EDITORIAL

From Incidence to Intervention: A Comprehensive Look at Breast Cancer in South Africa

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ABSTRACT

The formidable impact of breast cancer extends globally, with South Africa facing pronounced challenges, including significant disparities in breast cancer screening, treatment and survival along ethnic and socioeconomic lines. Over the last two decades, breast cancer incidence has increased and now accounts for a substantial portion of cancers in women. Ethnic disparities in terms of screening, incidence and survival exacerbate the issue, leading to delayed diagnosis among Black patients and highlighting healthcare inequities. These concerning trends underscore the urgency of enhancing breast cancer screening while mitigating treatment delays, although obstacles within the healthcare system impede progress. The intersection of breast cancer and human immunodeficiency virus (HIV) further complicates matters and particularly affects the Black population. Tackling the aforementioned disparities in breast

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cancer in South Africa mandates a multifaceted strategy. Robust screening efforts, particularly those targeting marginalised communities, are crucial for early detection. Concurrently, expedited treatment initiation is imperative. Addressing HIV-related complexities requires tailored interventions to ensure effective care. These multifaceted disparities require pan African research and cooperation as well as tailored interventions to enhance breast cancer care within the African region.

Keywords : Breast cancer; South Africa; Sub-Saharan Africa; Incidence; Mortality; Ethnicity; Screening; Treatment; Human immunodeficiency Virus (HIV) comorbidity

Key Summary Points

The incidence of breast cancer in South Africa has been steadily increasing over the last 20 years.

South Africa, a low- to middle-income country, has a lower incidence of breast cancer than high-income countries, but a higher mortality rate.

The relatively higher mortality rate is likely due to lower screening rates, lower access to healthcare and a higher frequency of triple-negative breast cancer in patients of African ancestry.

Many of these problems can be solved through the use of new digital screening methods, more education on breast cancer and the implementation of community outreach programmes.

EDITORIAL

Breast cancer is the most common cancer in women worldwide, with 2,261,419 new cases diagnosed in 2020. It is also the leading cause of cancer-related death in women globally,

including South Africa [1]. The course of breast cancer incidence in South Africa over the 20-year period from 2000 to 2020 shows a steady increase in the number of breast cancer cases (Fig. 1a), including patients of African, European and mixed ancestry. This increase is reflected in data from both the South African National Cancer Registry (NCR) and the International Association of Cancer Registries (IACR). Regardless of the source of the data, the absolute number of new breast cancer cases has doubled in the past 20 years and now accounts for 14–30% of all cancers in women [2] (Fig. 1b). It is not clear, however, whether this increase in breast cancer is due to an overall increase in all cancer types as there has only been a slight increase in the proportion of breast cancer cases to total cancer cases (Fig. 1b). Overall, the age-standardised rate (ASR) shows a very slight increase, although there has been a marked increase in the ASR for South Africans of European ancestry. In some parts of the country there has been a significant annual increase in the number of breast cancer cases recorded, such as in the Eastern Cape Province where a cancer registry reported a 61% increase in the number of breast cancer cases over the period 1998–2012 [3].

