

# Differences in Age, Stage and Biology of Breast Cancer Presentations at A Private Breast Unit in Johannesburg Before and During The COVID-19 Pandemic

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## ABSTRACT

**Objective:** Prior to the 2020 Coronavirus disease 2019 (COVID-19) pandemic, breast cancer (BC) was already a major healthcare concern globally, including in South Africa (SA). The pandemic forced adjustments in BC management and may have also impacted BC presentation characteristics due to social behavior changes. The aim of this study was to describe BC presentations before and during the COVID-19 pandemic at a single facility in SA.

**Materials and Methods:** A retrospective record review was conducted to compare BC presentations before and during the COVID-19 pandemic. The "before" period spanned 11 January 2019 to 31 March 2020 and the "during" period spanned 1 April 2020 to 20 December 2021. The variables analysed included patient age, BC stage at presentation, and tumor biology.

**Results:** A total of 731 patients were seen in the "before" period, and 636 in the "during" period. While there was a significant (p<0.0001) decrease in the mean number of patients who presented to the unit per month during the pandemic, no significant differences were observed in age, BC stage at presentation, or tumor biology between the two study periods.

**Conclusion:** Despite a significant reduction in new BC cases during the COVID-19 pandemic in SA, patient age, BC stage, and tumor biology remained unchanged. The rapid implementation of digital tools for healthcare management is likely to have played an important role in maintaining patient access to care.

Keywords: Breast cancer; pandemic; age; stage; biology; presentation

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#### **Key Points**

- A 36.7% decrease was noted in the number of patients presenting with breast symptoms during compared to before the pandemic.
- No significant differences were observed in patient age at presentation, breast cancer (BC) stage, or tumor biology between BC patients presenting before and during the Coronavirus disease 2019 pandemic.
- It was hypothesized that the lack of difference in presenting characteristics may be attributed to inadequate BC screening in South Africa, even before pandemic restrictions, whereas in the West, severe restrictions on access to BC screening resulted in later stages at presentation.
- The absence of this pattern in this study may also be due to Milpark Breast Cancer Centre of Excellence adaptations for managing care during pandemic restrictions.
- These adaptations included online communication between members of the multidisciplinary team, allowing for quick diagnosis of breast cancer stage and biology.

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# Introduction

Breast cancer (BC) was already a significant healthcare concern in South Africa, as well as globally, prior to the 2020 Coronavirus disease 2019 (COVID-19) pandemic (1). However, little research exists on how the pandemic may have affected BC presentation in low- and middle-income countries (LMICs).

The existing literature highlights the ongoing prevalence of BC globally, with South Africa facing additional diagnostic and management challenges due to widespread poverty and limited resources. Despite efforts to address BC, projections show the burden of BC in sub-Saharan Africa will double by 2030 (2).

Research suggests that the pandemic led to disruptions in healthcare access and delays in cancer diagnosis and treatment (3), attributed to resource diversion and fears of COVID-19 infection (4). While some studies suggest no significant changes in BC stage at diagnosis during the pandemic (5), there is a lack of data on how the COVID-19 pandemic has affected BC diagnosis and management in LMICs.

Given the evident disruptions caused by the COVID-19 pandemic and the lack of specific data on its effects on BC presentation and management in LMICs, investigating changes in BC presentation trends during the pandemic is warranted. Understanding these trends may be helpful when adapting BC management strategies and delivering quality care in South Africa and similar settings. The aim of this study was to fill existing gaps in the literature regarding BC diagnostic trends during the pandemic. Specifically, changes in patient age, BC stage, and tumor biology at presentation were investigated in a South African population before and during the COVID-19 pandemic.

## Materials and Methods

#### **Study Design**

This study was a retrospective cohort review. It was conducted at the Netcare Milpark Breast Cancer Centre of Excellence (BCCE), which is a private breast unit in Johannesburg, South Africa. A secondary electronic database, the Medical Information Technology Database Accreditation System was used to collect data from the Milpark BCCE. Data from all patients who were exclusively diagnosed and treated for the first time at the BCCE during our study period were collected. Patients included in this study were above the age of 18 years and provided informed consent for their data to be used for research purposes.

