



Cross-sectional Study

Analysing the trends in breast surgery practice during COVID-19 pandemic: A comparative study with the Pre-COVID era

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ABSTRACT

Background: The emergence of coronavirus disease 2019 (COVID-19) pandemic has crippled the healthcare systems all over the world. Cancer treatment is indispensable and disruption in its provision can lead to unanticipated consequences. No local data exists that has quantified the impact of COVID-19 pandemic on breast cancer surgery in a lower middle-income country (LMIC), therefore, the present retrospective comparative cohort study is directed to determine the trends in breast surgery operative volumes and its outcomes at our institution in Pakistan.

Materials and methods: Data was collected retrospectively from Pre-COVID-19 and COVID-19 era to determine impact of the current pandemic on breast cancer management practices and outcomes.

Results: Cohort results showed a decline in the number of surgeries during COVID-19 era. A total 149 cases were operated during study period vs. 231 during same Pre-COVID-19 i.e. a 35.5% drop in cancer surgeries. In early COVID-19 time frame, only 4 patients had breast reconstruction, 12 out of 149 (8.05%) surgical candidates were identified having positive COVID-19 status preoperatively and one ASA class 3 patient caught COVID-19 post-surgery and succumbed to virus.

Conclusion: Pandemic has a negative effect on cancer management in a LMIC with compromised access and care of cancer patients.

1. Introduction

The intractable outbreak of coronavirus disease 2019 (COVID-19) pandemic has made drastic changes in the world of work. Besides a continuous threat to public health, the economic and social derangements threatens the long term subsistence and well-being of millions of people. The beta coronavirus or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the infecting pathogen accountable for this fatal ongoing pandemic, had made its first attack in Wuhan, China on 17th November 2019 [1,2]. Since then, it has spread globally claiming 4,666,334 lives and infecting 226,844,344 individuals from all across the globe by 17 September 2021 [3]. The outbreak of COVID-19 has been running a course of rise and fall with new variants and up till now, the world has faced four spells of this contagion with each spell being more severe in intensity and causing more casualties from the preceding one [4].

Pakistan a lower-middle-income nation has a restricted amount of budget to spend on healthcare and coupled with a finite supply of resources is constantly grappling with the third wave of COVID-19 by taking unprecedented measures to counter the deleterious reverberations of its crisis and to prevent itself from being caught in a dreadful situation faced by its neighboring countries like India and Iran [5,6]. As per the government's official portal, Pakistan has recorded 1,223,841 cases and 27,206 deaths due to COVID-19 by 19 September 2021. Therefore, the government has imported substantial doses of various vaccines effective against COVID-19 in order to curb the perilous spread of this contagion and successfully administered 72,986,511 doses of it in a population of over 212 million people [7].

Since the outset of this disease, the healthcare organizations all over the world have incorporated necessary changes in their system to provide unprejudiced essential health services to every patient and particularly to those battling cancer amidst the current unfurling health crises

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as data has clearly underscored the fact that cancer patients can easily become victims of SARS-CoV-2 virus infection and are more prone to develop serious complications as compared to general population [8,9]. As a result, American Society of Breast Surgeons (ASBrS), the National Accreditation Program for Breast Centers (NAPBC), the National Comprehensive Care Network (NCCN), European Society for Medical Oncology (ESMO) and other oncology institutions devised a structured framework on the management approach of breast cancer cases in parallel to conserving resources for utilizing them in the ensuing public health crises spawned by COVID-19 [10,11]. In our previously published work, we concluded that timely implementation of these health policies and multidisciplinary participation in our institution maintained infectivity and fatality at a lowest possible rate among breast cancer cases despite of high constraints to health resources [12].

However, not enough research has explored the change in the breast surgery operative volume brought on by the rapidly evolving nature of the ongoing pandemic. Hence, we conducted a study to assess the consequences of COVID-19 outbreak on the surgical management of breast cancer patients in our institution by comparing the volume of breast surgeries performed and its outcomes before the global pandemic era versus those operated during the unravelling pandemic. We hope that this study will be a contribution from a developing country to the management policies of breast surgery clinical practice and will add to the body of literature.

