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Epidemiology and clinical characteristics of breast cancer in Ethiopia: a systematic review

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Abstract

Background According to GLOBOCAN 2020 Breast cancer is the most common cancer among women and the prevalence is increasing worldwide and in Ethiopia. This review assessed studies conducted in Ethiopia on the clinical features and epidemiology of breast cancer.

Methods Data base search conducted PubMed, Google Scholar African Journals Online (AJOL), Cumulative Index of Nursing and Allied Health Literature (CINAHL) and Hinari without time restrictions. The search keywords included; prevalence and pattern, clinical presentation, histological and molecular subtypes, and management. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline to identify, search, extract articles, and report this systematic review. The protocol was registered in PROSPERO, ID: CRD42023403320.

Results Twenty studies were included in the review with 33,369 participants and 3 were community-based and 17 were hospital-based. In all except two reviewed studies, breast cancer is the most common cancer among women of Ethiopia. The most frequent presenting symptom was a breast lump/mass and commonly affected side was right breast. Most patients presented at a late stage and they were premenopausal age group. The commonest histology type is ductal carcinoma, that the most prevalent receptor was estrogen receptor positive, and the most common molecular subtype was Luminal A in pathology samples. Surgery is main stay of treatment and the most common surgical technique practiced in Ethiopia is modified radical mastectomy.

Conclusion Breast cancer incidence is rising, and it accounts for the major cancer burden in the country. There is a need for additional awareness-raising and health education because delayed presentation are critical problems throughout Ethiopia. For planning and monitoring cancer patterns, comprehensive demographic and clinical data from a population or facility-based registry are needed in the regions. The available treatment options are still limited in Ethiopia it needs infrastructural development.

Keywords Breast Cancer, Systematic review, Epidemiology, Ethiopia

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Introduction

The World Health Organization (WHO) report shows that in 2020, 2.3 million women were diagnosed with breast cancer, making it the most common cancer with 685,000 deaths worldwide. It continues to cause more disability-adjusted life years (DALYs) in women worldwide than any other cancer. Deaths from breast cancer are high in African countries due to poor health infrastructure, poor vital records, delayed health-seeking behavior, and low community awareness [1].

Breast cancer incidence and mortality rates in the world have increased over the last three decades. Study done on Breast cancer incidence and mortality from 1990 to 2016. In 60 out of 102 countries, the incidence of breast cancer has more than doubled, while the death rate has doubled in 43 out of 102 countries [2]. By 2030, it is predicted that there will be 2.7 million new cases worldwide each year and 0.87 million deaths from breast cancer [3].

A country assessment showed that breast cancer is the most common cancer illness in Ethiopia, accounting for 16,133 (20.9%) of all cancer cases and 9,061 (17.5%) of all cancer-related deaths [4]. Approximately 80% of breast cancer cases in sub-Saharan Africa are detected at late stages (stage III or IV), compared to 15% in high-income countries [5].

Breast cancer arises from the epithelium lining the milk ducts, known as invasive ductal carcinoma. This is the most common subgroup (50–80%), followed by the group arising from the glandular tissue of the breast lobules [6]. Based on mRNA gene expression levels, breast cancer can be classified into molecular subgroups. The four main intrinsic subtypes of breast cancer (Luminal A, Luminal B, HER2-enriched, and basal-like). Regarding Hormone status of breast cancers ER-positive tumors account for almost 70% of all breast cancers in Western populations [7, 8]. The TNM system for cancer staging refers to the classification of a tumor based on a list of factors, including the degree of disease affecting the main tumor (Tis to T4), regional lymph node status (N0 to N3), and distant metastases (M0 or M1) (0 to IV) [9].

When choosing a treatment plan, the type of breast cancer and its stage are often considered. Patients with breast cancer are often given several types of treatment. The current choices are radiation therapy, surgery, chemotherapy, hormonal therapy, biological therapy, and chemotherapy [10]. According to studies from underdeveloped countries, stage I and stage II have five-year survival rates of 90% and 65%, respectively, while stage III and stage IV have rates of only 33% and 6%, respectively [11].

Until April 2022, the Tikur Anbesa Specialized Hospital (TASH) was the only center in the country that offered radiotherapy. As of April 2022, Ethiopia has two additional functional radiation therapy centers: Jimma University Medical Center (JUMC) in the southwest of the country and Hiwot Fana Specialized Hospital at Haramaya University in the eastern part of the country.

