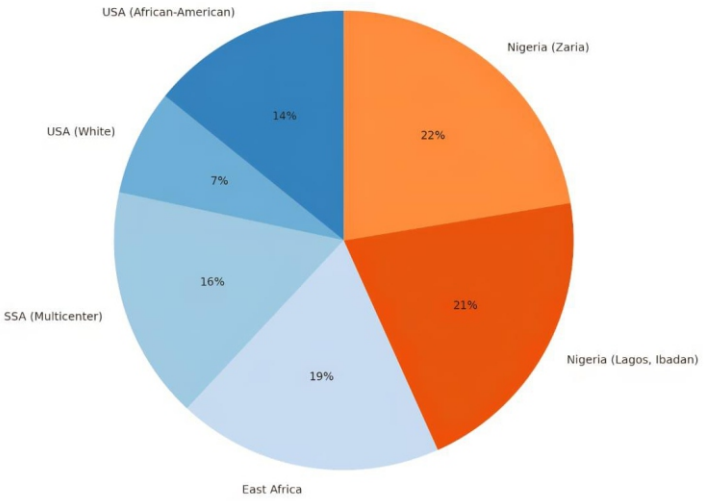

Figure 1: prevalence of TNBC by Region

TNBC prevalence across the selected studies. It clearly shows the higher proportions reported in Nigeria (28–30%) and East Africa (25%), compared with the USA White population (10%). The chart highlights the higher burden of TNBC in Nigeria and SSA compared to global averages.

Results

TNBC accounts for approximately 15–20% of all breast cancers globally. Its prevalence is higher among younger women, women of African descent, and those with BRCA1/2 mutations. In high-income countries (HICs), TNBC incidence ranges between 10–15%, while in Sub-Saharan Africa, reported rates are between 20–35% [22-24]. Nigerian studies show similarly high burdens, with TNBC constituting 25–30% of breast cancers [25-27] (Table 2).

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Table 2: Comparative Epidemiology of TNBC

Region	TNBC Prevalence	Common Age Group	Notable Risk Factors	References
Global (HICs)	10–15% of breast cancers	40–50 years	BRCA mutations, family history	[22,23]
Sub-Saharan Africa	20–35%	35–45 years	Younger age, high-grade tumors, delayed diagnosis	[24,25]
Nigeria	25–30%	30–45 years	Late-stage presentation, socioeconomic factors	[26,27]

Histopathological and Molecular Features: Globally, TNBC tumours are typically high-grade invasive ductal carcinomas, characterized by basal-like molecular subtypes. Sub-Saharan cohorts show higher histological grade, larger tumour size, and more frequent lymph node involvement compared to Western cohorts [28-30]. Nigerian studies report similar trends, with over 70% presenting at advanced stage (III–IV) and showing basal-like immunophenotypes [31] (Figure 2).

