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RESEARCH

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Impact of the COVID-19 pandemic on the pathologic diagnosis and treatment of breast cancer in a university hospital in Brazil

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Abstract

Purpose The COVID-19 pandemic has led to the need for extraordinary restrictions and adjustments in health services, which may have compromised cancer screening and oncological treatments. The aim of our retrospective study was to evaluate the impact of the COVID-19 pandemic on breast cancer pathologic diagnosis, presentation, and treatment in a university hospital in Brazil.

Materials and methods We extracted data from the medical records of all patients who were diagnosed with breast cancer and underwent treatment in a Southeast University Hospital in Brazil from March to December between 2018 and 2021. The primary objective was to compare breast cancer diagnosis, stage, and oncology treatments during the COVID-19 pandemic (2020–2021) with a prepandemic control cohort (2018–2019).

Results We collected data for 116 patients and 500 breast surgical specimens. There was a -12% decline in the diagnosis of new cases of breast cancer during the pandemic. The decrease was most pronounced when comparing 2019 and 2020 (-50%), and a recovery in the number of diagnoses was noted in 2021 compared to 2019 (+7.1%). In terms of therapeutic surgical approaches, an increase of 29.73% occurred during the pandemic period. The increase was most pronounced when comparing 2018 and 2020 (+41.18%). Overall, stage distribution and other tumor characteristics did not show statistically significant differences between the pandemic and prepandemic cohorts.

Conclusions Our results showed a decrease in the number of new breast cancer diagnoses (-12%) during the pandemic compared to the prepandemic period. However, the number of therapeutic surgical approaches performed increased, and a recovery in the number of breast cancer diagnoses during 2021 has been noticed. Concerted measures are needed to minimize the long-term negative impact of the COVID-19 pandemic on delayed diagnosis.

Keywords COVID-19, Pandemic, Breast cancer, Stage, Diagnosis, Treatment

Background

The novel coronavirus infection has spread worldwide since January 2020 (Wu and McGoogan 2020), and a global pandemic was declared by the World Health Organization (WHO) in March 2020 (Freer 2021). According to official data, as of September 2023, 37,796,956 cases and 705,775 accumulated deaths had been recorded in Brazil (Brasil 2023; Who 2023).

Although breast cancer is the most prevalent cancer in women worldwide, between the 1980s and 2020, there has been a drop in mortality in high-income countries

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due to early diagnosis and treatment (World Health Organization 2023). In Brazil, according to the National Cancer Institute (Instituto Nacional de Cancer José Alencar Gomes da Silva – INCA), in 2023, of the 362,730 new cases of cancer (except nonmelanoma skin cancer) expected in women, breast cancer corresponded to 30.1% (Instituto Nacional do Câncer, INCA (Brasil) 2023). Because of this, the Brazilian public health system provides breast cancer mammography screening exams for women aged 50 to 69 (Migowski et al. 2018). For those with atypical results, a biopsy is performed at a primary or secondary service, and in the case of malignancy, the treatment is provided at a tertiary cancer center. However, during the coronavirus pandemic, extraordinary measures such as quarantine and reorganization of the health system were implemented to limit viral spread and flatten the curve of COVID-19 cases. In Brazil, the INCA recommended the postponement of screening programmes in some places (INCA 2020). Additionally, the Brazilian National Health Service (Agência Nacional de Saúde – ANS) advised the temporary suspension of non-urgent procedures and exams during quarantine (Agência Nacional De Saúde Suplementar (ANS) 2023). These measures, in addition to patients' fear of contracting COVID-19 and their consequent hesitation to maintain their medical evaluations, led to a significant slowdown in breast cancer diagnostic procedures and treatments (Oncoguia 2023; Vanni et al. 2020). This reality raised concerns about the potential negative impact on breast cancer patients since the time to diagnosis and treatment initiation can negatively impact prognosis. In the United States, a conservative analysis has already estimated that almost 10,000 excess deaths from breast and colorectal cancer will occur in the next decade due to the effect of COVID-19 on cancer screening and treatment, i.e., an approximately 1% increase in deaths (Sharpless 2020).

Our study aimed to evaluate the impact of disruptions in oncology patient care, resulting from the COVID-19 pandemic, on breast cancer diagnosis, presentation, and surgical treatments among patients from the region covered by a Brazilian Southeast university hospital.