Rationale of the study

Based on a preliminary search, we couldn't find compressive evidence at the country level regarding breast cancer patients' epidemiology and clinical profile. Therefore, a thorough examination of the existing evidence on breast cancer would aid in understanding breast cancer epidemiology and clinical profile in the country. This review provides evidence for the development of future strategies that are especially suited to the Ethiopian population.

Study objective

This study aimed to generate country wide evidence on epidemiology and clinical characteristics of breast cancer in Ethiopia.

Methods

The PROSPERO international prospective register of systematic review database checked for already-done or ongoing systematic reviews with the same objective before the data collection process started. The protocol of this review is registered in ID: CRD42023403320. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline to identify, search, extract articles, and report this systematic review [12].

Search strategy

The electronic databases and search engines PubMed, Google Scholar African Journals Online, Cumulative Index of Nursing and Allied Health Literature and Hinari were searched until June 20, 2023. The MeSH terms and key words were as follows: breast cancer, breast neoplasm, prevalence, epidemiology, Sign, Symptom Presentation, histology, molecular subtype, and management of breast cancer. The MeSH keywords were combined using Boolean operators (AND/OR), and Ethiopia's name was appended at the end. To enhance the number of articles included and lower the number of missing articles, hand searching was done on the citations and references listed in the eligible articles (Tables 1 and 2).

Eligibility criteria

Selection of study and extraction

As shown in the PRISMA flowchart, all articles identified from the electronic database searches were imported into Zotero and Duplicates were removed. Further Exclusion of articles conducted using title and abstract screening. Articles with full text were assessed for eligibility and further full text exclusion done on those articles which do

Table 1 Searching protocol of systematic review on the epidemiology and clinical characteristics of breast cancer in Ethiopia

Breast cancer OR Breast carcinoma OR Breast tumor OR Breast malignancy	AND	Epidemiology OR Prevalence OR Incidence OR pattern OR Trends	AND	Sign OR Symptom OR Presentation OR molecular subtype OR histology OR Diagnosis OR Stage OR Treatment	AND	Management OR Surgery OR Chemotherapy OR radiotherapy OR Hormonal therapy OR Immunotherapy	AND	Ethiopia

Table 2 Inclusion and exclusion criteria of the systematic review on the epidemiology and clinical characteristics of breast cancer in Ethiopia

Eligibility Criteria for including studies in the review	
i. Population, or participants and conditions of interest	Patients with Female breast cancer of any age, stage,
ii. Interventions/Exposure/item of interest	Epidemiology, Clinical presentation, histological and molecular subtypes, Management
iii. Comparisons or control groups	Not applicable
iv. Outcomes of interest	Epidemiology and clinical characteristic
v. Setting	Ethiopia
vi. Study designs	All type of study (exception included in exclusion criteria)

Criteria for excluding studies not covered in inclusion criteria

- Studies done Only Male breast cancer
- Studies done Regarding knowledge, practice and attitude of breast self-examination and screening, identify risk factors, quality of life, survival and patient experience
- Studies designs systematic reviews, randomized controlled trials, and experimental studies
- Studies conducted outside Ethiopia
- If only the abstract, review papers, reports, and commentaries
- studies in other languages other than English

not have a clearly written result. FGD and BTT extracted data simultaneously and independently, and any disagreements were resolved after independent review by the TGD and YDS. Finally, we extracted relevant information from each literature using an Excel spreadsheet template to avoid missing important information when preparing the results of the review or for future cross-checking. The extracted data includes first author's name, year of publication, study design, location, prevalence and pattern, Presenting Symptom, Stage at presentation, Histology findings, Molecular Features and Treatment.

Data analysis

The extracted data were further categorized into institution-based and community-based according to the setting in which the studies took place and further sorted according to the institution in which the studies were conducted. The methodological quality of the included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist [13].