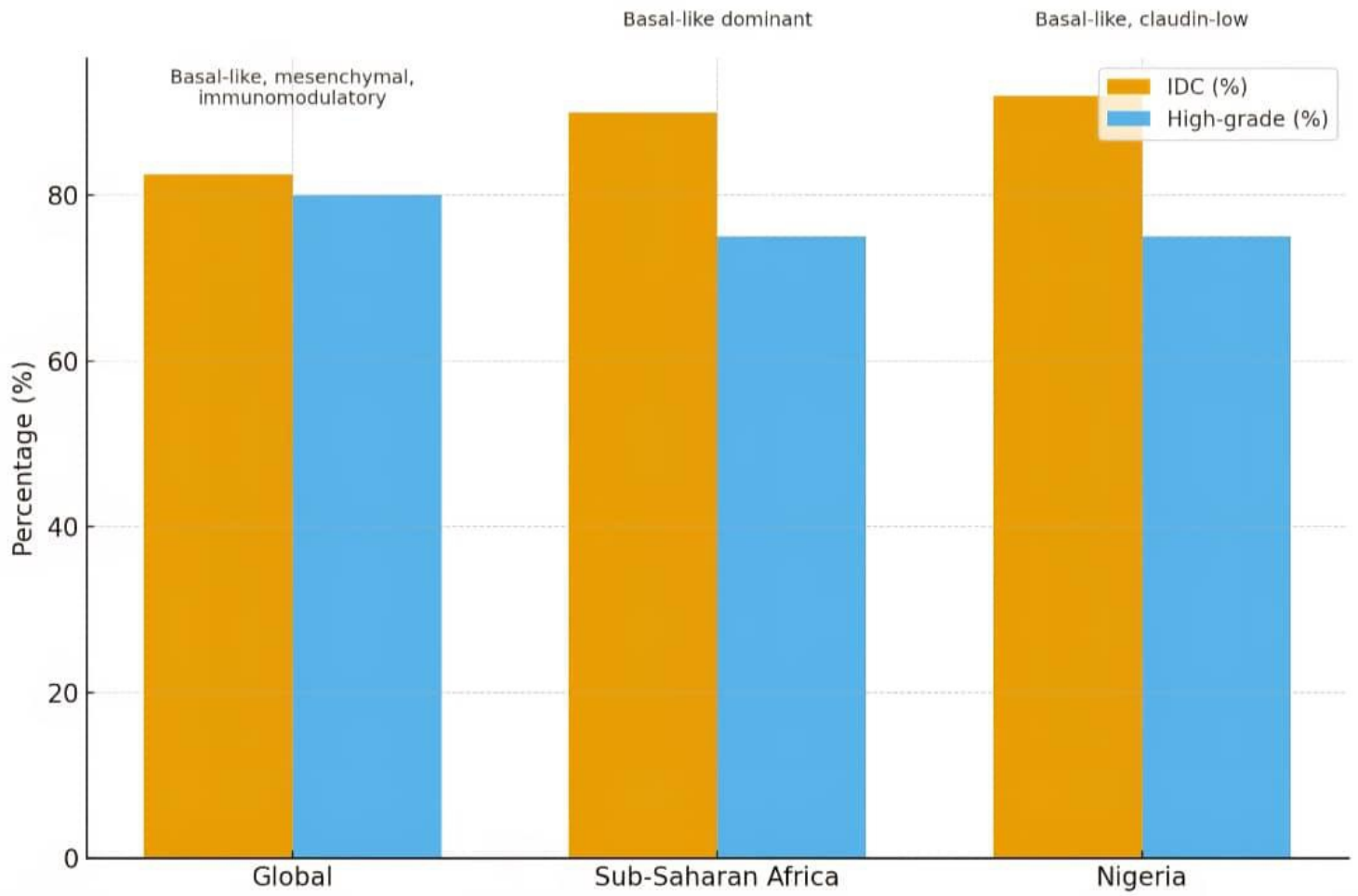

Figure 2: Comparative Histopathologic features of TNBC

IDC = Invasive ductal carcinoma; Molecular subtypes annotated above bars. Data adapted from global, Sub-Saharan African, and Nigerian TNBC studies [28–31].

Clinical Presentation and Outcomes: In Western countries, TNBC often presents at earlier stages due to screening programs. In contrast, patients in SSA and Nigeria frequently present with large tumours, nodal involvement, and metastasis at diagnosis [32-34]. Consequently, survival outcomes are poorer: 5-year survival rates in HICs exceed 70%, compared to 30–50% in SSA, and <40% in Nigeria [33,34]. (Figure 3)