Methods

Study design and population

This is a local population-based retrospective, observational study. We collected data from electronic files at the Pathology Laboratory of the Clinic Hospital of the Federal University of Triangulo Mineiro (HC-UFTM), Brazil. HC-UFTM consists of a tertiary center that assists 27 small cities and provides exams, diagnostic procedures, and treatments (surgery, radiotherapy, and chemotherapy) related to breast cancer. All patients who had a histopathological diagnosis of breast cancer and/or underwent breast cancer surgical treatment at HC-UFTM from March to December 2020–2021 were evaluated and considered the pandemic cohort. We compared this group with patients who matched the same criteria from March to December in the years 2018–2019, defined as the prepandemic cohort. We defined the periods due to the onset of lockdown measures.

This study aimed to evaluate COVID-19's effects on breast cancer diagnosis, surgical treatment, and presentation in patients receiving care within the public health network (SUS) at HC-UFTM. The primary objective was to compare the number of diagnoses and surgical treatments and the stage distribution during the COVID-19 pandemic with a historical cohort of the prepandemic period. The study utilized the eighth edition of the American Joint Committee on Cancer (AJCC) TNM classification to define the initial staging of breast cancer. Secondary endpoints were categorized based on the type of surgical procedure, tumor maximum diameter, grading, immunohistochemical profile, and administration of neoadjuvant chemotherapy.

A total of 500 breast surgical specimens from 439 patients were evaluated in the study. After aplying inclusion and exclusion criteria the cohort study included a total of 116 patients (Fig. 1). Cases that had been formally sent for consultation or a second opinion but in which the patient did not undergo surgical treatment at HC-UFTM were excluded from the analysis ($n=323$ patients).

The local Ethics Committee approved the study (CAAE number: 54257821.7.0000.8667).

Data collection

We reviewed the electronic files from the Pathology Laboratory at the School of Medicine of the Federal University of Triangulo Mineiro (HC-UFTM), Brazil, for each patient, including biopsy requests, histopathologic reports, and type of specimen, to obtain the following information: date of diagnosis, date of surgical treatment, type of surgical procedure, tumor maximum diameter, histologic tumor type and grading, pathological and prognostic stage, immunohistochemical profile, and administration of neoadjuvant chemotherapy.

The type of surgical procedure was distinguished between breast conservative surgery and mastectomy. Breast conservative surgery encompassed all treatments involving the excision of a portion of the gland, while modified mastectomy entailed the total excision of the breast.

The study's tumor characterization data included the maximum tumor diameter, pathological and prognostic staging based on the 2018 American Joint Committee on Cancer (AJCC) TNM classification 8th edition, and histological grade determined using

