Review

Received: 2025-03-12
Accepted: 2025-06-28

BCCR
2025, No 2, Vol 17 :000-000
www.bccrjournal.com

Connecting the Dots: A Narrative Exploration of Breast Cancer Risks in Sub-Saharan African

Ugwu Emmanuel Chika[1], Dike Ujunwa Precious[* 2,3] Ahuchaogu King-David [1, 4]

1

1 Faculty of Pharmaceutical Sciences, Enugu State University of Science and Technology, Enugu, Nigeria.
2 Department of Clinical Pharmacy and Management, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Rivers, Nigeria
3 African Community for Systematic Reviews and Meta-analyses, Cross-River, Nigeria.
4 Pharmacy Council of Nigeria (PCN) Headquarters, Abuja, Nigeria

*Corresponding author
Dike Ujunwa Precious
Donald Ekong Block A, University of Port Harcourt, Rivers, Nigeria
Email: udike188@uniport.edu.ng

ABSTRACT

Africa contribute significantly in the global burden of breast cancer. Crucial efforts have been made to understand the landscape of breast cancer in sub-Saharan Africa (SSA). This article specifically examines the the existing evidence to better understand the risk factors that shape the epidemiology of breast cancer within the SSA region. This article sets off by discussing the epidemiology of breast cancer in SSA, with emphasis on how disparities occur in the region. The article explored the incidence rate across various countries in SSA. The article explored the various risk factors associated with breast cancer in SSA including genetic factors, relevant biomarkers, hormonal factors, reproductive factors, and some disparities in treatments amongst others. Genetic mutations in BRCA1 and BRCA2 genes were discussed, buttressing how they contribute to the occurrence of breast cancer in the region. Certain biomarkers were also identified as risk factors of breast cancer and deserving of mention is the kaiso biomarker. Hormonal and reproductive factors such as age, breastfeeding time, family history, and body hormones such as estrogen, and progesterone amongst others were identified as common risk factors of breast cancer in SSA. The poor treatment strategies and regimens in breast cancer care in SSA is also associated with breast cancer outcome, leading to an overall impact on the epidemiology of breast cancer in SSA. Evidence-based recommendations were also made to improve breast cancer care in SSA. Recommended techniques to addressing breast cancer care rely on genetic insights primarily aimed at informing a technologically-inclined future progress and research.

Keywords:Sub-Saharan Africa; Risk factors; Breast Cancer; Genetics

INTRODUCTION:

Globally, breast cancer represents a critical issue for public health, with reports indicating approximately 2.3 million individuals were newly diagnosed in the year 2020 [1]. The prevalence of this disease shows regional disparities, but it is especially acute in Sub-Saharan Africa (SSA) [2], where it stands as the most common cause of cancer-related deaths among the female population [3]. Breast cancer's origins in this area is influenced by the region's distinct socioeconomic, cultural, and environmental factors [4].

The complexity of breast cancer, acknowledged as resulting from a significant mix of genetic, hormonal, environmental, and sociocultural influences, has been the focus of recent scientific investigations [5,6]. Despite these efforts, there is still much to learn about the precise factors that influence the rates and outcomes of breast cancer in SSA. Genetic predisposition is recognized as a significant determinant of breast cancer risk, with certain gene variants showing susceptibility to the disease [7,8]. In SSA, few studies have identified specific genetic mutations associated with an increased risk of breast cancer, highlighting the need for improved research efforts to understand the genetic nature of the disease in the region [2,3]. However, hormonal factors, such as early menarche, late menopause, and nulliparity, have long been implicated in breast cancer etiology [2,3]. In SSA, where access to reproductive healthcare and family planning services is often limited, hormonal imbalances may worsen the state of breast cancer risk and this underscores the importance of addressing reproductive health disparities through breast cancer prevention efforts. Additionally, Lifestyle and environmental factors, including urbanization, dietary changes, and sedentary lifestyles, are evolving at an alarming rate in SSA, potentially impacting breast cancer risk [3]. Furthermore, infectious agents such as human papillomavirus (HPV) and Epstein-Barr virus (EBV) have been implicated in breast cancer pathogenesis [1-3]. Healthcare disparities within SSA countries present significant challenges in the early diagnosis and management of breast cancer [3]. Disparities in form of limited access to screening programs, late-stage diagnosis, and inadequate treatment options contribute to poor outcomes and high mortality rates [1,3-5]. Sociocultural beliefs and stigma surrounding breast cancer further contribute to these challenges, hindering early detection and obscuring treatment-seeking behavior of patients [3]. Furthermore, economic constraints, including poverty and financial barriers, amplifies the barriers to accessing essential healthcare services, eventually intensifying the inequalities in breast cancer care in SSA regions [3]. The culmination of these factors is an incomprehensible healthcare system which ecourages the ineffective delivery of breast cancer care in SSA. The role of risks of breast cancer in SSA has been treated with less importance; however, this review aims to examine the existing evidence to better understand the risk factors that shape the epidemiology of breast cancer within the SSA region.