The statistics provided by the IACR differ from those reported by the South African NCR, with the number of new breast cancer cases in 2020 being much higher in the IACR data than in the NCR data (15,491 versus 9259). These differences are due to the different strategies used to tally the statistics. The NCR is a collection of pathology-based cancer surveillance figures based on the curation of cancer diagnosis data from histology, cytology and bone marrow aspirate and trephine samples; these samples have been collected, analysed and then reported on annually [4]. The IACR data are based on the South African NCR and Eastern Cape Province Cancer Registries. The final numbers are an approximation derived from the national mortality estimates and then applied to a model using mortality:incidence ratios from cancer registry data in neighbouring countries [1]. The reliability and effectiveness of the NCR data have also been called into question. In addition, the NCR does not record data
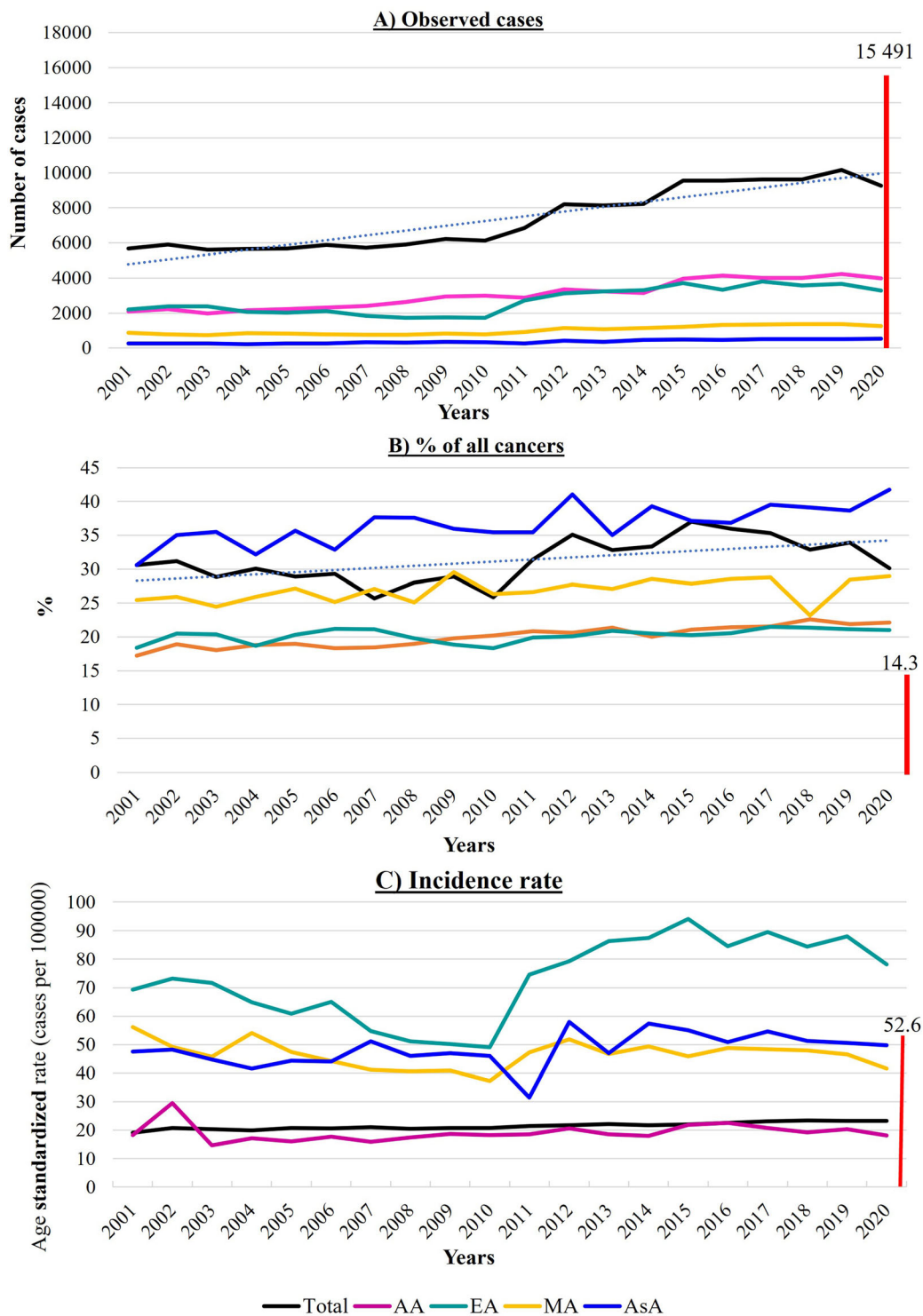
Fig. 1 Breast cancer incidence in South Africa. Incidence data for breast cancer in South Africa are presented as the total number of cases (**a**), the percentage of breast cancer cases among all cancer cases (**b**) and the age standardised rate, which reflects the number of cases per 100,000 individuals (**c**). The data plotted from 2001 to 2020 were obtained from the NCR. The red bars represent IARC data from 2020. *AA* African ancestry, *EA* European ancestry, *MA* Mixed ancestry, *AsA* Asian ancestry, *IARC* International Association of Cancer Registries, *NCR* National Cancer Registry

such as age, stage of presentation and clinico-pathological features and has no standardised descriptive pathology reporting [4]. Studies that have aimed to examine the catchment rate of breast cancer cases within the South African NCR showed that most hospital breast cancer cases were captured in the NCR database [5].

South Africa is a low-to-middle-income country (LMIC) and, similar to all other LMICs, it has a lower reported incidence rate of breast cancer than high-income countries (HICs). In most cases LMICs have a higher mortality rate for breast cancer than HICs despite having a relatively lower incidence. However, the mortality rate in South Africa is lower than that in most LMICs and is near to the rate recorded for most HICs. It should be noted that this lower mortality rate still does not reflect the lower incidence rate of breast cancer in South Africa compared to HICs with the same mortality rate, suggesting a poorer outcome for a greater percentage of patients with breast cancer in South Africa compared to their HIC counterparts [6, 7]. Breast cancer rates in South Africa differ based on ethnicity, with an incidence of one in 13 among white women and one in 81 in African women [8].