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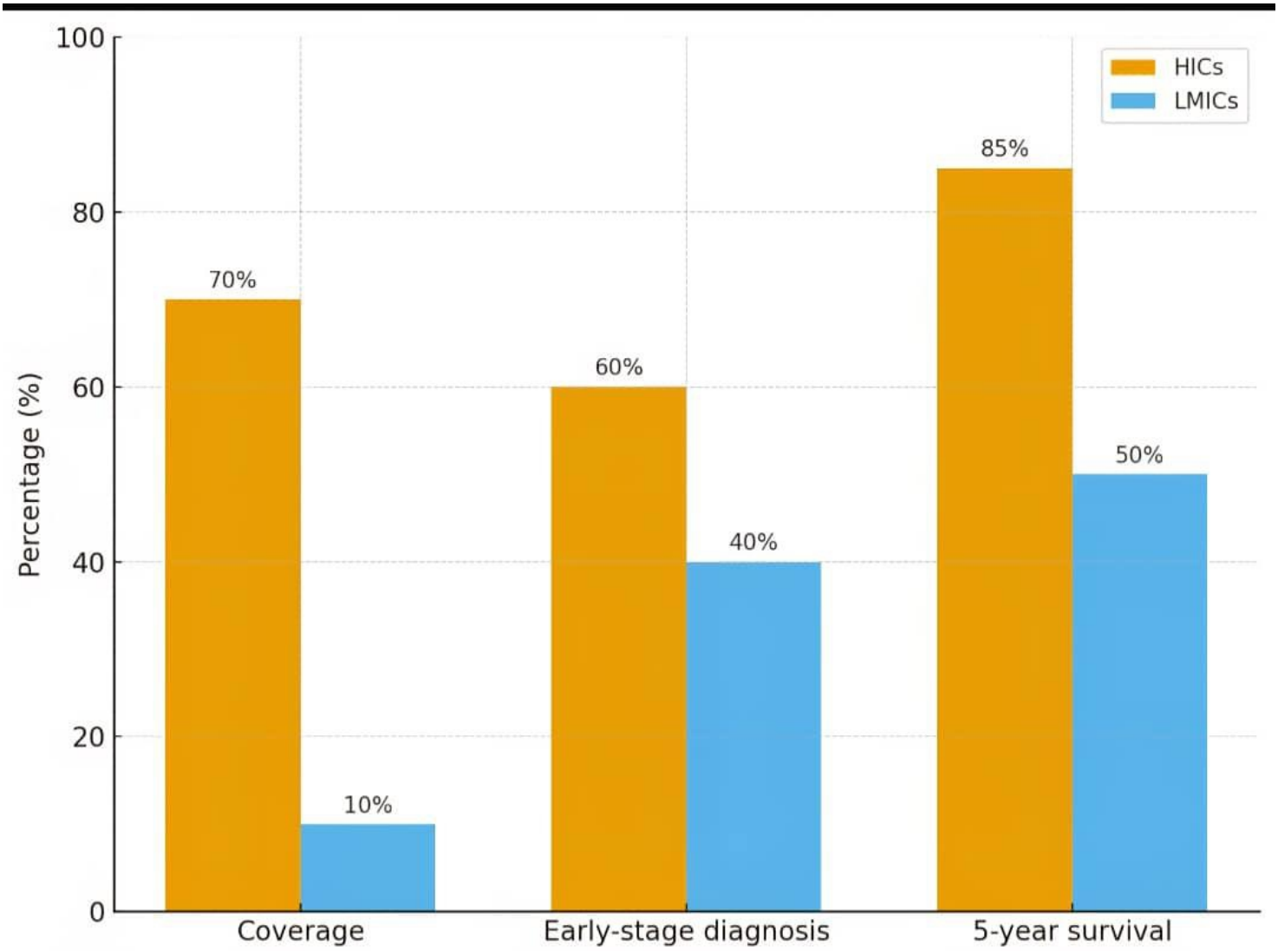

Figure 3: Survival Outcomes of TNBC

Comparison of breast cancer care indicators between High-Income Countries (HICs) and Low- and Middle-Income Countries (LMICs), showing disparities in screening coverage, early-stage diagnosis, and 5-year survival. Data synthesized from global oncology reports [32-34].