Epidemiology of breast cancer in SSA

Breast cancer holds the position of being the primary cause of cancer-related fatalities among women worldwide [9,10]. Projections indicate a substantial surge in cancer cases globally by 2030, with estimates suggesting an increase surpassing 85% [3]. However, within the confines of SSA, the prevalence of breast cancer appears comparatively lower than in high-income countries [9,11]. African-American women, despite exhibiting a lower incidence, face a higher fatality rate from breast cancer compared to White-American women [11]. Moreover, African-American women encounter an elevated risk of early-onset, high-grade, node-positive, and hormone receptor-negative breast cancer [11]. These similarities to hereditary breast cancer have prompted speculation that genetic transmission might contribute to the risk factors [10,11]. With the global prevalence of breast cancer on the rise, SSA contributes significantly to both cases and related deaths, thereby necessitating a thorough examination of the epidemiological trends, patterns, and projections concerning incidence and mortality by various healthcare stakeholders and governments in SSA. GLOBOCAN 2018 data reveals variations in age-standardized breast cancer incidence rates across SSA, with Eastern Africa recording 29.9 per 105 person-years, Middle Africa at 27.9, Southern Africa at 46.2, and Western Africa at 37.3 [12]. Surprisingly, despite these concerning figures, only a handful of SSA nations have been featured in global cancer incidence publications like "Cancer Incidence in Five Continents" [12]. However, studies indicate a notable annual percentage change (AAPC) in breast cancer incidence rates over specific periods in the region. For instance, Kampala, Uganda, experienced an AAPC of 4.5% between 1991 and 2006, while Harare, Zimbabwe, saw a rate of 4.9% between 1991 and 2010 [12]. Recent research focusing on cancer trends among individuals

aged 60 and above in SSA demonstrated a consistent annual increase of 5% in breast cancer incidence rates in Harare and Kampala, with slower increments observed in women under 60 [12,13]. Despite appearing to exist with a lower breast cancer incidence compared to other regions, SSA faces challenges due to limitations in data accuracy [12]. This brings attention to the importance of carefully interpreting the results. Projections for the future suggest that SSA would likely continue to bear the signifcant portion of breast cancer cases compared to other regions [12,13].

Genetic Factors and Biomarkers of Breast Cancer in SSA

Genetic factors have become significantly important in delivering care to cancer patients and major improvements have been witnessed in the type of care provided for people who have cancers of genetic origin. The major genetic mutation associated with breast cancer is in the BRCA1 and BRCA2 genes [14–16]. Other forms of mutation exist in breast cancer patients; however, these make up a low proportion of the cases that have been examined [15]. BRCA1 and BRCA2 mutations have been greatly associated with breast cancer among women living with breast cancer in SSA countries such as Nigeria, Uganda, and Cameroon [15]. A high number of these breast cancer cases in SSA are of pathogenic or likely pathogenic origin (L/LP) or variants of uncertain significance (VUS) [15]. The prevalence of these mutations in SSA is highly indicative of genetic risk factors for breast cancer on the continent. Additionally, the BRCA1 and BRCA2 mutations in women increase the chances of being diagnosed with breast cancer early in life [16]. Breast cancer is also likely to develop in both breasts of women with BRCA1 and BRCA2 mutations [16]. Also, having a relative who has breast cancer has been shown to increase the risk of having breast cancer [16, 17]. The advancement in testing and care provided to patients has been attributed to being able to diagnose women with cancer of genetic origin; however, precautions must be taken when taking this direction of care and testing, as not all women need to undergo genetic testing [16].