Results

Study selection and characteristics

A total of 352 articles were found from electronic data base searching on the search engines and databases. All of these search results exported to Zotero computer

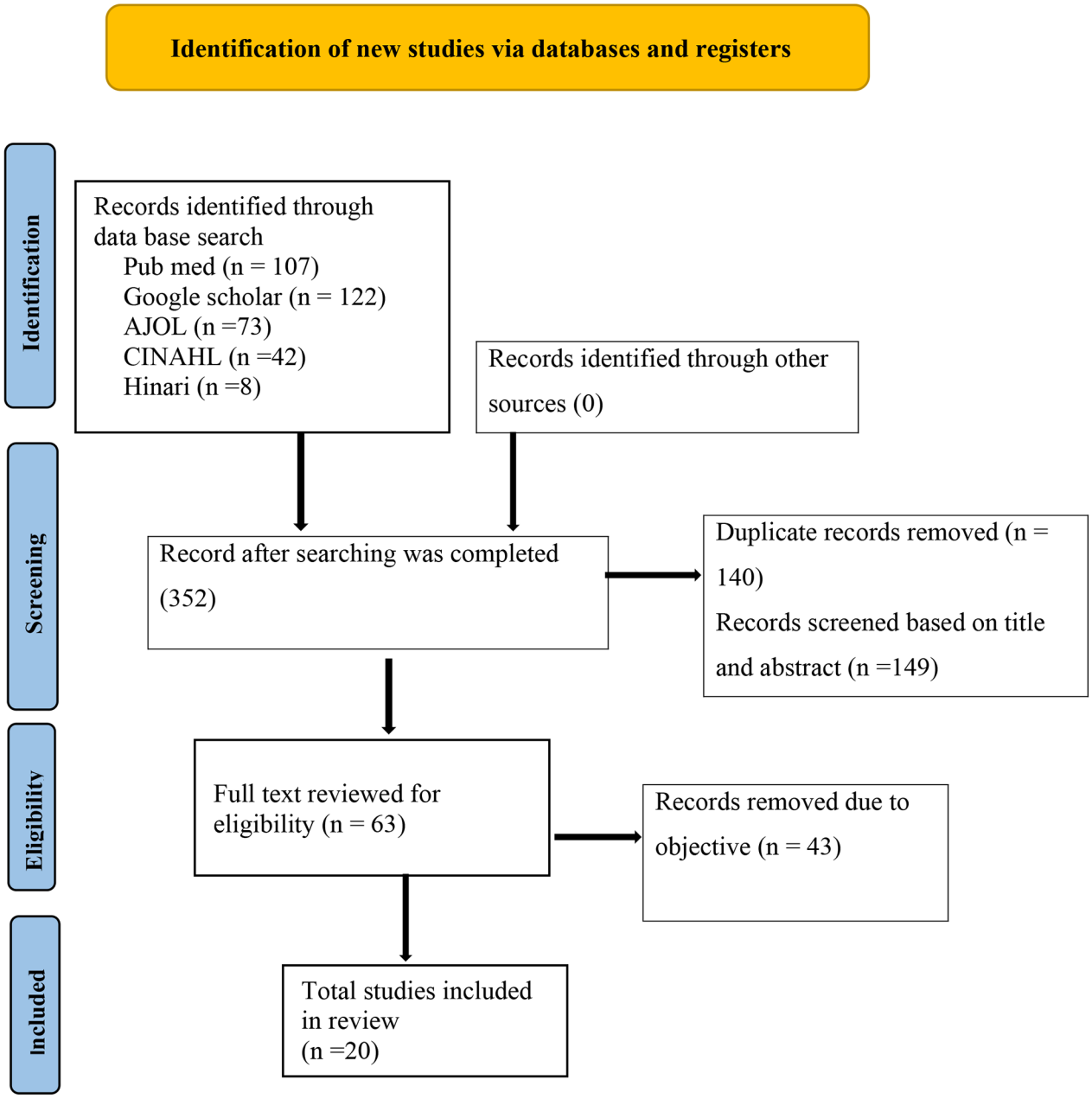


Fig. 1 PRISMA flowchart for article Search and Selection Process

software, where 140 duplicate records were removed and 149 were removed after being screened based on title and abstract. Further 43 articles were removed based on an objective of the review. Finally, 20 eligible articles, which enrolled 33,369 participants, were included in the systematic review (Fig. 1).

Most of the studies were conducted in Tikur Anbesa specialized hospital (TASH)(6/20), which was only hospital with radiotherapy treatment in the country until April 2022. Articles based on the study setting: 3 (15%) articles were community-based, and 17 (85%) articles were hospital-based. Based on study design, 9 (45%) articles were cross-sectional, 10 (50%) retrospective chart reviews, and one retrospective cohort.

Prevalence and pattern

Five studies assessed the prevalence and pattern of breast cancer in the country. All hospital-based studies showed the prevalence of breast cancer compared to other cancers. Breast cancer accounts for 15.2–26% of all cancers [14, 15] and from female cancer 29.3–37% [11, 16].