2. Materials and Methods

A retrospective comparative cohort study was performed in the Section of Breast Surgery at tertiary care cancer unit. Ethical approval was granted by the Institution's Research Ethics Committee (reference number: 2020-5418-14043) before the initiation of the research project and was carried out according to the principles of the Helsinki Declaration [13]. Informed consent is not required due to the observational nature of the research. The study has been registered with German Clinical Trials Register (DRKS) (Registration ID: DRKS00026114, https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00026114) and fulfilled the reporting guidelines of STROCCS criteria [14].

A total of 800 medical record files were reviewed including all breast cases who registered for the first time in hospital having Breast cancer, survivors, patients receiving systemic treatment for Stage IV disease and visited breast clinic for follow up/response assessment or evaluation for screen detected abnormalities, benign breast conditions or lumps or visited breast clinic for second opinion from March 1, 2019 to 31st March 2021. We found that during the pre-pandemic period i.e. from 1st March 2019 to 14th March 2020, 231 patients had surgeries for breast cancer, 101 had procedures either for benign conditions or had diagnostic image guided surgeries, 25 found to have Stage IV disease, 12 patients who were booked for surgery were lost to follow-up and 144 patients cancer survivors visited clinic. Thus, a total of 513 patient files were assessed. On the other hand, during the pandemic period (15th March 2020-31st March 2021), 149 patients were operated for proven breast cancer, 35 patients were having benign breast disease, 18 were Stage IV patients, 35 patients were booked for surgery but lost to follow-up (Declined surgery as contacted through Hotline service because of COVID Situation) and 50 were breast cancer survivors. Thus, 287 medical records were assessed during the second time-period.

For comparative analysis, Breast cancer patients were stratified into two cohorts (Group A and Group B). Group A comprised of all patients who underwent surgery for proven breast cancer before the onset of COVID-19 pandemic i.e. between 1st March 2019 and 14th March 2020 while Group B included all those patients who were operated between 15th March 2020 and 31st March 2021, this time period coincides with the COVID-19 outbreak era. Those patients were not accrued in the study whose medical records were either incomplete or lost to follow-up or receiving primary systemic treatment for their metastatic disease.

Demographic, clinicopathological and treatment characteristics data of all the study participants was extracted from the institutional medical records using a data collection proforma designed specifically for this research. Following parameters of the study population were included in the analysis: age at diagnosis, comorbidities, tumour pathology, tumour grade, stage and molecular subtype of breast carcinoma, institution of neoadjuvant chemotherapy/hormonal therapy, waiting time for surgery, type of surgical procedure performed, pre-operative COVID-19 RT-PCR test done or not, its result, length of post-operative hospital stay, occurrence of any COVID-19 symptoms post-operatively during hospital stay or within one week after discharge or development of any complication after surgery, waiting time for postoperative oncological consultation and commencement of adjuvant chemotherapy or radiotherapy.

Waiting time for surgery was enumerated as number of days from initial histological diagnosis of cancer to the date of surgery for patients who were advised upfront surgery. For patients who received neoadjuvant chemotherapy it was calculated as the number of days from the last chemotherapy cycle administration to the date of surgery performed. Following the hospital's guidelines, all the elective breast cancer surgeries were performed after having negative SARS-CoV-2 test done within 72 h pre-operatively. Patients who were found positive during this test, their surgery was re-scheduled as soon as the COVID-19 RT-PCR test came out negative after 14 days (Fig. 1).

Data analysis was carried out by making use of SPSS Statistics 26 (IBM Corporation, Armonk, NY, USA). The categorical data were reported as frequencies and percentages while continuous variables were described as mean/median and interquartile range (IQR). To evaluate the differences between the Pre-COVID-19 and COVID-19 cohorts, a Chi-square/Fisher's exact test was employed for categorical variables and an independent-t-test/Mann Whitney test was utilized for continuous variables using a p-value of less than 0.05 as statistically significant.