Discussion

Triple-negative breast cancer (TNBC) remains a disproportionately high burden among women of African ancestry, characterized by a higher prevalence, earlier onset, and more advanced disease at diagnosis compared to Western populations [35,36]. Systematic reviews report TNBC prevalence rates of 20–35% in Sub-Saharan Africa (SSA), significantly exceeding the 10–20%range observed globally [37]. Multicenter Nigerian and West African studies corroborate these findings; one Nigerian multicenter review documented TNBC frequencies ranging between 41% and 52% across regions, while a Southeast Nigerian cohort reported a prevalence of 35.7% with a large proportion presenting at stage III/IV disease [38-40]. These observations mirror global epidemiological trends linking TNBC with women of African descent [41].

Molecular profiling highlights TNBC's heterogeneity. The luminal androgen receptor (LAR) subtype, identifiable via AR immunohistochemistry (IHC), occurs in approximately 11–38% of Nigerian TNBC cases [42-44]. Conversely, quadruple-negative breast cancers (QNBCs) lacking ER, PR, HER2, and AR account for 75–80% of TNBCs in West African cohorts and are associated with aggressive clinical behavior and poorer prognoses [45]. The presence of AR-positive TNBC highlights a potentially targetable subgroup, emphasizing the need for further exploration of AR-directed therapy in resource-limited settings [46,47].

Globally, TNBC management has advanced with PARP inhibitors (e.g., adjuvant olaparib in BRCA-mutated early breast cancer) and immune checkpoint inhibitors (e.g., pembrolizumab in neoadjuvant and metastatic settings), which have significantly improved outcomes in selected populations [36-38]. However, their use remains limited in SSA due to infrastructural constraints, high costs, and restricted access to biomarker testing (PD-L1, BRCA mutation status) [36]. National initiatives such as the Clinton Health Access Initiative have improved access to essential chemotherapy but have not achieved equitable delivery of these novel therapies [35].

Survival outcomes in SSA remain considerably lower. While 5-year overall survival (OS) for TNBC exceeds 70% in high-income countries, SSA outcomes remain below 50%, largely attributable to late-stage presentation and limited treatment options [39]. For instance, a Southeast Nigerian study reported 59% 5-year survival for stage III disease, markedly lower than early-stage survival in Western cohorts [29].

To address these disparities, strategic priorities include:Enhanced diagnostic capacity: Scaling standardized IHC (ER, PR, HER2, AR) with robust quality control to guide

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treatment [2,34]. Molecular characterization: Expanded genomic profiling of Nigerian TNBC cases has identified recurrent TP53 and BRCA1 mutations, as well as novel African-specific variants, underscoring the need for locally relevant drug discovery [38].Adaptive treatment pathways: Developing pragmatic chemotherapy regimens tailored to regional availability, including simplified protocols validated by pragmatic trials.Community-driven implementation models: Programs such as Project Pink Blue demonstrate effective grassroots breast cancer awareness, screening, and navigation services, improving early detection and care access [36].

In summary, addressing TNBC disparities in SSA, particularly Nigeria, requires multifaceted strategies integrating affordable diagnostic tools, context-specific treatment algorithms, oncology and pathology workforce training, and African-centric research that captures both biological diversity and system-level determinants of inequity.

Diagnosis approach: Accurate TNBC classification depends on high-quality pathology and standardized receptor testing. ASCO/CAP guidelines for ER/PR (2020) and HER2 (2018–2023) testing emphasize pre-analytic rigor (cold ischaemia limits, fixation protocols), validated antibodies, and reflex ISH for equivocal HER2 to minimize false negatives and ensure reproducibility [49-52]. In low-resource settings such as Nigeria and Sub-Saharan Africa (SSA), limited immunohistochemistry (IHC) capacity, inconsistent fixation, and lack of external quality assurance (EQA) contribute to misclassification [52-54].

Key biomarkers and testing priorities:

- ER/PR/HER2: Mandatory for all invasive breast cancers; defines TNBC status [49-51]
- PD-L1: Drug-specific assays (e.g., 22C3 CPS, SP142) guide immunotherapy eligibility; harmonization efforts aid test selection [55,56]
- Germline BRCA1/2 and HR genes: Recommended for TNBC ≤60 years or strong family history; informs PARP inhibitor and platinum use [57,58].
- Tumour-Infiltrating Lymphocytes (sTILs): Feasible, reproducible prognostic marker predicting chemotherapy and immunotherapy response [59,60].
- HRD/genomic-scar assays: Support platinum/PARP selection but are largely unavailable in SSA; BRCA status and pathology features substitute [58,61].
- Circulating tumour DNA (ctDNA): Promising for early relapse detection and trial-based treatment adaptation [62,63].