A community-based study done using the Addis Ababa City Cancer Registry (AACCR) showed the incidence of breast cancer (2012–2013) to be 31.5% of all female cancers [17] and a study done during 2012–2015 from AACCR and six regions showed breast cancer constituted 33% of all cancers in women and 23% of all cancers [18].

According to a study done at Hawassa University Comprehensive Specialized Hospital (HUCSH) from 2013 to 2019, the number of women diagnosed with breast cancer in hospitals has increased from 69 (12.3%) In 2013, 106 (19%) in 2019 [19].

A study from Gondar University Comprehensive Specialized Hospital (GUCSH), showed breast cancer accounts for 76 (14.1%) of all cancers [15] and finding from TASH showed breast cancer accounts for 26% of female cancers [14].

A study conducted at St. Paul's Hospital Millennium Medical College (SPHMMC), of all malignancies, breast cancer accounted for 587 (29.3%) in 2019, making it the second most common disease after cervical CA [16].

Presenting symptom

Fourteen studies reported Age at diagnosis. The median age ranges 38-55.8 years [19, 20] and mean age ranges 42.1–47.5 years [16, 21].

Premenopausal patients represent the majority of female breast cancer patients at the time of diagnosis, with the median age being between 40 and 46 years (14,15,17,19,23,2829). Breast lumps or masses were the most common presenting symptoms in all studies, followed by breast pain and ulceration [20, 22–25]. A study conducted at the GUCSH, where 65 (79%) patients presented with breast mass and breast ulceration in 15 patients (18%) [26].

Similar findings from two university hospitals (Gondar and Felege Hiwot University Comprehensive Specialized Hospital) (GUCSH and FHCSH) revealed that breast lump or mass was the most common presentable symptom in 328 (88.4%), followed by painful wound in 161 (43.4%) [22].

A study at Dessie Referral Hospital (DRH) showed 117 (57.4%) patients presented with breast lumps, followed by breast pain in 70 (34.3%) [25]. A multicenter study in Addis Ababa showed that breast lumps were found in 344 (78.0%) patients, followed by pain in 53 (10.2%) patients [24].

Regarding lymph node involvement, the findings from GUCSH and FHCSH showed that (320, 86.3%) and DRH 30, (14.7%), had a lymph node involvement at presentation [22, 25]. According to studies done at the GUCSH and TASH, breast CA commonly affects the right breast 48 (59%), and, 160 (38.4%) respectively (26, 19 and 27)and unlike others finding from HUCSH showed left breast in is commonly affected 302 (54%), and the upper outer quadrant was the most commonly involved according to the findings from TASH 154 (78.2%) ,40 (9.6%) [27, 28].

Stage at presentation

Nine studies included stage at presentation. Eight studies showed most of the patients presented in late stages (stage III and stage IV), and the prevalence of advanced stages ranges from 57 to 71.2% in (22, 19, 29, and 25). This was shown in a study conducted in GUCSH and FHCSH, in which 53 (14.3%) patients were diagnosed at stage IV and 211 (56.9%) patients were diagnosed at stage III [22]. According to HUCSH findings, 24 (12.2%) were diagnosed with stage IV disease, 113 (57.4%) with stage III disease, and 160 (30.4%) with early-stage disease [19].

Findings from DRH showed 82 (40.2%) and 53 (25.5%) were diagnosed with stage IV and stage III, and early stage presentation was 69 (33.8%) [27]. TASH stages at diagnosis: 74 (57%) were diagnosed at stages III and IV. Stage III: 63 (48.5%); Stage IV: 11 (8.5%) [29].

Unlike the previous papers, a finding from the TASH showed that the majority of patients 56(59%) of patients presented with early and late stages accounted for 40(41%) [30].

Histology findings

Nine studies included histologic findings and in all reviewed studies, ductal carcinoma is the most prevalent histology type. The prevalence of ductal carcinoma in studies done in SPHMMC, (GUCSH and FHCSH), GUCSH, and HUCSH studies was 479 (81.6%), 347 (93.5%), 61 (74%), and 156 (79.2), respectively [16, 22, 26, 28]. Out of nine studies 5 studies were from TASH. Ductal carcinoma is the most common histology type in TASH, followed by lobular carcinoma, with a prevalence ranging from 55.3 to 83.7% [20, 27, 29–31].