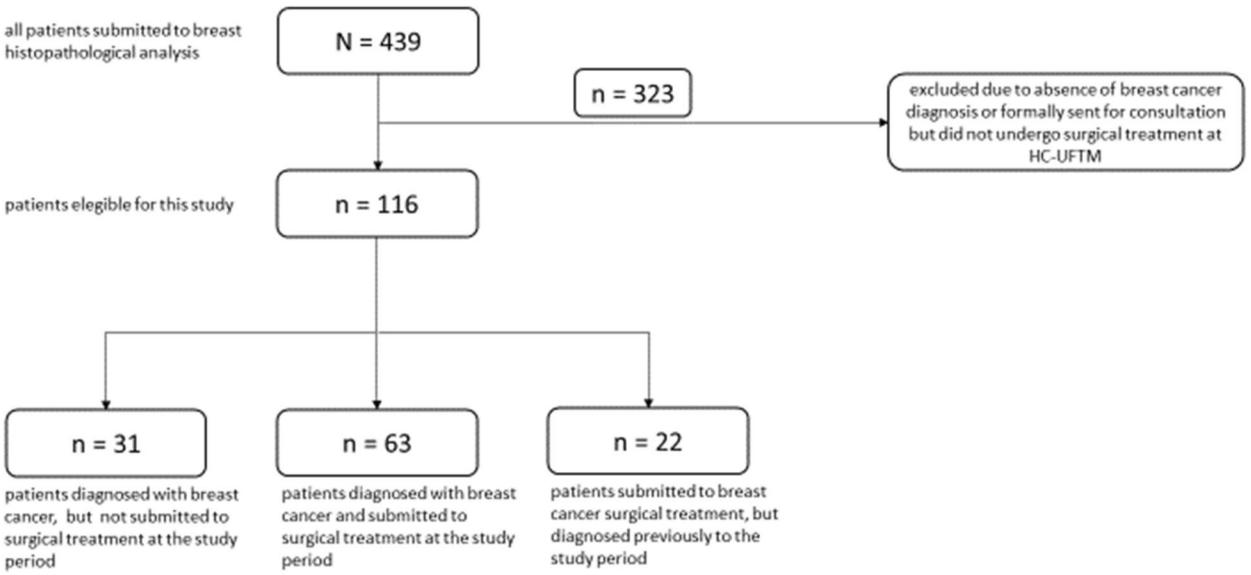

Fig. 1 Flow chart of the cohort study design

the Nottingham combined histological grading system. Moreover, the molecular subtype of each tumor was identified based on the expression of surrogate markers estrogen receptors, progesterone receptors, HER2, and Ki67 through immunohistochemical analysis. Tumors were classified as luminal A, luminal B, triple-negative, or HER2-positive based on the criteria set forth by the World Health Organization's Breast Tumor Classification (2019).

Some information was not present in the medical records or histopathological reports and was therefore not included in the analysis.

Statistical analysis

The collected data were tabulated in Microsoft Office Excel 2010 and analyzed using SPSS statistical software version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables were characterized using absolute and relative frequencies. Tumor stage, surgical procedure, grading, immunohistochemical profile, histological type, and administration of neoadjuvant chemotherapy between the two periods were compared using Fisher's exact test. We analyzed the maximum diameter as a continuous variable using means and standard deviations, and its normality was evaluated using the Kolmogorov–Smirnov test. The Mann–Whitney U test was used for data with skewed distribution. We performed all statistical analyses using SPSS software version 23.0 (IBM Corp., Armonk, NY, USA). A p value < 0.05 was considered statistically significant.

Results

Between March and December in 2018, 2019, 2020, and 2021, a total of 116 patients received a new diagnosis of breast cancer and/or underwent breast cancer treatment at HC-UFTM and were included in our analysis. Most patients were female, white and age older than 50 years (Table 1).

Considering the period analyzed, a total of 94 cases of breast cancer were diagnosed, with 22 cases (23.4%), 28 cases (29.8%), 14 cases (14.9%), and 30 cases (31.9%)

Table 1 Total patients demographic characteristics

Characteristic	N	%
Sex		
Female	114	98.3
Male	2	1.7
Age, years		
≤ 30	1	0.9
31–40	14	12.1
41–50	31	26.7
51–60	31	26.7
61–70	22	19.0
71–80	13	11.2
81–90	3	2.6
≥ 90	1	0.9
Ethnicity		
Missing	9	7.8
White	63	54.3
Multiracial	37	31.9
Black	7	6.0

in 2018, 2019, 2020, and 2021, respectively (Fig. 2). Fifty cases (53.2%) were diagnosed in the PPC and 44 cases (46.8%) in the PC (Fig. 3). There was a decline (-12%) in the diagnosis of breast cancer during the pandemic; this decrease was most pronounced when comparing the period between March and December of 2019 and 2020 (-50%). However, a recovery in the number of diagnoses was noted in 2021, with a 7.1% increase over the 2019 period, as shown in Fig. 2.

Considering cancer treatment procedures in the period analyzed, there was an increase (75%) in patients undergoing neoadjuvant therapy in the PC, although the difference was not statistically significant ($p=0.370$). In the PPC, neoadjuvant chemotherapy was carried out in 12 patients (32.4%), while 21 patients (43.8%) were submitted to neoadjuvant chemotherapy in the PC. In terms of therapeutic surgical approaches, a total of 85 patients underwent breast surgery between March and December in 2018, 2019, 2020, and 2021, with 17 (20%), 20 (23.5%), 24 (28.2%), and 24 (28.2%) surgeries conducted in each of those years, respectively (Fig. 4). There was an 11 (29.73%) increase during the pandemic period (Fig. 5). The increase in cancer surgery records was most pronounced when comparing March and December of