An important aspect of breast cancer risks also include the associated biomarkers. The term “biomarker” is a derivative word from “biological marker”, meaning a disease indicator within the human body, specific enough to show the difference in the health status of a patient and a healthy person, which in turn shows the interplay between the body’s biological form and health hazards. An important emerging biomarker for increasing the risk of breast cancer is the androgen receptor [18]. Clinical therapy for breast cancer can be initiated, instructed, and guided using breast cancer biomarkers due to the association of certain biomarkers with cancer development [18].

An important cancer subtype that has received recent scholarly attention is the aggressive triple-negative breast cancer (TNBC). The prevalence of this cancer subtype in Africa is well established, and studies show that this is highest in West Africa [19]. It is significantly characterised by the absence of three regular biomarkers: progesterone and oestrogen receptors and human epidermal growth factor receptor 2; hence, it cannot be treated using tamoxifen or other targeted chemotherapy [19, 20]. However, this has received attention over the years due to recent progress made in identifying the biomarkers associated with such cancer subtypes [20, 21]. Of particular imprtance is the recent identification of Kaiso as a potential biomarker in TNBC in African women [21]. Kaiso is a tumorigenic transcription factor that has target genes well associated with the onset of tumors as well as cancer invasion and metastatic stages in cancer [21]. Additionally, there has been tremendous improvement in identifying other forms of biomarkers for TNBC. These biomarkers include those found in the blood (VEGF/VEGFR and IL-8), in the body cell nucleus (BRCA1/2, GR, and TP53), in the cytoplasm of the cell (PIK3CA, PTEN, pAKT/pS6/p4E-BP1), and on the surface of the cell (EGFR, IGFBP, C-Kit, and PD-L1) [20]. These findings underscore the need to understand breast cancer as a complex disease characterized by a nexus of interactions between body proteins, DNA, and other body components, ensuring a more sophisticated and clinical approach to therapy in breast cancer in SSA.

Hormonal and Reproductive Factors: Associations, Interactions, and Modifiable Influences

Certain reproductive factors are significant considered as risks for breast cancer. There are modifiable and non-modifiable factors. Modifiable factors are risk factors individuals have influence on by the lifestyles. They are risk factors that can be controlled or changed. In a study in the UK, modifiable factors accounted for 23.1% of breast cancer cases[22]. Examples of modifiable factors affecting breast cancer are low parity, delayed childbearing, alcohol consumption, short breastfeeding time, oral contraceptive use, later marriage, smoking [23,

24]. Non-Modifiable factors are risk factors the individual has no control over. Examples of non-modifiable risk factors are age, hereditary, younger menarche, genetic factors, family history of breast cancer, anthropometric status etc [24,25]. All these factors in turn affect the reproductive system and hormonal balance hence increasing the chances of breast cancer.

Number of children is a reproductive factor affecting the rise of breast cancer. It has been observed that having at least a child reduces the risk of breast cancer in comparison with nulliparous individuals [26]. Hence, the risk also reduces with an increase in number of children. However, there is a twist; the risk of breast cancer increases if the first child is had after 30 years. Closely related is the age of first pregnancy. A study in South Africa reports that women who had their first child at the age of 30 years or older had double risk when compared with their counterparts who had at 16 years or younger [27]. The risk is increased by 3% for every year delayed while it decreases with having multiple pregnancies at a younger age [28], hence, age of first pregnancy is another risk factor. Breasts of nulliparous women contain unseperated lobules with high growth index and concentrations of steroid hormone receptors. These breasts are more vulnerable to carcinogenic attack and are the sites of origin of breast carcinomas [29].

Furthermore, breastfeeding prevents pre and post-menopausal breast cancer. Breast feeding does this through inducing hormonal changes in the body, excretion of carcinogenic agents, increased breast separation, delayed ovulation amongst others among other mechanisms [30]. Breast feeding also delays the start of a new mother's menstrual periods, hence decreasing exposure to hormones such as estrogen [31]. Extended period of breast feeding also separates the ductal epithelial cells hence protecting against carcinogens and further increasing prolactin hormone that may further cause a separation of ductal epithelial cells [32].