#### **Study Period**

The study was divided into two time periods: patients presenting between 1<sup>st</sup> January 2019 and 31<sup>st</sup> March 2020 (a total of 15 months prior to the South African national COVID-19 lockdown) and those presenting during the national lockdown from 1<sup>st</sup> April 2020 to 20 December 2021 (a total of 20 months).

## Variables

Variables included patient age at first presentation with BC, the stage of disease at which they presented, and the biological characteristics of their BC. Patients ages were divided into three categories: those who presented at less than 36 years of age, those aged between 36 and 54 years, and those who were older than 54 years of age.

The stage of BC at first presentation was divided into eight groups according to the American Joint Committee on Cancer  $7^{th}$  edition classification system. Patients diagnosed with more than one tumour

were classified according to the tumour of higher stage. The patients who were classified under "unknown stage" consisted of those for whom a stage was not determined at the time of data collection. This group consisted of patients whose data were not available, or not correctly recorded into the database.

Biological type of BC at first presentation was stratified according to the four primary BC molecular subtypes: luminal A, luminal B, human epidermal growth factor receptor 2 (HER2), and triplenegative BCs. Patients who presented with more than one tumor of different molecular subtypes were categorised according to the more aggressive subtype with regard to treatability and clinical behaviour.

## **Statistical Analysis**

Data analysis was performed using Stata 17.0 BE - Basic Edition (Manufacturer: StataCorp LLC; phone: +19796964600; email: support@stata.com). Deidentified data containing age, stage, and molecular subtype were obtained from the BCCE database curator and then further stratified by the two study sub-periods.

The continuous variable of age was grouped into three ordinal categories. A t-test was performed to determine if there was a statistically significant difference in the mean age. To determine if there were statistically significant changes in the ratios of age, clinical stage and molecular subtype, a chi-square test was performed. Lastly, an Exact Poisson test was performed to compare the number of patients seen before and during the COVID-19 Pandemic. Confidence intervals (CIs) of 95% were used. A *p*-value of <0.05 was considered significant.

## **Study Ethics**

Ethical approval was obtained from the Wits Human Research Ethics Committee (approval number M220952, date: 12.10.2022). Study site permission was obtained from the hospital CEO and database curator (approval number UNIV-2023-0009, date: 31.03.2022). All enrolled patients provided consent prior to the inclusion of their data in the database for anonymized research.

## Results

## **Study Cohort**

A total of 1,364 patients were included in the study. Patients were known with primary BC and were diagnosed and treated at the BCCE between 1 January 2019 and 20 December 2021. A total of 731 patients were included in the pre-COVID study period, and 636 patients presented during the COVID period.

#### **Patient Presentation Rate**

During the COVID-19 pandemic, there was a significant decrease in the number of patients presenting with BC per month compared to the pre-pandemic period (p<0.0001) (Figure 1). In the first period the mean number of patients per month was 48.7 versus 31.8 patients per month during the pandemic.

## Age

The mean age of patients was 32.26 years (95% CI: 31.37–33.15) before the COVID-19 pandemic and 32.20 years (95% CI: 31.06–33.15) during the pandemic (p = 0.83). A chi-square test was also performed to compare the differences in each age group before and during the pandemic. Across all three age groupings, there was no significant difference in age at presentation (p = 0.19). Table 1 below shows patient age at BC presentation in both study sub-periods.



# Stage

**Figure 1.** Number of patients seen per month before and during the COVID-19 pandemic. Figure 1 shows an initial decline in patient numbers at the onset of the COVID-19 pandemic, followed by fluctuating trends during the COVID-19 pandemic period

COVID-19: Coronavirus disease 2019

Most patients during the study period presented to the BCCE with a single tumour and, therefore, a single stage of BC. BC stages are shown in Table 2. A chi-square test was performed, and the differences in BC stage at presentation between the two study periods were not significant (p = 0.12).

## Breast Cancer Molecular Subtype

Molecular subtypes were classified as luminal A, luminal B, HER2+, triple-negative, or unknown based on their initial biopsy for all patients in the study. Comparison of the proportions of each of these subtypes in the two study periods is shown in Table 3. Overall, there was no significant difference in the distribution of patient tumour biology before and during the COVID-19 pandemic (p = 0.24).