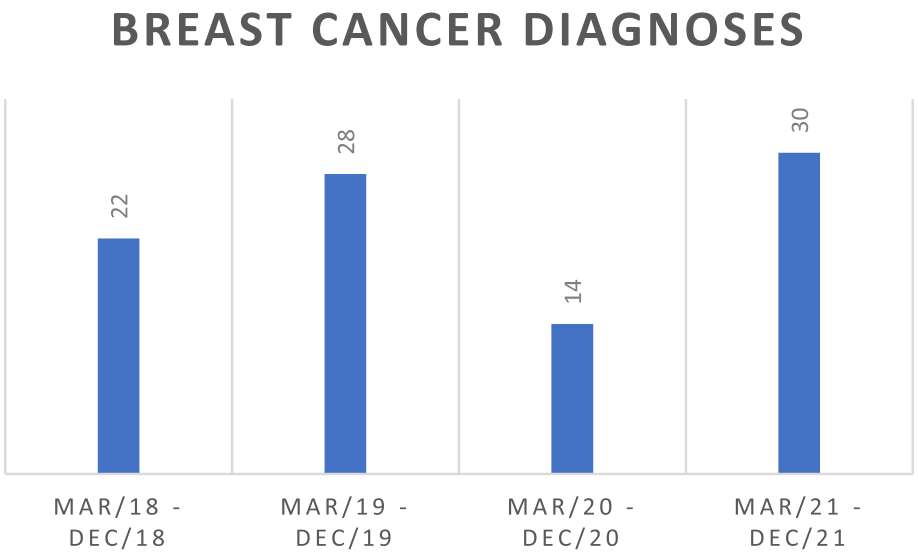

Fig. 2 Breast cancer diagnoses during 2018, 2019, 2020 and 2021

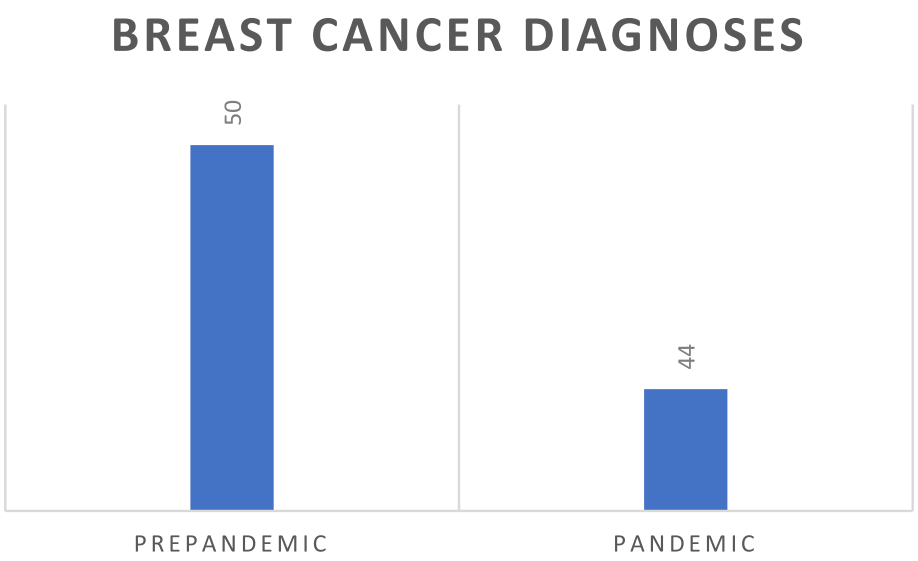

Fig. 3 Breast cancer diagnoses during and prior to the COVID-19 pandemic

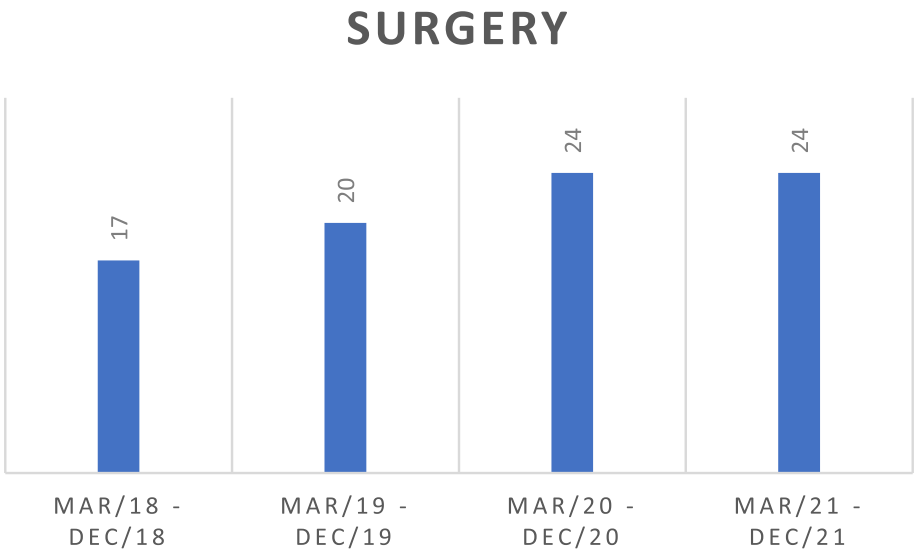

Fig. 4 Breast cancer surgeries during 2018, 2019, 2020 and 2021

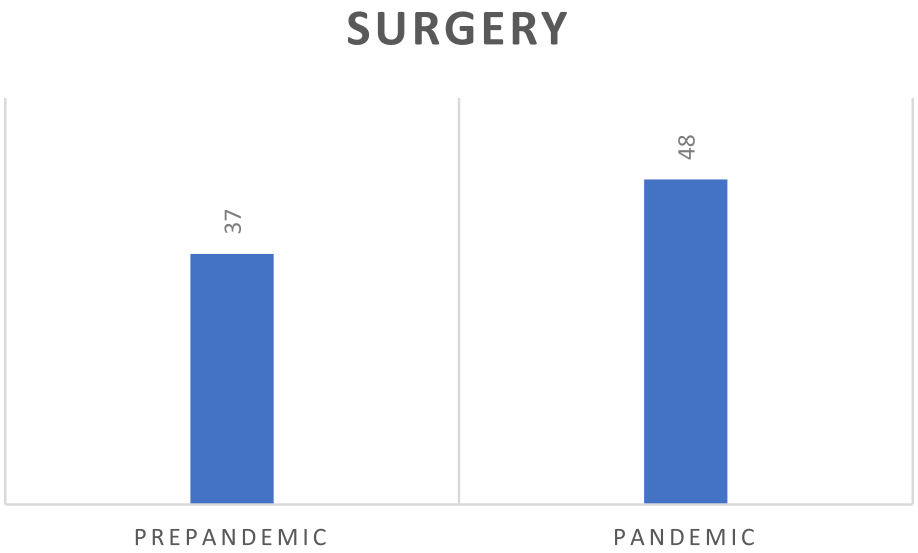

Fig. 5 Breast cancer surgeries during and prior to the COVID-19 pandemic

2018 and 2020 (+41.18%). Regarding types of surgery, breast conservative surgery was performed in 18 (48.6%) patients in the PPC, while the number was 19 (51.4%) for mastectomy. In the PC group, 22 patients (45.8%) underwent conservative surgery, and mastectomy was performed in 26 patients (54.2%). These parameters did not show any statistically significant difference ($p=0.829$). Types of surgery and their relative p values are shown in Table 2.

The pathological tumor size did not present a statistically significant difference between the groups ($p=0.811$). The mean tumor diameters were 2.2 cm (SD ± 1.49) in the PPC and 2.65 cm (SD ± 2.90) in the PC, while the median was equal (2 cm) in both groups. The distribution between the groups did not show a

Table 2 Breast cancer types of surgeries during and prior to COVID-19 onset

Surgery type	Prepandemic		Pandemic		*p* value
	N	%	N	%	
Mastectomy	19	51.4	26	54.2	0.829
Conservative	18	48.6	22	45.8	

statistically significant difference in the number of more advanced pathological stages ($p=0.750$). Additionally, the incidence of lymph node positivity was similar between the two groups ($p=1.000$). In the prepandemic group, there were 15 cases (45.5%) with lymph node metastasis, and in the pandemic group, 20 cases (44.4%) were positive for metastasis. Moreover, the pathological staging pN did not present a statistically significant difference ($p=0.240$). There was a 200% increase in metastatic breast cancer disease during the pandemic. Six patients (12.5%) presented with distant metastasis in the PC compared to two patients (5.4%) in the PPC, although the difference was not statistically significant ($p=0.457$). Table 3 shows the TNM distribution of the two groups (prepandemic and pandemic).