Estrogen and progesterone are hormones implicated in breast cancer. Estrogen acts as a catalyst for cancer growth due to it's ability to elicit the division and proliferation of breast tissue, a process that carries the risk for cancer causing mutations. The progesterone Receptor on its side modulates estrogen receptors α (ER). Triple negative is a term used to define clinical assays for estrogen receptor ER1, progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) [33]. Oral contraceptive use over a long period of time increases the chances of breast cancer by increasing exposure to estrogen and thereby influence the risk of cancer by changing the endogenous hormonal milieu [34]. Production of estrogen declines after menopause and major source of oestradiol is by conversion of androgen precursors (mainly androsteredione) in extraglandular tissues e.g adipose tissue [35]. The buildup leads to high serum concentration of oestradiol which is implicated breast cancer after menopause. Alcohol also increases estrogen level by interfering with estrogen pathway causing decreased long and frequent cycles amongst others [36].

Breast Cancer Outcome and Quality of Life in SSA: Determinants, Disparities and Interventions.

It has been projected that in this decade, beginning from 2020-2029, around 416,000 women will die from breast cancer in SSA, however with conscious efforts like down staging and improved treatment, around a third of the death can be averted [37].

While breast cancer has a good prognosis in high income countries, the reverse is the case in low and middle-income countries. Multiple deaths due to breast cancer are reflected in a high breast cancer mortality with the deaths in SSA double that in Western Europe [38]. The African Breast Cancer –Disparities in Outcome (ABC-DO) gives a 3-years report aimed at identifying reasons for poor prognosis especially in Africa. In the study, it was reported that survival is very low, across the countries, with around 40% in Nigeria, 45-50% in Uganda and Zambia and around 56-59% in South Africa and Namibia, this is in contrast to white Namibian women who had up to 96% recovery [39]. A similar 5-year study estimates that survival of breast cancer in SSA is less than 50% in comparison to black and white women in the U.S with 73% and 85% recovery respectively [40, 41].

Improved survival was recorded for women diagnosed at stages 1 and 2 than for those diagnosed at stages 3/4 [42]. Younger age has also be associated with poorer prognosis [43]. Quality of treatment is another determinant. Affordability, availability, accessibility, quality, and acceptance by patients are factors that can affect treatment.

Breast cancer requires the expertise of clinical oncologist to manage, however, there is a short supply of the medical team. A study revealed that there is approximately 1 clinical oncologist per 1000 incident patients, 1 clinical oncologist per 325 incident patients in Namibia, and 1 clinical oncologist to 10,167 patients in Ethiopia [44,45], compared to 1 per 137 incident patients in USA. Sadly,

over 40% of those with advanced breast cancer don't receive chemotherapy. It is estimated that in Africa, there is less than 1 RT machine per million people, compared to almost 15 RT machines per million people in North America [46]. The NCCN Harmonized guidelines for SSA identified this problem, and has remedied by providing guidelines that can be followed in absence of RT facilities.

Futhermore , some patients do not complete their treatment regimen due to some factors ranging from lack of funds, inadequate bed space, and in some cases of feeling well after early therapy thus non-adherence [47]. Breast cancer management requires a multidisciplinary approach and this is not always available in most hospitals in SSA.

A study involving 2,228 patients with breast cancer showed that the survival and life outcome of patients are greatly influenced by impact of last stage, lack of treatment, tumor biology, positive HIV status, and age. Also, little education, poor awareness, rural residence, and lower socioeconomic status were associated with poorer survival outcomes. Survival improvement (up to 22%) was achievable through downstaging and availability of basic treatment. Patients from Namibia showed better outcomes compared with patients from South Africa, Uganda, Zambia and Nigeria [45].

Moreover, it is hypothesized that poor survival from breast cancer in Africa is attributed to in descending order of magnitude: late stage at diagnosis, lack of access to and compliance with appropriate treatment, tumour aggressiveness and comorbidities [46].

Techniques, Genetic Insight, and Future Directions

While traditional approaches to breast cancer care are vital, integrating novel techniques and genetic insights can improve treatment strategies in the region, ultimately improving patient outcomes.

