ORIGINAL ARTICLE

Clinical Course, Behaviour and Staging of Breast Cancer at the Time of Presentation During the Era of COVID-19 Pandemic

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ABSTRACT

Objective: To explore the repercussions of COVID-19 pandemic on clinical course, behaviour, and staging of breast cancer

Methodology: This observational study, during the span of COVID-19, included all patients reported as breast cancer on histopathology in breast care clinic of MINAR Cancer Hospital, Pakistan. Clinical behaviour, details of histopathology including tumor type, Estrogen Receptors (ER), HER 2 Neu, and stage of disease at the time of presentation were recorded and analyzed for frequency and percentages.

Results: Mean age of diagnosis was 45.6 years with STD of ±10.75 with parity range of 0 to 8. Lesion was most frequent on left side. Only 37% patients were diagnosed at early stage. Total 63% patients presented with advanced disease with 13% patients having distant metastasis with bones being the commonest site. As many as 79% patients reported positive for ER and 74% for HER 2 Neu, while 84% patients breastfed children. Hormone intake history was positive in 32% patients.

Conclusion: COVID 19 pandemic has had a drastic effect on the outcome of breast cancer by hindering early diagnosis in our population. Adding to the preexisting paucity of screening programmes and deficit in infrastructure for early diagnosis, COVID 19 pandemic led to an increase in the preexisting high mortality rate.

Key Words: Breast cancer, COVID-19, delay in diagnosis, early detection, pandemic

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INTRODUCTION

Being the most common type of cancer in women worldwide[1], Breast Cancer is always a topic of discussion for international researchers. It gains importance because the main prognostic factor is the stage of the disease at the time of diagnosis[2]. The earlier the diagnosis, the better is the treatment with 5 years survival rate[3]. Breast Cancer has variable clinical presentations. Although mass screening and awareness programmes have lead to an increasing number of patients being diagnosed pre symptomatically worldwide, but these programmes are still deficient in our region[4]. Low literacy rate, beliefs in myths, poverty, and shortage of resources are aiding factors in late presentation. Lack of awareness for early warning signs and beliefs in myths are the most common recognized factors for delay in diagnosis in Pakistani women. Other factors for delay in early detection are a lack of effective mass screening programmes and scarce availability of diagnostic facilities at public sector institutes[5].

During the COVID-19 pandemic, lock-down was practiced worldwide as an attempt to control dissemination of disease by forcing people to stay confined at homes[6]. Fear of catching disease and strict restrictions on public transportation led to patients facing hindrances in approaching diagnostic medical facilities. Moreover, the convergence of most of the medical force towards control of the pandemic, led to a shortfall in medical services available to non-COVID patients. We initiated this research to analyze the influence of the COVID-19 pandemic on timely detection of breast cancer and to ascertain the number of individuals experiencing diagnostic delays attributable to COVID-19, while also considering existing factors that impede early detection.

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METHODOLOGY

After having approval from ethical committee with Ref No: M-3(13)/2018 of the institution, this observational study was conducted from January 2020 to June 2021 at the breast care clinic of MINAR Cancer Hospital Multan, Pakistan. It might reflect the total population sampling as it is the only institute in public sector of Southern Punjab with fully equipped breast imaging and breast cancer diagnostic facilities. Total population sampling helps to elaborate the complete picture of factors. Information was collected using a pro forma during the history-taking process. This data collection method ensured anonymity, maintained patient confidentiality, and avoided the disclosure of any identifying information.

All new patients presenting to breast care clinic with different breast related symptoms, were evaluated by triple assessment technique, including initial assessment on clinical examination and imaging followed by pathological evaluation.

Patients earning less than 20,000 PKR monthly were considered poor, those earning between 20,000 to 50,000 PKR lower-middle class, and those above 50,000 PKR were categorized as upper-middle class[7].

In this study, individuals with a graduation level were noted as highly educated, while those with undergraduate qualifications were considered to have lower levels of education[8].

All patients diagnosed for breast cancer on histopathology during this period were included in the study and were evaluated for liver, lung, bone, or brain metastasis by Abdominal Ultrasound, Bone Scan, Ct Scan/ X-ray chest, and CT Scan of Brain. All already diagnosed patients on follow up or treatment, non-cancer patients and patients who lost follow up were excluded from study.