Based on prognostic and predictive factors, the proportion of poorly differentiated tumors (grade III) was similar between the groups ($p=0.864$), and the percentage of grade III carcinomas did not rise throughout the pandemic. Among the PPC, grade III carcinoma was present in 31.4% of cases, while the number was 27.1% in the PC. There was a higher incidence of HER2 tumors during the pandemic (10.5% in the PC vs. 0% in the PPC), as well as triple-negative breast cancer (21.1% in the PC vs. 13.6% in the PPC), although the molecular classification based on immunohistochemistry did not present a significant difference ($p=0.225$). Thirty-five (94.6%) cases of PPC were invasive carcinoma compared to 42 (82.5%) cases of PC ($p=0.457$). Tables 4 shows the prognostic factors of the two groups.

Table 3 TNM distribution between prepandemic and pandemic groups

TNM	Prepandemic		Pandemic		*p* value
	N	%	N	%	
T					0.750
pTis	1	2.7	3	6.2	
pT1mi	0	0.0	1	2.1	
pT1	17	45.9	18	37.5	
pT2	11	29.7	17	35.4	
pT3	3	8.1	1	2.1	
pT4	4	10.8	5	10.4	
N					0.240
pN0	18	48.6	25	52.1	
pN1	11	29.7	12	25.0	
pN2	1	2.7	7	14.6	
pN3	3	8.1	1	2.1	
pNx	4	10.8	3	6.2	
M					0.457
pM0	35	94.6	42	87.5	
pM1	2	5.4	6	12.5	

Table 4 Prognostic factors: grading, immunohistochemical subtype, and lymph node metastasis

Prognostic factor	Prepandemic		Pandemic		*p* value
	N	%	N	%	
Grading					0.864
Low	8	22.9	13	27.1	
Intermediate	15	42.9	19	39.6	
High	11	31.4	13	27.1	
IHC subtype					0.225
Luminal A	5	22.7	6	31.6	
Luminal B	14	63.6	7	36.8	
HER2+	0	0.0	2	10.5	
Triple negative	3	13.6	4	21.1	
LN metastasis					1.000
Yes	15	45.5	20	44.4	
No	18	54.5	25	55.6	

LN Axillary lymph node, *IHC* Immunohistochemical

Both prognostic and anatomical pathological staging did not show any significant difference, with p values of 0.599 and 0.641, respectively. According to anatomical pathological staging throughout the time under study, the proportions of patients with breast cancer in stages I through IV were 18.2%, 51.6%, 18.2%, and 6.1% in the PPC group and 24.4%, 37.8%, 17.8%, and 13.3% in the PC group. In terms of prognostic staging, the proportion of patients with breast cancer in stages I through IV was 72.7%, 9.1%, 13.6%, and 4.5%, respectively, in the PPC, whereas stage I through IV was distributed as follows: 76.9%, 11.5%, 3.8%, and 0%, respectively, in the PC. Breast cancer anatomic and prognostic stages and relative p values are shown in Tables 5 and 6, respectively.

Table 5 Breast cancer stages according to the AJCC/UIC 8th edition TNM anatomic staging system

Stage	Prepandemic		Pandemic		*p* value
	N	%	N	%	
0	2	6.1	3	6.7	0.641
IA	6	18.2	11	24.4	
IB	0	0.0	0	0.0	
IIA	12	36.4	14	31.1	
IIB	5	15.2	3	6.7	
IIIA	1	3.0	4	8.9	
IIIB	2	6.1	3	6.7	
IIIC	3	9.1	1	2.2	
IV	2	6.1	6	13.3	

Table 6 Breast cancer stages according to the AJCC/UIC 8th edition TNM prognostic staging system

Stage	Prepandemic		Pandemic		*p* value
	N	%	N	%	
0	0	0.0	2	7.7	0.599
IA	14	63.6	15	57.7	
IB	2	9.1	5	19.2	
IIA	2	9.1	3	11.5	
IIB	0	0.0	0	0.0	
IIIA	1	4.5	0	0.0	
IIIB	2	9.1	1	3.8	
IIIC	0	0.0	0	0.0	
IV	1	4.5	0	0.0	