#### Table 1. Age of patients at diagnosis before and during the COVID-19 pandemic

Age at diagnosis	Frequency before COVID-19	Percentage before COVID-19	Frequency during COVID-19	Percentage during COVID-19	<i>p</i> -value
<36 years old	26	3.56	37	5.82	
36-54 years old	301	41.17	251	39.46	0.19
>54 years old	404	55.27	348	54.72	
Total	731	100.00	636	100.00	
COVID-19: Coronavirus disease 2019					

## Table 2. Clinical stage of patients seen before and during the COVID-19 pandemic

Clinical staging	Frequency before COVID-19	Percentage before COVID-19	Frequency during COVID-19	Percentage during COVID-19	<i>p</i> -value	
Stage 0	65	8.89	51	8.02		
Stage IA	203	27.77	168	26.42		
Stage IB	0	0.00	1	0.16		
Stage IIA	273	37.35	272	42.77		
Stage IIB	91	12.45	82	12.89	0.12	
Stage IIIA	47	6.43	32	5.03		
Stage IIIB	28	3.83	15	2.36		
Stage IIIC	0	0.00	2	0.31		
Unknown	24	3.28	13	2.04		
Total	731	100.00	636	100.00		
COVID-19: Coronavirus disease 2019						

## Table 3. Breast cancer type seen before and during the COVID-19 pandemic

Breast cancer type	Frequency before COVID-19	Percentage before COVID-19	Frequency during COVID-19	Percentage during COVID-19	<i>p</i> -value	
Luminal A	235	32.15	182	28.62	0.24	
Luminal B	219	29.96	219	34.43		
HER2	102	13.95	91	14.31		
Triple negative	86	11.76	63	9.90		
Unknown	89	12.18	81	12.74		
Total	731	100.00	636	100.00		
COVID 10: Concerning disease 2010; UED2; Upper pridemal equity factor excepter 2						

COVID-19: Coronavirus disease 2019; HER2: Human epidermal growth factor receptor 2

# **Discussion and Conclusion**

The COVID-19 pandemic resulted in significant adjustments to BC management both globally (3) and in South Africa. Changes included reductions in non-essential hospital visits, outpatient clinic consultations, and BC screening (6). Many elective surgeries were cancelled, and medical management strategies were altered (6).

A 2020 retrospective study conducted at Groote Schuur Hospital in South Africa found that 18% fewer BC surgeries were performed in 2020 compared to 2019 (7). Notably, a 21-day "Level 5" nation-wide lockdown was established in South Africa between 26th March and 16th April 2020 during the COVID-19 pandemic. During this period, all citizens and residents were confined to their homes except to obtain essential goods, seek emergency medical care, or if they were essential workers. Non-essential businesses were forced to close (8). Following the cessation of the Level 5 lockdown, strict regulations remained in place until the National State of Disaster was lifted two years later, on 5 April 2022. Throughout this period, various levels of restrictions applied, and citizens and residents were encouraged to stay at home and minimize non-essential contact with others. Many people also chose to avoid healthcare and social settings as far as possible due to fear of exposure to the severe acute respiratory syndrome coronavirus (4).

At the BCCE, new patients were still provided with in-person appointments for initial assessments. Patients and healthcare workers wore personal protective equipment, including face masks. Follow-up consultations were conducted virtually, and multidisciplinary team meetings were held online.

The results of the present study demonstrated a significant decrease in the number of patients who presented to BCCE each month during the pandemic compared to the number of patients seen per month prior to it. This finding aligns with a study conducted by Van Wyngaard et al. (7) which reported a 35.9% decrease in patients presenting with new breast symptoms per month between 2019 and 2020. However, a noticeable discrepancy exists between our study and that of Van Wyngaard et al. (7). Groote Schuur Hospital experienced a greater decline in patients presenting with BC compared to the private BCCE unit (9). Considering that Groote Schuur Hospital is a public institution, its patient cohort is likely to experience greater economic and social disadvantage (10). The population may have been more affected by access to transport due to the pandemic lockdown restrictions at the time (8).