3. Results

After reviewing 800 electronic medical records of breast cancer patients, a total of 380 subjects who underwent surgery in the above mentioned time period met the inclusion criteria of the present study. Of these 231 (60.79%) were operated in pre-pandemic period and thus were included in Group A while 149 (39.21%) patients had their surgery done in pandemic period and accrued in Group B (overall 35.5% decline in breast cancer surgeries) (Fig. 2). A total of 3252 patients visited the hospital during the pre-pandemic period. This value had been reduced to 2028 patients during the pandemic period. Thus, a decrease of 32.4% has been recorded in patients visiting the hospital.

As evident from Table 1, data analysis revealed statistically significant differences in the baseline characteristics of two study cohorts except for the mean age at diagnosis of ($p = 0.885$). Most of the patients were diagnosed with Invasive Ductal Carcinoma (IDC) upon histological examination representing 80.1% of cases in Group A and 77.9% of cases in Group B ($p < 0.001$). Relatively, Grade 2 disease was noticed in large proportion of study population of Group A than in patients of Group B [124 (53.8%) vs. 76 (51.0%), $p < 0.004$]. In Group A, half of the patients 143 (61.9%) were observed with Luminal Type as compared to Group B where substantial number of study subjects 104 (74.8%) were characterized with this molecular subtype respectively ($p < 0.002$). Approximately a great majority of cases 112 (48.5%) presented with stage II breast cancer in group A whereas in Group B, it contributed to 65 (43.6%) cases ($p = 0.023$). Neoadjuvant chemotherapy was administered to half of the patients 119 (51.5%) in Group A and 69 (46.3%) patients of Group B ($p = 0.032$).

Table 2 outlines the types of surgical intervention performed and management outcomes of the study population which demonstrated no major difference in the waiting time for surgery between Group A and Group B patients ($p = 0.487$) except for those patients who tested positive on pre-operative COVID-19 RT-PCR test 12/149 (8.05%).