Regarding the level of differentiation, studies conducted in TASH and HUCSH, showed that moderate differentiation carcinoma is the commonest type (177 (31.7%) and 91 (46.2%), followed by poor differentiation (155 (27.7%) and 72 (36.5%), respectively [28, 31]. Unlike the previous study findings, those from northern Ethiopia (GUCSH and FHCSH) and GUCSH showed that poor differentiation was the most common among types 140 (45.6%) and 30 (37%), followed by moderate differentiation in patients 79 (40.7%) and 14 (17%), respectively [22, 26].

Molecular features

Two studies from TASH looked at the prevalence of hormone receptors and molecular subtypes. Both papers showed that the most prevalent receptor was estrogen receptor positive, and the most common molecular subtype was Luminal A in pathology samples. In a study

from TASH in 2018, the prevalence of estrogen receptor positivity was 74 (65%), progesterone receptor positivity was 49 (43%), and HER2 positivity was 26 (23%). Regarding molecular subtype, the prevalence of Luminal A (ER+and/or PR+, HER2-) was 45 (40%), Luminal B (ER+and/or PR+, HER2+) was 30 (26%), HER2-enriched (ER-, PR-, HER2+) was 11 (10%), and Triple Negative/Basal like (ER-, PR-, HER2-) was 26 (23%) [30]. In a similar study from the same institution (2017), 137 biopsies were found to be ER+ (65.5%), PR+ (58%), and HER2 positive (28%) in a study, and the prevalence of molecular subtypes was shown to be Luminal A (54%), Luminal B (22%), HER2-enriched (6%), and Triple 29 Negative/Basal-like (18%) [29].

Treatment

Studies included in this review Reported modalities of treatment, including surgery, chemotherapy, radiotherapy, and hormonal therapy. Surgery remain the mainstay of management in many settings in Ethiopia, and the most prevalent surgical technique was modified radical mastectomy (MRM) [19, 22, 25].

Finding from GUCSH showed, surgery was done for all 82 patients of which 51 (62%) of patients underwent MRM, and 79 (96%) received chemotherapy. The commonest chemotherapy regimen is Adriamycin and Cyclophosphamide (AC). Hormonal treatment given to 60 (73%) and Tamoxifen 18 (22%) was the commonest type [26].

Surgery was performed in 357 (96.2%) patients by two university hospitals (GUCSH and FHCSH); chemotherapy was performed in 163 (43.9%); and hormone therapy was performed in 50 (13.5%) [22].

According to a study conducted at HUCSH, chemotherapy provided for all 559 (100%) patients and Doxorubicin, cyclophosphamide, and paclitaxel were the chemotherapy regiment was commonest. Hormonal therapy provided 168(30%) and Tamoxifen regiment was commonest hormonal therapy patients, and surgery (modified radical mastectomy) was done for 196 (35.1%) [19].

Chemotherapy was given for 275 (90.7) patients in TASH in 2019, with the most prevalent regimen being 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC) in 66.9% of cases. Surgery was done for 257 (85%) , combination therapy (surgery, chemotherapy, and palliative care) delivered to 189 (55.8%) and Radiotherapy was provided for 107 (35%) [21].

A similar study from TASH on 2013 Surgery was done for 902 (87%), and the majority had a modified radical mastectomy of 880 (95%). The majority of patients 893 (83%) also received chemotherapy, mainly anthracycline-containing chemotherapy (FAC)782 (73%). Hormonal therapy provided for 864 (81%) [31].

According to a study conducted at ACSH, 121 (65.1%) patients had surgery and 33 (17.7%) had chemotherapy, while the rest had both surgery and chemotherapy [30]. In TASH(2017), 192 (74%) patients received surgical intervention, the commonest being mastectomy 126, (65.6%); radiotherapy was provided for 53 (20.5%); and chemotherapy was provided for 231 (89.2%) patients [29].

Discussion

Breast cancer is the most common type of cancer in Ethiopia in most reviewed studies, where the prevalence ranges from 15.2 to 26% from all cancers [14, 15] and from female cancer 29.3–37% [11, 16]. The pattern of breast cancer is increasing in Ethiopia. A study from HUCSH showed the breast cancer rate in hospitals has increased from 69 (12.3%) in 2013 to 106 (19%) in 2019 [19] and Results from TASH showed changes in breast cancer between 1997 and 2012, with a prevalence in 2012 has increased by more than seven times compared 1997 [32].

finding from different studies support this review's finding which shows incidence increased by 1.44% per year from 1990 to 2017 and as for regional changes in incidence, all regions of breast cancer had increased incidence except North America, and the Middle East and North Africa had the largest increase in overall incidence [33]. In a similar study conducted between 2000 and 2012, incidence rates of breast cancer increased in South Korea, China, and the United Kingdom while decreasing in the United States [34]. The breast cancer incidence in Africa continues to increase and is projected to double by 2050.