Precision Medicine: One of the most promising avenues for personalized breast cancer treatment is precision medicine [49-51]. By leveraging genomic profiling and molecular diagnostics, healthcare providers can tailor treatment plans to individual patients based on their specific genetic makeup and tumor characteristics [49,50,52]. This approach allows for more targeted therapies, minimizing side effects and optimizing treatment efficacy [52].

Genetic Counseling and Testing: Genetic counseling and testing services play a crucial role in identifying individuals at higher risk of hereditary breast cancer due to specific gene mutations, such as BRCA1 and BRCA2 [53]. By identifying high-risk individuals early on, healthcare providers can implement appropriate preventive measures, such as increased surveillance or risk-reducing surgeries, potentially saving lives [53, 54].

Research and Innovation: Investing in research and innovation is essential for advancing our understanding of breast cancer genetics and identifying new therapeutic targets [55]. Collaborative research efforts between local and international institutions is essential in generating valuable insights into the drivers of breast cancer cases of genetic origin in SSA. This would eventually make way for the development of targeted therapies tailored to the region's population [56,57].

Access to Cutting-Edge Technologies: Ensuring access to up-to-date technologies, such as next-generation sequencing platforms and advanced imaging modalities, is critical for conducting genetic research and implementing personalized treatment approaches [57]. In other to bridge the gap in the knowledge of breast cancer genetics in resource-limited settings, there must be efforts to expand access to these technologies in SSA

Integration into Clinical Practice: Integrating genetic insights into clinical practice is essential for improving breast cancer care. To achieve this, there must be adequate provision of education and training for healthcare providers on genetic testing, interpretation of results, and personalized treatment approaches. Multidisciplinary collaboration between genetic counselors, oncologists, and surgeons, is also recommended in order to produce comprehensive care plans for patients based on genetic profiles.

Community Engagement and Empowerment: Engaging communities in discussions about genetic research and its implications for breast cancer prevention and treatment is crucial for building trust and addressing cultural sensitivities. This may be achived by empowering individuals with knowledge about their genetic risk factors. Additionally, available resources on breast cancer risks awareness can facilitate informed decision-making and improve health outcomes within the communities [53].

Conclusion

The concept of breast cancer in SSA is of utmost significance with most important aspects being the risks and factors associated with it, respresenting an integral part in the African healthcare sector of public health concern. The high prevalence of breastcancer in SSA

raises various interests including risk factors associated with this disease amongs SSA countries. Certain genetic factors and biomarkers have been implicated as factors associated with breast cancer in the region. Worthy of mention are the genetic mutations in the BRCA1 and BRCA2 genes as well as the prevalence of TNBC in women in SSA countries. Breast cancer epidemiology is also shaped by the presence of hormonal changes in females. Reproductive factors also contribute to the endemicity of breast cancer in SSA countries. The disparities within breast cancer care are well associated to with poor level of breast cancer outcomes in SSA. Low survival rates, high mortality rates, low staffing of oncology professionals, and impaired treatment regimen are of deserving mention. Finally, incorporating novel techniques and genetic insights into breast cancer management strategies in SSA holds tremendous promise for improving breast cancer care. These techniques range from precision medicine, to extensive research, genetic counseling, improved technology-based clinical practice, and community engagement to mention a few. These techniques harness the potential to shape the epideology of breast cancer in SSA countries, greatly mitigating the risks and factors associated with it.

Author Contributions:
Ugwu, Emmanuel Chika was responsible for the study's conception and design. All authors contributed, read and approved the final manuscript.

Competing interests:
The authors declare that they have no competing interests.