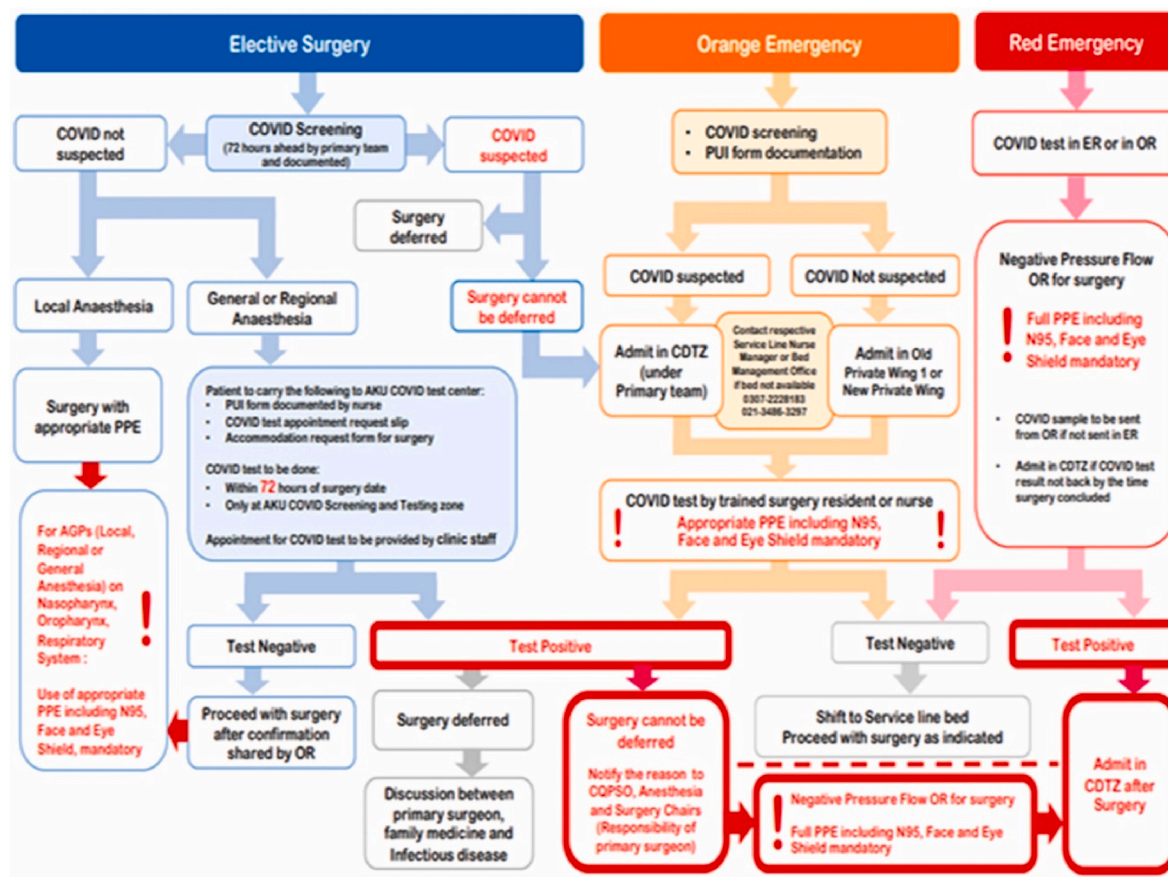


Fig. 1. COVID testing algorithm for surgery patients.

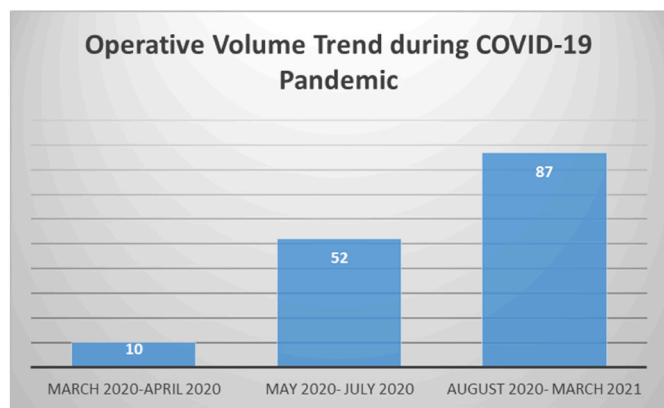


Fig. 2. Operative volume trend during COVID-19 pandemic.

Therefore their surgeries were performed between 14 days and 35 days as per WHO guidelines once they turned negative for COVID-19 virus. Fortunately, all of these infected patients were asymptomatic, isolated at home and were continuously monitored by the telehealth facilities of the hospital which connected them to their primary consultant and infectious disease specialist. In early 6 weeks of pandemic, only 10 cancer surgeries were performed while 04 patients who were hormone receptor positive scheduled for surgeries were cancelled and started on hormonal treatment to delay surgical intervention for at least 8 weeks giving a cancellation rate of 28.6%. Study results also identified that a large number of patients in the study were subjected to breast mastectomy which consisted of 154 (66.7%) cases in Group A and 104 (69.8%) cases in Group B. Likewise, more breast reconstruction surgeries were carried

out in Group A than in Group B (7.8% vs. 2.7%, $p < 0.013$). A decline in sentinel lymph node biopsy was recorded during COVID-19 pandemic [157 (67.9%) vs. 108 (72.5%), $p < 0.013$]. Post-operative hospital stay was minimised in patients of Group B in order to reduce nosocomial spread of COVID-19 virus (1.4 days vs. less than one day, $p < 0.001$). Despite it, one patient contracted the virus during its postoperative stay and expired [1/149 (0.67%)]. She was an ASA class 3 a 69 year old woman with multiple comorbid illnesses including hypertension, diabetes and severe COPD, operated under local anaesthesia for a breast conserving procedure.