Prognostic indicators: Traditional clinicopathologic variables (tumour size, nodal status, grade) remain foundational [64]. Pathologic complete response (pCR) after neoadjuvant therapy is strongly prognostic, with Residual Cancer Burden (RCB) scoring refining risk assessment [65.66]. sTILs independently correlate with better outcomes [59,60]. Germline BRCA carriers show distinct relapse patterns, and adjuvant olaparib improves invasive disease-free survival [58,67]. PD-L1 positivity enriches for chemo-immunotherapy benefit [55,56]. ctDNA detection post-treatment signals early relapse risk [62,63].

Implementation in SSA and Nigeria: Investment in pathology infrastructure,standardized handling, validated IHC, EQA participation, and workforce training is crucial [52,54,68].

A tiered testing model emphasizing universal ER/PR/HER2, selective BRCA and PD-L1 testing, and routine sTIL scoring maximizes clinical impact within constraints [52,54,59]. Regional collaboration, pooled procurement, and implementation research will accelerate access to biomarker testing and targeted therapies [68].

Clinicopathological Features of TNBC

Triple-negative breast cancer (TNBC) exhibits distinctive biological and clinical characteristics compared with other breast cancer subtypes. Patients are often younger at diagnosis, and tumors tend to be high-grade, rapidly proliferative, larger in size, and more likely to present with nodal involvement and early visceral or central nervous system metastases. These aggressive features are consistently reported in global literature, Sub-Saharan African (SSA) data, and Nigerian series [69,70]

TNBC disproportionately affects younger women, often in their mid-30s to mid-40s in SSA cohorts, which is notably younger than in high-income countries. This has implications for genetic risk assessment, fertility counseling, and treatment strategies [71-73].

Most TNBCs are invasive ductal carcinomas of no special type (IDC-NOS) and are predominantly grade 3. Contemporary studies show high rates of nuclear atypia, frequent mitoses, lymphovascular invasion, and larger tumor sizes compared to hormone receptor-positive cancers [74,75].TNBC is characterized by elevated Ki-67 expression, frequently >30–40%, which predicts higher rates of pathological complete response (pCR) to neoadjuvant chemotherapy. However, high Ki-67 also correlates with worse outcomes when pCR is not achieved, making its prognostic use context-dependent [76.77].A substantial proportion of patients in SSA present with stage III–IV disease, reflecting delayed access to diagnosis and care. Lymph node positivity is common and is a key determinant of poor survival in regional populations [71,74].Androgen receptor (AR) expression defines the luminal androgen receptor (LAR) subtype, while quadruple-negative breast cancer (QNBC; ER-/PR-/HER2-/AR-) is prevalent in West African datasets and carries a more aggressive course. Recognizing these phenotypes is essential for prognostication and trial selection [73]. TNBC has an early relapse peak within 3–5 years, with visceral (lung, liver) and brain metastases predominating. Combined with late-stage diagnosis, this explains high early mortality in SSA [74,75]. TNBC demonstrates high pCR rates to anthracycline-taxane ± platinum neoadjuvant chemotherapy. However, patients without pCR remain at high relapse risk, emphasizing the role of adjuvant escalation strategies, such as PARP inhibitors in BRCA1/2 carriers [76].Multiple Nigerian studies corroborate these findings: younger patient age, a predominance of high-grade tumors, nodal positivity, and frequent stage III–IV disease. These data highlight the urgent need for earlier detection, standardized diagnostics, and equitable access to multimodality care [69-71].