Discussion

In the present study, we evaluated COVID-19's effects on breast cancer diagnosis, surgical treatment, and presentation in patients receiving care in a university hospital. The results of our retrospective analysis showed a decrease in the number of breast cancer diagnoses (-12%) during the pandemic compared to the prepandemic period. Similar to our results, other studies have shown that the COVID-19 pandemic has adversely affected access to healthcare services worldwide, including those related to oncology (Buonomo et al. 2020). A reduction in the number of breast cancer diagnoses has been reported in Brazil (Negrao et al. 2022; Bonadio et al. 2021) during the pandemic period. The primary factor for the decrease in the number of breast cancer diagnoses could be attributed to the decline in the implementation of screening examinations such as mammography, along with the increased challenge in accessing healthcare facilities due to lockdown measures and patients' fear of contracting COVID-19. In the United States, according to a retrospective analysis that used the American College of Radiology National Mammography Database, the volume of screening mammographic examinations dropped to 36.3% between March and May 2020 compared to the same period in 2019, while in 2021, the screening mammography volume rebounded to 85.3% of the pre-COVID-19 level (Grimm et al. 2022). Rocha et al (Rocha et al. 2023) also noted a significant decrease in the percentage of mammograms performed within the public healthcare system in Brazil by 40% between 2019 and 2020. In 2021, even after the easing of stringent measures, the total number of mammograms was still 18% lower than the count in 2019 (Rocha et al. 2023). These data highlight the need for upcoming actions, as Brazil was already facing challenges in coordinating cancer screening and obtaining access to diagnostic procedures prior to the COVID-19 pandemic (Ribeiro et al. 2022).

In our series, the decrease in the diagnosis of new cases of breast cancer was not accompanied by a decrease in oncology surgeries. Similar to our results, Vanni et al. (Vanni et al. 2020) reported a cohort of patients who underwent breast surgery at four Italian breast units. In their series, among 432 patients, there was an increase in the number of therapeutic surgical approaches from 209 between March 11, 2019, and May 30, 2019, to 223 in the same period of 2020. Another study showed that, regardless of the cancer type, screening and diagnosis have been more significantly impacted than treatment in Brazil (Ribeiro et al. 2022), as shown in our study. We believe that the higher number of oncological surgeries during the lockdown may be related to the suspension of elective procedures, which allowed for an increase in the number of therapeutic surgical procedures for breast cancer at our university hospital. Regarding therapeutic procedures, our study also observed an increase in the absolute and proportional number of patients undergoing neoadjuvant chemotherapy; however, there was no statistically significant difference.

Our analysis has some limitations, which are important to highlight. Since our study is retrospective, observational, and locally population-based, causality could not be determined, and the small sample size may not be representative of the entire population of Brazil. The long-term effects of the pandemic on the detection, treatment and prognosis of breast cancer were not included due to the short timeframe between the onset of COVID-19 and our analysis. We believe that the therapeutic approaches to breast cancer remained consistent in our hospital, although the pandemic may have affected patient behavior and breast cancer screening coverage, which could have influenced the lower number of breast cancer diagnoses during the year 2020. Therefore, we believe a potential negative impact on BC stages at presentation and increased screening demand should be expected in the coming years, in Brazil and other countries. Thus, it is crucial to exert efforts to preserve essential cancer services and diminish the long-term negative impacts of the COVID-19 pandemic.

Conclusions

Our findings show that during the COVID-19 pandemic, there was a reduction in the number of new breast cancer diagnoses at HC-UFTM, mainly during the 2020 period. However, the number of therapeutic surgical approaches performed increased, and a recovery in the number of breast cancer diagnoses during 2021 has been noticed.

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Authors' contributions
RCI: literature review, data collection, analyzed and interpreted data, major contributor to manuscript writing, and proof reading. GAT: literature review, data collection, manuscript writing, and proof reading. SAZ: performed statistical analysis and proof reading. HG: literature review, idea, concept, analyzed and interpreted data, major contributor to manuscript writing, and proof reading.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
This study was approved by the ethics committee of Federal University of Triangulo Mineiro (CAAE number: 54257821.7.0000.8667).

Consent for publication
Not applicable.

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

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