Funding:
This work did receive no funding

Acknowledgments:
None

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021 May;71(3):209-49. https://doi.org/10.3322/caac.21660
2. Obafemi FA, Umahi-Ottah G. A review of global Cancer prevalence and therapy. J Cancer Res Treat Prev. 2023;1(3):128-47. Obafemi FA, Umahi-Ottah G. A review of global Cancer prevalence and therapy. J Cancer Res Treat Prev. 2023;1(3):128-47. https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011
3. Morhason-Bello IO, Odedina F, Rebbeck TR, Harford J, Dangou JM, Denny L, et al. Challenges and opportunities in cancer control in Africa: a perspective from the African Organisation for Research and Training in Cancer. The lancet oncology. 2013 Apr 1;14(4):e142-51. https://doi.org/10.1016/S1470-2045(12)70482-5
4. Saini G, Ogden A, McCullough LE, Torres M, Rida P, Aneja R. Disadvantaged neighborhoods and racial disparity in breast cancer outcomes: the biological link. Cancer Causes & Control. 2019 Jul 1;30:677-86. https://doi.org/10.1007/s10552-019-01180-4
5. Hiatt RA, Brody JG. Environmental determinants of breast cancer. Annual review of public health. 2018 Apr 1;39:113-33.
6. Gibbon S, Joseph G, Mozersky J, Zur Nieden A, Palfner S, editors. Breast cancer gene research and medical practices: transnational perspectives in the time of BRCA. Routledge; 2014 Mar 5.
7. Antoniou AC, Easton DF. Models of genetic susceptibility to breast cancer. Oncogene. 2006 Sep;25(43):5898-905. https://doi.org/10.1038/sj.onc.1209879
8. Turnbull C, Rahman N. Genetic predisposition to breast cancer: past, present, and future. Annu. Rev. Genomics Hum. Genet.. 2008 Sep 22;9:321-45.
9. Duggan C, Trapani D, Ilbawi AM, Fidarova E, Laversanne M, Curigliano G, et al. National health system characteristics, breast cancer stage at diagnosis, and breast cancer mortality: a population-based analysis. The Lancet Oncology. 2021 Nov 1;22(11):1632-42. https://doi.org/10.1016/S1470-2045(21)00462-9.
10. Ahmad A. Breast cancer statistics: recent trends. Breast cancer metastasis and drug resistance: challenges and progress. 2019:1-7.
11. Fregene A, Newman LA. Breast cancer in sub-Saharan Africa: how does it relate to breast cancer in Afri-

can-American women?. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2005 Apr 15;103(8):1540-50. https://doi.org/10.1002/cncr.20978
12. Joko-Fru WY, Jedy-Agba E, Korir A, Ogunbiyi O, Dzamalala CP, Chokunonga E, et al. The evolving epidemic of breast cancer in sub-Saharan Africa: Results from the African Cancer Registry Network. International journal of cancer. 2020 Oct 15;147(8):2131-41. https://doi.org/10.1002/ijc.33014
13. Pilleron S, Soerjomataram I, Charvat H, Chokunonga E, Somdyala NI, Wabinga H, et al. Cancer incidence in older adults in selected regions of sub-Saharan Africa, 2008–2012. International journal of cancer. 2019 Apr 15;144(8):1824-33.https://doi.org/10.1002/ijc.31880
14. Hayat M, Chen WC, Brandenburg JT, De Villiers CB, Ramsay M, Mathew C. Genetic susceptibility to breast cancer in Sub-Saharan African populations. JCO glob oncol. 2021 Dec;(7):1462–71.
15. Babatunde A, Yonglan Z, Paul N, Antony G, Timothy M, Toshio FY, et al. Prevalence of Inherited Mutations in Breast Cancer Predisposition Genes among Uganda and Cameroon Women. Cancer Epidemiol Biomarkers Prev. 2020;29(2):359–67.
16. American Cancer Society. Breast cancer risk factors you can't change [Internet]. [Cited 2024, April 4]. Available from: https://www.cancer.org/cancer/types/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html
17. National Cancer Institute. Genetics of Breast and Gynecologic Cancers (PDQ®)–Health Professional Version [Internet]. Updated: April 4, 2024. [Cited 2024, April 4]. Available from: https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq
18. Chan-Ping You, Man-Hong Leung, Wai-Chung Tsang, Ui-Soon Khoo, Ho Tsoi. Androgen Receptor as an Emerging feasible Biomarker for Breast Cancer. Biomolecules. 2022; Jan 4;12(1):72. doi: 10.3390/biom12010072.
19. Hercules SM, Alnajar M, Chen C, Mladjenovic SM, Shipeolu BA, Perkovic O, et al. Triple-negative breast cancer prevalence in Africa: a systematic review and meta-analysis. BMJ Open. 2022;12[5]:e055735.
20. Fleisher B, Clarke C, Ait-Oudhia S. Current advances in biomarkers for targeted therapy in triple-negative breast cancer. Breast Cancer (Dove Med Press). 2016;8:183-97.
21. Bassey-Archibong BI, Hercules SM, Rayner LGA, Skeete DHA, Smith Connell SP, Brain I, et al. Kaiso is highly expressed in TNBC tissues of women of African ancestry compared to Caucasian women. Cancer Causes Control. 2017 Nov;28(11):1295–304.
22. Brown KF, Rumgay H, Dunlop C, et al. The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. Br J Cancer 2018; 118: 1130–41.
23. Yeo W, Lee HM, Chan A, Chan EYY, et al. Risk factors and natural history of breast cancer in younger. Chinese women. World J Clin Oncol. 2014, 5, 1097-106.
24. Colditz GA, Bohlke K. Priorities for the primary prevention of breast cancer. CA Cancer J Clin 2014;64:186–94.
25. Hawk N, O'Regan R. Treatment of triple-negative breast cancer. Community Oncology. 2010;7(7):328-332
26. Karapanou O, Papadimitriou A. Determinants of menarche. Reproductive biology and endocrinology. 2010; 8(115):1477.
27. Kruger WM, Apffelstaedt JP. Young breast cancer patients in the developing world: incidence, choice of surgical treatment and genetic factors. South African Family Practice. 2007;49(9):18-24.
28. Mujagic Z, Srabovic N, Mujagic H. The role of prolactin in human breast cancer. J of Croat Soc Med Biochem. 2009;19(3):236-249.
29. Puri S, Mangat C, Bhatia V, Kalia M, Sehgel A, Kaur AP. Awareness of risk factors and aspects of breast cancer among North Indian women. Internet J Health. 2009; 8(2):1-12.
30. Lord SJ, Bernstein L, Johnson KA, Malone KE, McDonald JA, Marchbanks P A, et al. Breast cancer and hormone receptor status in older women by parity, age of first birth, and breastfeeding: A case-control