TNBC in both global and SSA settings is an aggressive, biologically distinct disease that disproportionately affects younger women. It is defined by high-grade, highly proliferative tumors with early visceral spread, frequent nodal involvement, and poor outcomes without pCR. Regional studies confirm late-stage diagnosis and substantial heterogeneity, including AR-positive and QNBC phenotypes, underscoring the importance of improving early detection, biomarker profiling, and treatment access.

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Current Treatment Options for TNBC: Triple-negative breast cancer (TNBC) is a biologically aggressive subtype lacking expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). As a result, systemic treatment relies primarily on cytotoxic chemotherapy, immune checkpoint inhibition in selected settings, targeted agents for biomarker-defined subgroups (e.g., germline BRCA/HRD), and antibody–drug conjugates (ADCs). Clinical trials remain essential for expanding therapeutic options. Multimodality care (surgery ± radiotherapy) remains central for localized disease, while systemic therapy decisions are guided by disease stage, residual disease after neoadjuvant chemotherapy (NACT), PD-L1 status in metastatic disease, and germline BRCA mutation status [78,79].

Early-Stage Disease – Curative Intent

Neoadjuvant Chemotherapy (NACT)is standard for many stage II–III TNBC patients, allowing tumor downstaging and assessment of chemosensitivity. Regimens commonly include anthracycline- and taxane-based combinations; platinum agents are added selectively to increase pathological complete response (pCR) rates, particularly in BRCA-mutated or high-risk patients [80].

Immune Checkpoint Inhibitors (ICI): Pembrolizumab combined with NACT, followed by adjuvant pembrolizumab, improved pCR and event-free survival in the KEYNOTE-522 trial. This regimen is FDA-approved and integrated into international guidelines for high-risk early-stage TNBC 78,79].

Adjuvant Capecitabine for Residual Disease: Patients with residual invasive disease after NACT derive significant benefit from adjuvant capecitabine, as demonstrated in the CREATE-X trial, which improved disease-free and overall survival [82].

Adjuvant PARP Inhibitor for BRCA Mutation Carriers: The OlympiA trial established adjuvant olaparib as a standard for patients with germline BRCA1/2 mutations and high-risk, HER2-negative early breast cancer, underscoring the importance of germline testing [83].

Residual High-Risk Disease and Biomarker-Guided Escalation: For patients with residual disease after NACT, adjuvant olaparib is recommended for BRCA mutation carriers, while capecitabine is appropriate for BRCA wild-type high-risk cases. Pembrolizumab continues post-NACT as per KEYNOTE-522 outcomes [83].

Metastatic Disease: Chemotherapy remains the cornerstone of TNBC treatment, with taxanes, anthracyclines, and platinum agents used as clinically appropriate [84]. In PD-L1–positive metastatic TNBC (CPS ≥10), pembrolizumab combined with chemotherapy has been shown in the KEYNOTE-355 trial to improve progression-free and overall survival [79]. Although atezolizumab initially received support for PD-L1–positive TNBC in the IMpassion130 study, its U.S. indication was later withdrawn, illustrating the evolving regulatory landscape [85]. Sacituzumabgovitecan, a Trop-2–targeted antibody-drug conjugate, significantly improved survival in heavily pretreated metastatic TNBC (ASCENT trial) and is now established as standard later-line therapy [81,85]. For patients with germline BRCA-mutated metastatic TNBC, PARP inhibitors such as olaparib (OlympiAD) and talazoparib (EMBRACA) are approved and preferred in this subgroup [82]. Targeted therapies, including the AKT inhibitor capivasertib combined with paclitaxel, have demonstrated improved outcomes in biomarker-selected patients harboring PIK3CA, AKT1, or PTEN alterations in the PAKT trial [86].

Other considerations in TNBC management include active participation in clinical trials, particularly those investigating novel immunotherapy combinations, antibody–drug conjugates (ADCs), and targeted kinase inhibitors. Biomarker testing for germline BRCA1/2 mutations, PD-L1 CPS, and HER2 status is essential to guide personalized treatment decisions. In resource-limited settings, emphasis should be placed on accurate receptor assessment, germline testing when feasible, and the use of cost-effective agents such as capecitabine, while patient-access programs can help facilitate the use of immunotherapies and ADCs [87].