This review showed commonest age group was from 40 to 46 years (7, 22, 23, 21, 16, 28, and 20) which similar finding other African studies [35–37].

Regarding stage at presentation, most of the patients presented with late stages (stages 3 and 4), with a prevalence range of 57–71.2% [19, 22, 25, 29]. which is supported by papers from Africa showed with 89.6% and 72.8% of breast patients in Kenya and Nigeria respectively presenting with advanced stage disease [38–40]. Studies in South Africa reported an advanced stage breast cancer incidence of 50 and 55% [40]. This review showed that early-stage (stages I and II) accounts for 15–35% [6, 8, 15, 27]. Similar findings were found in other developing countries, where only 20–50% of patients in the majority of low- and middle-income countries were diagnosed in these earlier stages [39].

Breast lump or mass is the most common presenting symptom in all studies from various parts of the country, ranging from 57.4 to 88.4% [22, 24–26].

Regarding histological findings of breast cancer in Ethiopia, the commonest histology is ductal carcinoma, followed by lobar carcinoma in all reviewed research and

prevalence ranges (55.3–93.5%) [16, 20, 22, 26–29, 31, 41].

The prevalence of hormone receptors and molecular subtypes is high; estrogen receptor positivity is the most common receptor and is found in more than 65% of breast cancer patients. In terms of molecular subtype, Luminal A (ER+and/or PR+, HER2-) is the most common finding in breast cancer biopsies, accounting for more than 40% of cases, while Triple Negative/Basal-like cases account for more than 15% of cases [20, 29]. Similar finding from studies from south Africa showed Estrogen Receptor is the commonest hormone receptors [39, 40].

This review showed surgery is the mainstay treatment for breast cancer in Ethiopia, and radiotherapy is only provided in the capital city on TASH. A similar study from Africa showed a mastectomy rate greater than 85% and a huge difference from Europe's breast cancer mastectomy of 30% [41].

Limitations of the study

Only English language articles were included.

Conclusion and recommendation

This review summarized the epidemiology, clinical and histological characteristics, and treatment modalities of breast cancer in Ethiopia. Breast cancer incidence is rising, and it accounts for the major cancer burden in the country. There is a need for additional awareness-raising and health education because delayed presentation is a critical problem throughout Ethiopia. For planning and monitoring cancer patterns, comprehensive demographic and clinical data from a population- or facility-based registry are needed. Currently, only one exists in the capital, the Addis Ababa City Cancer Registry (AACCR). There is a need to establish and strengthen histologic and pathology labs, as most hospitals are doing surgeries without histologic, molecular, or receptor identification since it helps with targeted therapy, according to what current best practice suggests. The available treatment options are still limited in Ethiopia; it needs Expanding radiation facilities is a major step toward improving outcomes for breast cancer patients.

Abbreviations

AACCR	Addis Ababa City Cancer Registry
ACSH	Ayder Comprehensive Specialized Hospital
BC	Breast Cancer
CA	Cancer
DRH	Dessie Referral Hospital
EPHI	Ethiopian Public Health Institute
ER	Estrogen Receptor
FHCSH	Felege Hiwot Comprehensive specialized hospitals
GUCSH	Gondar University Comprehensive Specialized Hospital
HER2	Human Epidermal Receptor
HUCSH	Hawassa University Comprehensive Specialized Hospital
IRB	Institutional Review Board
JUMC	Jimma University Medical Center
LMIC	Low- and Middle-Income Country
MeSH	Medical Subjects Headings
MRM	Modified Radical Mastectomy
PR	Progesterone Receptor
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SPHMMC	St. Paul's Hospital Millennium Medical Collage
TASH	Tikur Anbesa specialized hospital
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1

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Author contributions

FGD and BTT developed the protocol, reviewed the reference list, extracted data, and conducted the analyses. TDD and YDS assessed the quality of the data, ensured the absence of errors and arbitrated in case of disagreement. FGD developed the draft manuscript and TDD critically reviewed it. All authors have read and agreed to the published version of the manuscript.

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Data availability

All data generated or analysed during this study are included in supplementary file.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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