The South African National Department of Health declared diseases such as breast cancer to be a priority, leading to the creation of the National Breast Cancer Policy Guidelines. These guidelines remain to be fully implemented [9], but they highlight the importance of breast cancer screening as the most viable strategy for controlling the disease through early detection and treatment. South African recommendations for breast cancer screening include the recommendation that screening starts at the age of 40 years [10]. Screening for breast cancer is positively associated with socioeconomic position, level of education and employment (vs. not employed). In addition, it has been noted that screening is often neglected by patients of African ancestry due to time and financial constraints, a lack of knowledge about the disease and cultural influences [11, 12]. One of the major contributors to a lack of screening and poor breast cancer survival in South Africa is poor access to healthcare and limited resources,

which includes poor access to clinical breast examinations and screening imaging [13].

In South Africa, patients are more likely to present with late-stage (stage III or IV) breast cancer, with studies indicating that the incidence of advanced stage breast cancer in South Africa is between 50% and 57% [4, 7]. Differences in breast cancer diagnosis patterns are also influenced by ethnicity, with patients of European ancestry more likely to present with early-stage breast cancer, while patients of African ancestry are more likely to present with advanced disease [12]. Triple negative breast cancer (TNBC) is also diagnosed at higher rates in South Africa, resembling the prevalence of TNBC seen in the African American population of the USA [14–16].

The treatment of breast cancers in South Africa standardly occurs at tertiary hospitals, which are located in urban areas. These treatments include surgery, radiation therapy and/or chemotherapy. Because of their cost, the availability and use of receptor-based targeted therapy, such as anti-HER2 agents, are limited in South African public hospitals [14]. As such, South African public hospitals frequently experience delays in the initiation of breast cancer treatment, which affect the timely administration of adjuvant chemotherapy, radiotherapy, or endocrine therapy. These delays, in turn, are associated with poorer survival among women treated with upfront surgery. In addition, lack of transport for those living more than 20 km from the hospital is another barrier to treatment. Language and communication problems also play a role in treatment delay, especially in those who are non-English speakers [17, 18]. Treatment outcomes for breast cancer in South Africa vary wildly with geographical location and socioeconomic status of the patient [17]. The very large socioeconomic disparity within the South African society severely affects health status and patient outcomes. This disparity is reflected in the existence of two separate healthcare systems within South Africa: a public healthcare system funded by the government, and a private healthcare system run by private companies and used by those who are able to afford to pay for a medical aid scheme. These two healthcare systems are associated with

different outcomes due to treatment access, implementation and speed of delivery [19].

In terms of comorbidities, the high prevalence of human immunodeficiency virus (HIV) infection in South Africa and the nature of HIV means that breast cancer is commonly diagnosed together with concurrent HIV infection. Patients with HIV, when diagnosed with breast cancer, are commonly of a younger age and are at a more advanced stage of disease than patients who are HIV negative. Treatment of these patients is more complicated, resulting in poorer outcomes [20]. Patients who are HIV positive are more likely to undergo breast cancer screening because patients with chronic conditions undergo screening as part of their care or screening is just more convenient because these patients spend more time at healthcare facilities [21].

Personalised medicine promises to revolutionise the screening, diagnosis and treatment of breast cancer. This is a long-awaited groundbreaking change in the approach to managing the disease, with individuals and populations receiving tailor-made medical solutions. These changes will be made possible through the use of high-throughput technologies, such as next-generation sequencing. These technologies will generate large amounts of "omics" data which will be scored and managed in large databases through the use of artificial intelligence (AI). AI can then apply machine learning to select and recognise patterns and features within these data to make decisions regarding treatment or recognise the features to make accurate diagnoses or prognoses [22].

The gathering and screening of large amounts of digital information also has its drawbacks; for example, this approach could lead to discrimination based on specific molecular signature, since AI can discriminate either on purpose of accidentally based on the thoughts and opinions of its creators or teachers. This can lead to misdiagnoses or inappropriate treatment recommendations due to a specific group being ignored by the AI engine [23]. This challenge is particularly important in sub-Saharan Africa (SSA) as the representation of individuals of population groups in teaching datasets may be skewed towards those of European ancestry since the large bulk of studies into the molecular patterns in breast cancer have been performed in this population group. Such a development is known as data bias, while societal bias may occur when older datasets or databases are used that classify data using outdated terms or classifications [24]. Societal bias can result in individuals that fall outside of certain classifications being ignored, resulting in misdiagnoses and poor treatment selection [25]. Another important issue is the giving of informed consent by the patient for their data to be used in numerous unforeseen fashions. This leads to issues surrounding privacy and the protection of information [26]. Once again this is compounded by the collection of large volumes of data as the accidental disclosures of health-related data are more likely to occur as the volume of data collected increases [27]. As previously mentioned, the greatest barrier to the implementation of precision medicine in SSA is the lack of population-specific data, which is why encouraging clinical trial participation in under-represented population groups is of the utmost importance for breast cancer screening, diagnosis and management. Up to now, the participation of members of non-European descent in clinical trials remains fairly low compared to that of patients of European descent [28]. This problem can be partially alleviated through community outreach and education programmes.