The number of postoperative complications were consistent between the two time periods (mean 4.0, $p < 0.001$) which included haematoma, seroma formation, wound infection and flap necrosis. All of these patients were managed as outpatients and none of them required re-admission in hospital. In addition, no major change in the waiting time for postoperative oncological consultation was detected between the two study groups (mean 2.0 days, $p < 0.001$). Waiting time for adjuvant chemotherapy (mean 7.0 days, $p = 0.484$) as well as waiting time for radiotherapy (mean 7.0 days, $p = 0.484$) did not differ between Group A and Group B.

4. Discussion

This is the first study reporting impact of SARS-CoV-2 virus on surgical care of breast cancer patients during this pandemic era overall from a lower middle-income country. This virus has remained inciting panic for Pakistan, being a lower middle-income country (LMIC) with limited health care budget and fragile health care system. Not only were there challenges due to the pandemic but also the health care system had to deal the myths and false beliefs associated with COVID-19 country wide which contribute to a negative impact on the outcome [12]. Our

Table 1
Demographic and clinicopathological data of breast cancer patients.

Variable	Total n = 380	Group A (01/3/2019–14/3/2020) n = 231 (60.79%)	Group B (15/3/2020–31/3/2021) n = 149 (39.21%)	p-value
Age in years	380	51 (IQR, 22–78 years)	51 (IQR, 27–76 years)	0.885
Comorbidities	380			<0.001
Diabetes	39	33 (14.3%)	6 (4.0%)	
Hypertension	110	52 (22.5%)	58 (38.9%)	
Valvular Heart Disease	01	01 (0.4%)	0 (0%)	
None	230	145 (62.8%)	85 (57.1%)	
Tumour Pathology	380			<0.001
Invasive Ductal Carcinoma	301	185 (80.1%)	116 (77.9%)	
Invasive Lobular Carcinoma	24	14 (6.1%)	10 (6.7%)	
Ductal Carcinoma in Situ	22	16 (6.9%)	6 (4.0%)	
Metaplastic Carcinoma	13	8 (3.5%)	5 (3.4%)	
Papillary Carcinoma	12	6 (2.6%)	6 (4.0%)	
Others	8	2 (0.8%)	6 (4.0%)	
Tumour Grade	380			<0.004
Grade 1	26	11 (4.7%)	15 (10.1%)	
Grade 2	200	124 (53.8%)	76 (51.0%)	
Grade 3	154	96 (41.5%)	58 (38.9%)	
Molecular Subtype (missing n = 10)	370			<0.002
Luminal Type	247	143 (61.9%)	104 (74.8%)	
Triple Negative	76	50 (21.64%)	26 (18.7%)	
Her 2 enriched	47	38 (16.45%)	9 (6.5%)	
Tumour Stage (Pathological)	380			0.023
Stage 0	63	36 (15.6%)	27 (18.1%)	
Stage I	77	45 (19.5%)	32 (21.5%)	
Stage II	177	112 (48.5%)	65 (43.6%)	
Stage III	63	38 (16.4%)	25 (16.8%)	
Neoadjuvant Chemotherapy	380			0.032
Yes	188	119 (51.5%)	69 (46.3%)	
No	192	112 (48.5%)	80 (53.7%)	

study showed that the overall number of breast cancer surgeries had declined when comparing to Pre-COVID-19 era with compromised cancer care.

During this exceptional situation to avoid delays in surgical care of breast cancer patients, multi-disciplinary teams including breast surgeons have been working continuously to modify the management of breast cancer patients, guidelines have been formulated and followed to avoid unforeseen complications among breast cancer patients [12].