Key Advances and Future Directions in TNBC: Triple-negative breast cancer (TNBC) remains among the most aggressive breast cancer subtypes. However, recent advances are reshaping its management. Immunotherapy has emerged as a major breakthrough: immune checkpoint inhibitors such as pembrolizumab and atezolizumab, when added to chemotherapy, have improved survival outcomes in both metastatic and early-stage TNBC—particularly in PD-L1–positive and high-risk populations [88].

Targeted therapies now offer precision-based treatment options. PARP inhibitors like olaparib and talazoparib extend survival in patients with germline BRCA1/2 mutations, establishing biomarker-guided treatment as a cornerstone strategy [89]. Additionally, antibody–drug conjugates (ADCs) such as sacituzumab govitecan have demonstrated substantial activity in heavily pretreated metastatic TNBC, providing durable clinical responses with manageable toxicity [90].

Molecular profiling reveals TNBC's heterogeneity. Subtypes such as basal-like, mesenchymal, immunomodulatory, and luminal AR (LAR) TNBC are now being used to guide therapeutic selection [91]. Emerging strategies include AR antagonists for LAR-TNBC, PI3K/AKT/mTORinhibitors in pathway-activated tumors, and novel ADCs targeting Trop-2, HER2-low, and additional surface markers [92].

Liquid biopsy technologies, such as circulating tumor DNA, exosomes, and fragmentomics, are increasingly explored for early detection, minimal residual disease monitoring, and real-time treatment guidance [93]. Integration with multi-omics and artificial intelligence promises to enhance predictive biomarkers and optimize precision medicine approaches.

Future directions emphasize personalized therapy, rational immunotherapy combinations, and expanding access in low- and middle-income countries, where late-stage presentation and limited infrastructure significantly impede outcomes. Collectively, these advances are narrowing the therapeutic gap in TNBC and bringing hope for improved survival and quality of life.

Challenges in the Management of TNBC in LMICs: Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer, and its management in LMICs is hindered by systemic barriers across clinical, infrastructural, financial, and policy domains. These challenges contribute to poorer outcomes compared to high-income countries, emphasizing the need for context-specific strategies.

Late Presentation and Advanced Disease: In LMICs, TNBC frequently presents at stage III or IV, primarily due to limited awareness, lack of screening programs, sociocultural stigma, and reliance on alternative medicine [94,95]. Early detection remains rare, unlike in high-income settings where screening and awareness campaigns are well established [95].

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Inadequate Diagnostic Capacity: Accurate TNBC diagnosis relies on immunohistochemistry (IHC) and molecular profiling, but many LMICs face shortages of trained pathologists, IHC reagents, and reliable laboratory infrastructure [96,97]. This often results in misclassification, poor disease documentation, and a lack of biomarker-driven treatment selection [98].

Limited Access to Novel Therapies: Advanced TNBC treatments, such as PARP inhibitors, immune checkpoint inhibitors, and antibody–drug conjugates, show proven survival benefits but remain largely inaccessible in LMICs due to high costs, regulatory gaps, and weak distribution systems [98,99]. Consequently, chemotherapy remains the mainstay, despite higher toxicity and suboptimal efficacy.

Oncology Workforce Shortages: A severe deficit of oncologists, pathologists, radiologists, and specialized nurses hampers optimal care [100]. For example, Nigeria has fewer than 100 clinical oncologists serving over 200 million people [101]. Limited expertise delays diagnosis, lengthens treatment pathways, and restricts access to radiotherapy and advanced surgery.

Financial Barriers and Out-of-Pocket Costs: The absence of universal health coverage forces many patients to pay out-of-pocket, leading to treatment delays or abandonment [102,103]. The financial burden is especially high for TNBC due to intensive chemotherapy regimens and limited availability of affordable alternatives.