study. Can Epidemiol Biomark Prev. 2018; 17:1723.
31. Fung TT, Hu FB, Hankinson SE, Willett WC, Holmes MD. Low-carbohydrate diets,Dietary Approaches to Stop Hypertension-style diets, and the risk of postmenopausal breast cancer. Ame J Epidemiol. 2011;174(6):652-660.
32. Celik S, Aksoy G. Identification of risk factors for breast cancer for women in Istanbul. Open Nurs J. 2007; 1:6-12.
33. Anderson BO, Ilbawi AM, El Saghir NS. Breast cancer in low and middle income countries (LMICs): a shifting tide in global health. Breast J. 2015;21:111–8.
34. Islami F, Liu Y, Jemal A, Zhou J, Weiderpass E, Colditz G, et al. Breastfeeding and breast cancer risk by receptor status–a systematic review and metaanalysis. Ann Oncol 2015;26:2398–407.
35. Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Maso L. Worldwide thyroid-cancer epidemic? The increasing impact of overdiagnosis. N Engl J Med 2016;375:614–7.
36. Lauby-Secretan B, Scoccianti C, Loomis D, Benbrahim-Tallaa L, Bouvard V, Bianchini F, et al. Breast-Cancer Screening — Viewpoint of the IARC Working Group. N Engl J Med 2015;372:2353–8.
37. Ferlay J, Ervik M, Lam F, et al. Global cancer observatory: cancer today. 2018. https://gco.iarc.fr/today/onlineanalysis. Accessed [Dec 1, 2019].
38. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359–86.
39. Coghill AE, Newcomb PA, Madeleine MM, et al. Contribution of HIV infection to mortality among cancer patients in Uganda. AIDS. 2013; 27: 2933–42.
40. Galukande M, Wabinga H, Mirembe F. Breast cancer survival experiences at a tertiary hospital in sub-Saharan Africa: a cohort study. World J Surg Oncol 2015;13:220.
41. Coleman MP, Quaresma M, Berrino F, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). Lancet Oncol 2008;9:730–56.
42. Kantelhardt E, Zerche P, Mathewos A, et al. Breast cancer survival in Ethiopia: a cohort study of 1,070 women. Int J Cancer 2013;135:702–9.
43. Keegan TH, Press DJ, Tao L, et al. Impact of breast cancer subtypes on 3-year survival among adolescent and young adult women. Breast Cancer Res 2013;15:R95.
44. Mathew A. Global survey of clinical oncology workforce. J Glob Oncol .2018;4:1–12.
45. Joko-Fru, W. Y., Griesel, M., Mezger, N. C. S., Hämmerl, L., Seraphin, T. P., Feuchtner, J., Wabinga, H., N'da, G., Mathewos, A., Kamaté, B., Nsonde Malanda, J., Gnangnon, F. H. R., Chesumbai, G. C., Korir, A., Lorenzoni, C., Zietsman, A., Borok, M. Z., Liu, B., Thomssen, C., McGale, P., … Kantelhardt, E. J. (2021). Breast Cancer Diagnostics, Therapy, and Outcomes in Sub-Saharan Africa: A Population-Based Registry Study. Journal of the National Comprehensive Cancer Network : JNCCN, 20(13), 10.6004/jnccn.2021.7011. https:// doi. org/10.6004/ jnccn . 2021.7011.
46. Abdel-Wahab M, Bourque JM, Pynda Y, et al. Status of radiotherapy resources in Africa: an International Atomic Energy Agency analysis. Lancet Oncol 2013;14:e168–175.
47. Egwuonwu OA, Anyanwu SN, Nwofor AM. Default from neoadjuvant chemotherapy in premenopausal female breast cancer patients: what is to blame? Niger J Clin Pract 2012;15:265–9.
48. McKenzie F, Zietsman A, Galukande M, et al. African Breast Cancer— Disparities in Outcomes (ABC-DO): protocol of a multicountry mobile health prospective study of breast cancer survival in subSaharan Africa. BMJ Open 2016;6:e011390. doi:10.1136/bmjopen-2016-011390
49. Olopade OI, Grushko TA, Nanda R, Huo D. Advances in breast cancer: pathways to personalized medicine. Clinical Cancer Research. 2008 Dec 15;14(24):7988-99. https://doi.org/10.1158/1078-0432.CCR-08-1211
50. Subhan MA, Parveen F, Shah H, Yalamarty SS, Ataide JA, Torchilin VP. Recent advances with precision medicine treatment for breast cancer in-