The first wave of COVID-19 occurred from March to July 2020 hence based on institutional guidelines, cancer surgery was offered to a limited group of breast cancer cases; it was a time when the COVID -19 infectivity rate was high (279,146 reported cases) with an ongoing understanding about transmission, control, treatment, and impact on immunocompromised cancer patients [7]. In first 6 weeks, only 10 cancer surgeries were performed with a reduced level of care for breast cancer patients. 04 patients who were hormone receptor positive scheduled for surgeries in early 6 weeks were cancelled and started on hormonal treatment to delay procedures for at least 8 weeks (cancellation rate of 28.6%), it was a time when COVID Surg Collaborative also anticipated that cancellation rate would be 37.7% for cancer surgeries during peak 12 weeks of outbreak [15].

Subsequently hospital had developed a policy of having mandatory negative COVID-19 RT-PCR test within 72 h of proposed surgical date to

Table 2
Surgical and management outcomes of breast cancer patients.

Variable	Total n = 380	Group A (01/3/2019–14/3/2020) n = 231 (60.79%)	Group B (15/3/2020–31/3/2021) n = 149 (39.21%)	p-value
Waiting time for surgery	380	4.4 (IQR, 4.0–4.5 days)	4.4 (IQR, 4.0–4.5 days)	0.487
Pre-operative COVID-19 test Result (n = 149)	–	–	Positive 12 (8.05%)	–
Surgical Intervention	380			<0.013
BCS	122	77 (33.3%)	45 (30.2%)	
Mastectomy	258	154 (66.7%)	104 (69.8%)	
Reconstruction	22	18 (7.8%)	4 (2.7%)	
SLNB	265	157 (67.9%)	108 (72.5%)	
Post-operative Hospital Stay	380	1.4 (IQR, 1.0–1.5 days)	Less than one day	<0.001
Post-operative complications	380	4.0 (IQR, 4.0–5.0)	4.0 (IQR, 3.0–4.0)	<0.001
Waiting time for postoperative oncological consultation	380	2.0 (IQR, 2.0–3.0 days)	2.0 (IQR, 2.0–3.0 days)	<0.001
Waiting time for chemotherapy	380	7.0 (IQR, 7.0–8.0 days)	7.0 (IQR, 7.0–8.0 days)	0.484
Waiting time for radiotherapy	380	7.0 (IQR, 7.0–8.0 days)	7.0 (IQR, 7.0–8.0 days)	0.484

provide essential care with safety for all. The term elective for cancer cases was revisited understanding the fact that delay could have impact on stage progression and psychological well-being and quality of life of patients hence cancer lists were prioritized. A total 52 cases were operated in May–July 2020 period which was nearly equivalent to pre-COVID-19 era. During this period Breast conservation vs mastectomy remained the same as compared to pre-COVID-19 period. Subsequently from August 2020 till May 2021, infectivity rate had passed through second and third waves with sharp rise to a steep decline but fortunately each wave had less powerful impact as compared to other LMICs like India, despite it we found that number of cancer surgeries had dropped to 106 as compared to 131 in pre-COVID-19 era at our institution. Worldwide data from different cancer centers had reported several reasons for decline in cancer surgeries and less efficient cancer care during first peak i.e., March to May 2020 [16,17]. A multicenter study from Netherland associated this decline to reduce referrals from National screening programs and General practitioner practices with drop in T1-T2No cases [17].

During first wave none of the patients were offered reconstructions as per guidelines to reduce operating room time, post-operative hospital stay and to avoid reconstruction associated issues with anticipated several clinic visits if they developed any post-reconstruction complication which could be associated with increased risk of hospital acquired COVID-19 infection. A study from Italy showed reduced surgical procedures during pandemic with marked decrease in reconstructive procedures similar to our study results ($p < 0.001$) [16]. This is in line with recommendations from ESMO to keep breast reconstructions as low priority [11]. Contrary to that from August 2019 to May 2020 the rate of reconstructions had increased at our institution, all these patients had relatively smooth post-operative course with no major reconstruction related complications like infection, wound dehiscence or reconstruction failure and numbers were comparable to figures performed in same period in 2019.