Weak Cancer Registries and Data Systems: Cancer registries in LMICs are often underdeveloped, with poor coverage and inadequate data quality [104]. This impedes accurate disease surveillance, policy-making, and participation in international clinical trials.

TNBC management in LMICs is constrained by late presentation, inadequate diagnostic infrastructure, unaffordable therapies, workforce shortages, financial toxicity, and weak health data systems. Addressing these systemic gaps requires investments in early detection, affordable diagnostics, targeted therapy access, workforce training, and robust cancer registries.

Research Gaps and Future Perspectives: Despite substantial advances, significant research gaps persist in the management of triple-negative breast cancer (TNBC). First, heterogeneity at molecular and clinical levels remains poorly characterized in low- and middle-income countries (LMICs), where genomic profiling is limited by infrastructural and financial constraints. Consequently, the true burden of molecular subtypes such as basal-like, mesenchymal, and immunomodulatory TNBC is under-reported in Africa and other LMICs compared to high-income settings [105,106].

Second, biomarker discovery and validation remain insufficient. While PD-L1, BRCA1/2, and tumor mutational burden have shown promise in predicting response to immunotherapy and PARP inhibitors, reproducibility across diverse ethnic groups and healthcare systems is lacking [107,108]. Moreover, few African-led genomic studies have addressed population-specific mutations that may influence disease biology or therapeutic response [109].

Third, limited clinical trial participation in LMICs hampers equitable evidence generation. Most pivotal immunotherapy and targeted therapy trials are conducted in North America, Europe, and Asia, with minimal African representation [110]. This restricts generalizability and perpetuates disparities in access to novel regimens.

Future perspectives emphasize: (i) expanding molecular characterization using cost-effective next-generation sequencing in LMICs; (ii) integrating multi-analyte biomarkers (ctDNA, CTCs, exosomes) into routine monitoring; (iii) broadening clinical trial inclusion across Africa and other resource-limited regions; (iv) development of low-cost biosimilar and generic PARP inhibitors to bridge treatment inequities; and (v) advancing implementation research to adapt precision oncology into real-world LMIC contexts [111,112].

Bridging these gaps requires global collaborations, region-specific genomic studies, and equitable trial designs. Strengthening research capacity in LMICs will be crucial to ensure TNBC patients worldwide benefit from precision medicine innovations.

Conclusion

Triple-negative breast cancer remains a highly aggressive subtype of breast malignancy, characterized by distinct molecular features, poor prognosis, and limited therapeutic options compared to hormone receptor–positive or HER2-enriched tumors. Despite advances in immunotherapy, PARP inhibitors, and novel antibody-drug conjugates, outcomes remain suboptimal, especially in low- and middle-income countries (LMICs), where late presentation, inadequate diagnostic infrastructure, and restricted access to novel agents persist. Integrating molecular classification with tailored treatment strategies holds promise for precision oncology in TNBC. Bridging the gap between cutting-edge discoveries and real-world implementation is critical to reducing the global survival disparity.

Recommendations

Expand Access to Molecular Diagnostics: Prioritize wider availability of immune histochemistry, genomic profiling, and biomarker-based testing to facilitate precision treatment of TNBC, particularly in LMICs.

Promote Early Detection and Community Awareness: Strengthen public health education, screening initiatives, and culturally tailored awareness campaigns to reduce delays in presentation and diagnosis.

Develop Context-Appropriate Treatment Protocols: Establish regionally adapted clinical guidelines that optimize the use of cost-effective chemotherapy regimens while incorporating novel agents such as immunotherapies and PARP inhibitors where resources allow.

Enhance Clinical Research Representation: Expand inclusion of Sub-Saharan African populations in global and regional clinical trials to generate evidence that reflects local disease biology and treatment responses.

Invest in Health System Capacity: Strengthen oncology infrastructure, workforce training, and equitable access to essential cancer medicines and supportive care.

Advance Research Priorities: Encourage studies on genetic predispositions, molecular heterogeneity of TNBC in African women, and health system or socio-cultural factors influencing outcomes.

Conflicts of interest: none

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