The predominant role of community health workers in providing educational programmes targeting breast cancer is believed to be extremely important in the fight against breast cancer. The aim of such education is to provide information on breast health, disease and the signs and symptoms of breast cancer. Such knowledge may also inform the public about the methods for breast cancer screening and treatment options, both of which would help to alleviate fears and lead to a greater number of women going for screening and seeking help for their health concerns. These health programmes could also assist in education on reproductive health by, for example, lowering the transmission of sexually transmitted infections, such as human papillomavirus (HPV), which is a risk factor for breast cancer [29].

Educational programmes would also be useful in informing women which risky behaviors other than sexual behaviors contribute to the development of breast cancers, including excess alcohol consumption, smoking, obesity, a fatty diet and the use of hormone replacement therapy. An analysis of the literature indicated that these educational programmes are most effective when both men and women receive education, and that this education should be given to people at all stages of life from the young to the old [30].

In general, South African women have a moderate level of knowledge of breast cancer risks [31, 32]. The extent of this knowledge varies in different regions of the country, with knowledge of breast cancer symptoms being lower in women assayed in the province of Limpopo [32] compared a parallel socioeconomic population in the Western Cape Province [31, 33]. Studies indicate that South African women assume breast cancer is common and curable if detected early [32, 33], and many women have positive attitudes toward care seeking, despite the common scenario of some women delaying seeking medical attention [32]. Delays in care seeking can be attributed to cultural influences, fatalism, fear of stigma, a preference for traditional medicine [34], fear of a positive diagnosis, fear of pain and cost [33].

Community engagement, which is defined as mutually beneficial actions that promote power sharing and mutual respect between healthcare workers or researchers and community members [35, 36], is vital in terms of increasing breast cancer awareness and redressing disparities in the screening and treatment of breast cancer. The aim of community outreach programmes are to understand what is going on in a specific, affected community as well as to engage with key stakeholders in that community, such as community leaders, to help implement changes in the approach to breast cancer. Community outreach and engagement allows for the for bi-directional exchange of knowledge and education, which is necessary for the elimination of breast cancer disparities, and strategies for breast cancer include assisting patient navigation, the design and development

of interventions, setting up advisory boards/patient boards and the use of community mentors. Patient navigation facilitates healthcare access, resulting in increases in the number of women who undergo screening, diagnosis and treatment [37, 38]. Well-implemented patient navigation initiatives can result in increased breast cancer screening, earlier diagnosis [39–41], and the earlier initiation of treatment [39]. Intervention development involves consultation with the community when developing or implementing effective interventions. This leads to more favourable outcomes as it allows these strategies to be tailored to a specific community [42, 43]. Advisory boards provide structure to the partnership [44]. They typically comprise individuals who are as representative as possible of the target research community or population. In terms of breast cancer management and treatment, such advisory boards have been successfully used to design community- and population-specific treatments [45, 46] and develop interventions for risk factors, such as stress [47]. Finally, there are community mentors, who are people who have an innate understanding of breast cancer based on previous experience, such as a mentor who has been directly affected by the disease as a recovering patient, and/or they are close to a person suffering from breast cancer. These individuals are part of the target community and are therefore trusted and can communicate and spread the information on breast cancer more easily.

The high burden of breast cancer and the strain it places on South African society and its healthcare system makes it an important problem requiring multiple approaches. Research ranges from social research, tracking the social factors influencing screening and care seeking, to research into the molecular basis of the disease in African populations. These strategies will improve the quality of epidemiological data, which will in turn refine cancer registries. An analysis of breast cancer research across the SSA region showed that compared to the actual breast cancer burden, current research is not geared towards resolving the issues surrounding breast cancer in SSA [48]. As such, future research should focus on dealing with African

problems and ensuring that a database of molecular characteristics and breast cancer subtypes be established that is specific to African women.