cluding triple-negative sub-type. Cancers. 2023 Apr 8;15(8):2204. https://doi.org/10.3390/cancers15082204

51. Swathi NL, Chakrabarti M, Muzzamil M, Hamdar H, Jaber A, Chamoun A, et al. Precision Medicine: Insights From Case Studies and Cutting-Edge Technologies. InMedical Robotics and AI-Assisted Diagnostics for a High-Tech Healthcare Industry 2024 (pp. 257-280). IGI Global. DOI: 10.4018/979-8-3693-2105-8.ch017
52. Pinker K, Chin J, Melsaether AN, Morris EA, Moy L. Precision medicine and radiogenomics in breast cancer: new approaches toward diagnosis and treatment. Radiology. 2018 Jun;287(3):732-47. https://doi.org/10.1148/radiol.2018172171
53. Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, Caughey AB, Doubeni CA, et al. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer: US Preventive Services Task Force recommendation statement. JAMA. 2019 Aug 20;322(7):652-65. doi:10.1001/jama.2019.10987
54. Piccinin C, Panchal S, Watkins N, Kim RH. An update on genetic risk assessment and prevention: the role of genetic testing panels in breast cancer. Exp Rev Anticancer Ther. 2019 Sep 2;19(9):787-801. https://doi.org/10.1080/14737140.2019.1659730
55. Carpenter WR, Reeder-Hayes K, Bainbridge J, Meyer AM, Amos KD, Weiner BJ, et al. The role of organizational affiliations and research networks in the diffusion of breast cancer treatment innovation. Medical care. 2011 Feb 1;49(2):172-9. DOI: 10.1097/MLR.0b013e3182028ff2
56. Curigliano G, Criscitiello C, Andrè F, Colleoni M, Di Leo A. Highlights from the 13th St Gallen International Breast Cancer Conference 2013. Access to innovation for patients with breast cancer: how to speed it up?. ecancermedicalscience. 2013;7. Doi https://doi.org/10.3332%2Fecancer.2013.299
57. Obeagu EI, Obeagu GU. BRCA Mastery: Redefining Breast Cancer Care through Cuttingedge Diagnosis and Management. Elite J Med. 2024;2(2):55-66.