There were no significant differences in patient age at presentation, BC stage, or tumor biology between BC patients presenting before and during the pandemic. This aligns with findings of multiple similar international studies, including one in Rochester, New York, by Tonneson et al. (5), which found that tumor biology did not change during the pandemic. A similar finding was reported at a university referral centre hospital in northern Italy (11). The lack of significant changes in age or tumour biology, both in the present study and other international studies, is likely attributable to the fact that these variables are not directly affected by the pandemic itself nor any of its associated restrictions. This is because such restrictions do not impact major non-modifiable risk factors for BC, including age, sex, and genetic predisposition (12).

In addition, there were no significant changes in BC stage at presentation. In contrast, a 2021 European case-control study found

that delayed management of BC patients resulted in more advanced disease at presentation (13). Similarly, when comparing "pre-COVID" to "COVID-era" data, The American Society of Breast Surgeons reported that BC patients presented with more advanced-stage disease, particularly stage III BC, in the latter period (14). Cairns et al. (14) attributed this shift to severe restrictions in BC screening in the USA during the pandemic.

A 2022 systematic review by Li et al. (15) analysed 74 studies assessing the impact of the COVID-19 pandemic on BC screening and diagnosis. The review found a reduction in BC screening volume and a higher proportion of advanced-stage BC during the pandemic. However, of the 74 studies included, 41% were from North America, 35% from Europe and only one study was from Africa. This highlights either a lack of cancer screening programs in Africa or insufficient reporting of the data from existing programs, both of which warrant further attention. The lack of African data also limits direct comparisons between the findings of the present study and those of international studies, as differences in healthcare infrastructure, population demographics, and screening practices may play a significant role (15). In the South African public healthcare sector, there is no existing national BC screening program (16). The use of BC screening among private medical aid users is also suspected to be minimal in South Africa and across Africa as a whole. Given that BC screening in South Africa was already inadequate before the COVID-19 pandemic, it is logical that a further decrease in screening may not have significantly impacted BC stage at diagnosis. The lack of changes in BC stage and biology in the two periods of this study may also be attributed to the BCCE's coordination of care, particularly its emphasis on online communication between members of the multidisciplinary team, which enabled the timely diagnosis of BC stage and biology. These adaptations likely contributed to maintaining quality of care throughout the COVID-19 pandemic.

#### **Study Limitations**

Two major limitations of this study are the omission of race categories and the study's location at a single private institution. It is well recognized that racial composition in South African patient populations often mirrors socioeconomic disparities (17). Consequently, as a private healthcare unit, the BCCE is likely to predominantly serve a wealthier socioeconomic minority (18). It is essential to consider this disparity to ensure that BC research and treatment accurately reflect the diversity of South Africa's population. Future studies should aim to include data from both public and private breast units to provide a more representative analysis. Moreover, further research from South Africa and other LMICs is needed to assess the long-term impact of the COVID-19 pandemic on BC presentation, diagnosis, and care in public healthcare settings.

During the COVID-19 pandemic, the BCCE's use of digital solutions facilitated clear communication, ensuring swift BC diagnosis and management despite national restrictions. We recommend the continued use of digital tools, such as online communication platforms implemented in the peak of the COVID-19 pandemic, to facilitate multidisciplinary meetings at BCCE. These platforms improved meeting attendance and reduced the time to diagnosis at the BCCE (19). The integration of digital technologies not only enhances patient care through communication but also improves patient access to healthcare.

BC remains a significant burden on both South African and global healthcare systems. This study highlights the importance of adapting

BC management strategies to local contexts. The findings of this study can serve as a framework for further BC research in the context of global healthcare emergencies, particularly within the South African public health sector.

#### Ethics

**Ethics Committee Approval:** Ethical approval was obtained from the Wits Human Research Ethics Committee (approval number M220952, date: 12.10.2022). Study site permission was obtained from the hospital CEO and database curator (approval number UNIV-2023-0009, date: 31.03.2022).

**Informed Consent:** All enrolled patients provided consent prior to the inclusion of their data in the database for anonymized research.

#### Footnotes

## Authorship Contributions

Surgical and Medical Practices: C-A.B.; Concept: C.M., C-A.B.; Design: C.M., C-A.B.; Data Collection or Processing: N.K., D.d.C., D.v.L.; Analysis or Interpretation: N.K., D.d.C., D.v.L.; Literature Search: N.K., E.D.; Writing: N.K., D.d.C., E.D., A.M., C.M., C-A.B.

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