Breast cancer incidence and mortality are increasing in Africa [49, 50], with the prevalence of breast cancer predicted to double in SSA by 2050 [50, 51]. An interesting study has shed light on the impact of the Human Development Index (HDI) on the average age at diagnosis in countries of SSA. This study reported that in countries with a high HDI the average age of diagnosis is 56.5 years compared to an average age of 48 years in low HDI countries [51].

In South Africa, as in other SSA countries, racial disparities are also observed. The African Breast Cancer-Disparities in Outcomes (ABC-DO) prospective cohort study showed that Namibian white women had a relatively favourable outcome compared to Namibian Black women, with a 3-year survival rate of 90% versus 56% [52]. The study excluded South African white and Asian groups due to their low representation in the general population. South African Black women and those of mixed ancestry were included. The results were consistent with those found in Namibian women, with South African Black women having a lower 3-year survival than those of mixed ancestry. It is also worth noting that in all of the different countries included in the study, all of the Black groups had lower survival compared to all of the non-Black groups [52].

Late-stage cancer at diagnosis is common in SSA, with 64.9% of women being diagnosed with stage III and IV disease, among whom 18.4% are diagnosed with stage IV cancer at presentation [51]. Factors that affect healthcare-seeking behaviour in SSA include cultural beliefs, stigma, supernatural forces, perceptions of beauty in light of the possibility of mastectomy and accessibility to diagnostic and treatment facilities [50]. A low level of education was also associated with late presentation, as was limited knowledge of breast cancer [53]. The authors of a Togolese cohort study deduced that the distance from healthcare facilities, fear of diagnosis, lack of breast self-examination and the type of initial consultation (i.e. consultation with a traditional healer) were predictors of late presentation [54].

In order to reduce late-stage diagnosis, early breast cancer detection is required. Breast cancer screening has proven to be beneficial in HICs that use mammography in national screening programmes. Mammography is not readily available in SSA, necessitating methods such as breast self-examination and clinical breast examination [55]. Predictors of screening include education level, increased age, having health insurance and high socioeconomic status [56]. The scarcity of mammography facilities has led to the consideration of using handheld breast cancer screening equipment, such as iBreast Exam [57].

Treatment data are scarce in SSA despite the importance of such data for assessing the quality of care and setting healthcare priorities and standards. Breast cancer requires multimodality treatment to successfully reduce mortality. Where the data are available, treatment abandonment is observed, and it can be as high as 38% in Nigeria [58]. The use of multimodality treatment necessitates the formation of multidisciplinary tumour boards, a strategy that has been shown to improve patient outcomes. Despite an abundance of evidence, there remains a shortage of multidisciplinary tumour boards in developing nations, including SSA [59]. Targeted receptor therapy, such as Trastuzumab, is inaccessible to women in many countries in SSA due to its high cost. Significant discounts would be needed to make targeted receptor therapy affordable to LMICs [60].

In South Africa, as often found in other SSA countries, HIV is a comorbidity to breast cancer. In Namibia, HIV mainly affects Black women, with a rate of 14.8% compared to 2% in non-Blacks [61]. HIV-positive women who are diagnosed with breast cancer have a lower survival rate than their HIV-negative counterparts [62]. It is postulated that for women in the HIV-positive group, increased drug toxicity and drug-drug interactions while being treated for breast cancer lead to poorer outcomes compared to their HIV-negative counterparts [63, 64].

Generally, South Africa is comparable to other SSA countries, as also shown by similar

racial disparities in breast cancer outcomes, the scarcity of receptor target therapies, the high prevalence of comorbidities (i.e. HIV), limitations in breast cancer screening and late presentations. Although there are country-specific variations, similarities are abundant. Some African countries, such as the Ivory Coast, have set up a multidisciplinary platform (oncologists, surgeons, pathologists, radiologists) to better manage this disease. In terms of screening, early diagnosis by self-examination, screening in women aged > 40 years, mammography, ultrasound-guided biopsy puncture and the assignment of a Gleason score are the standard screening methods used for breast cancer in most countries. In most African countries, education and information on breast cancer screening, symptoms and treatment are also distributed via mass media, such as television. Despite these strategies and tools, many SSA countries have many patients with progressive breast cancer, as is the case with South Africa. This article provides an overall view of the common problems related to the management of breast cancer in SSA, highlighting a number of aspects specific to the region. It can be concluded from this article that breast cancer should be considered to be a public health problem and that an International Multidisciplinary Platform (IMP) should be set up to enable communication and the sharing of experiences from different countries and lead to collaboration, with much more emphasis on education and screening via digital platforms.

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Declarations

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