As far as waiting time for surgery is concerned there was no difference between pre-COVID-19 and COVID-19 eras. Sentinel node biopsy was offered as per routine as institution was having an enough supply of Nano colloid available. Likewise, previously cited study conducted in Italian Breast Unit also reported no change in use of sentinel lymph node biopsy before and during COVID-19 pandemic ($p = 0.84$) however they reported that patients who were on the operating lists during the COVID-

19 pandemic had to wait slightly longer for their surgical intervention than the patients scheduled for their surgery before the COVID-19 pandemic (49.11 vs. 46.39 days) [16]. On the contrary, study from Canadian cancer center showed no major difference in surgical care as compared to Pre-COVID-19 era with improved waiting time which they associated with low impact of COVID-19 in their center and to better team based care [18].

During the pandemic time hospital had made policy to discharge stable patients as early as possible hence post-operative hospital stay was reduced in this era to reduce exposure and simultaneously to reduce workload to health care providers, patients were connected to team members via teleconsultations to monitor their health condition and to address wound related issues. Anecdotal evidence proved that patients were also satisfied as it reduced hospital encounters which is evidently a high transmission pocket [19].

In comparison to developed countries, Pakistan does not have any National Cancer Screening Program nor having a stringent General practitioner practice system, our workload is based on cases who presented with self-discovered lumps or diagnosed with breast cancer at other hospitals, only <2% of cases at our center treated after being picked on Screening. We found that fears associated with COVID-19 was the strongest reason for decline in elective cancer surgeries at our center, there were diagnosed cancer cases who deliberately missed their clinic and surgery appointments for several months and presented afterward with upgrade stage during this era. We also found a fear to get treatment in a hospital such as ours which offers COVID-19 related care in a designated area entirely separated from the main hospital, this was also the strongest reason to delay treatment. Many patients who were contacted through telecommunication sought alternative therapies like spiritual healing, herbal, or homeopathic treatment as they were waiting for pandemic to over before they sought proper cancer treatment. Prospectively collected data showed that rate of stage III disease at presentation has increased up to 38% (25–30% in pre-COVID-19 era) and stage IV by 14% as compared to our institutional figure of 7–10% every year since 2010. Pakistan has been experiencing a 4th wave currently with almost 100% infective cases of the Delta variant in Karachi, hoping to curb disease successfully without conceding further care.

There were certain limitations to our study, the first being a single center experience from a private sector and the other having a small sample size, however to the best of our knowledge this study is one of the few studies showing the impact of COVID-19 on surgical care of cancer patients from lower- and middle-income countries (LMICs). Further research should be conducted in this regard including all the public and private sector institutions to better understand the impact of prevailing pandemic on breast cancer surgery and to enhance understanding for unforeseen other future pandemics.

5. Conclusion

COVID-19 pandemic has had reverberations on the breast surgery oncologic practice at our institution with marked decline in number of surgical interventions despite of timely planning and strategizing breast cancer management. This likely resulted from fear among community and cancer patients to acquire COVID-19 infection from hospital territories leading to lesser cancer diagnosis and treatment. Later on, patients presented with an advanced cancer stage demanding more aggressive treatment. Therefore, the findings of our study warrant strengthening of current breast cancer management policies and stringent infection control measures to provide uninterrupted standardized cancer care in the ensuing and future pandemics.

Ethical approval

Ethical exemption was obtained from Institution's Ethical Review Committee (reference number: 2020-5418-14043) which waived documentation of informed consent due to the observational nature of the

study.

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Author contribution

Conceptualization, Methodology: LMV, DJ. Data curation: LMV, AJ, AN. Software, Formal analysis: NK, LMV, DJ. Investigation: LMV, DJ, TS. Writing - Original Draft: LMV, DJ. Writing - Review & Editing: All authors. Final approval of the Article: All authors. Accountability for all aspects of the work: All authors.

Registration of research studies

Name of the registry: German Clinical Trials Register (DRKS).

Unique Identifying number or registration ID: DRKS00026114.

Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00026114.

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Data statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103342>.

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