Details of demographic features including age, family history, marital status, parity, education level, socioeconomic status and work status were recorded. Answer to questions were recorded in pre-designed pro forma. Time of onset of symptoms, reasons for delay in seeking medical advice, knowledge about breast cancer and significance of early detection, beliefs in myths, and social or cultural values were gathered.

SPSS 26 software was used for data analysis. Frequency was expressed in percentages. Relationships between variables were determined by Chi Square test.

RESULTS

Total 3,864 patients reported to the breast care clinic of MINAR Cancer Hospital, Multan. Out of these, 379 patients were found to have (Breast Imaging-Reporting and Data System) BIRADS 5 lesions on mammography and ultrasound. All patients with BIRADS 5 lesions were subjected to ultrasound guided Trucut biopsies for histopathology correlation. Total 297 biopsies turned out to be carcinoma. Patients diagnosed with carcinoma were of ages from 20 to 70 years with the mean age of 45.6 years with STD of ±10.75. Age-wise distribution is shown in Table 1. Parity ranged from 0 to 8 while mean value for parity was 4 with STD of ± 1.75. Fifty-two per cent (154) patients had lesions in left breast. Only 37% (109/297) patients were diagnosed at an early stage that is defined as stages I and II. Sixty-three per cent (188/297) patients were categorized in late stages i.e. Stage III and IV. Prevalence of group staging is shown in Table 2 and Graph 1. Thirty per cent (89/297) patients had positive nodal disease at the time of presentation. Nodal involvement is shown in Graph 2. Total 13% (39/297) patients were having distant metastasis. Bones were the commonest site for distant metastasis at the time of presentation. Out of these, 18 were positive for bones, 15 for lungs, and 6 for liver metastasis. Summary of clinical course and behaviour are shown in Table 3. Relevance of the stage of disease to literacy, socioeconomic status, and living areas is shown in Table 4. Receptor status of tumor cells revealed positive estrogen receptor (ER) in 79% (235) cases while progesterone receptor (PR) was positive in 74% (220) and HER 2 was positive in 70% (208) cases. Invasive ductal carcinoma remained the most frequent histology type forming 82% of total. Other types in descending frequency were medullary, lobular, mucinous, and papillary carcinomas.

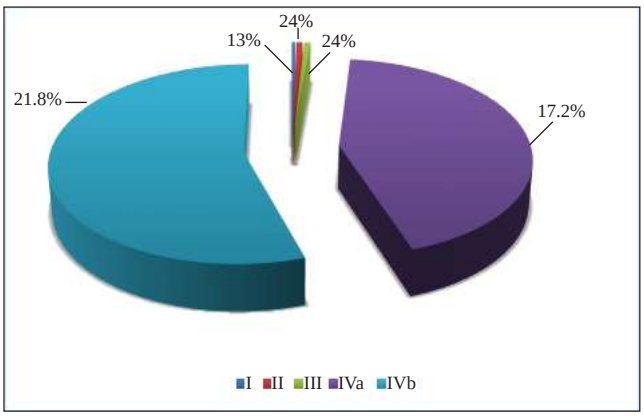
We subdivided delays in two types:

a. Delay on the patients' part
b. Delay on the system's part

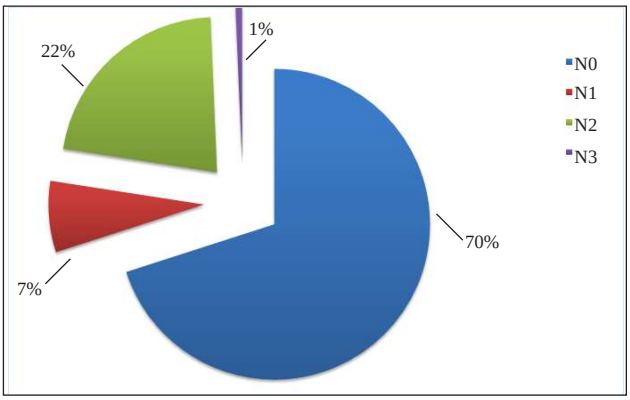
As our system is providing services for diagnosis of breast cancer on one to two days' delay, that was not significant. So, the main part of delay shown in our study was late reporting of patients for diagnostic services. Lack of awareness for relevance of successful treatment on early detection remained the most common factor. Other factors were low literacy rate, beliefs in myths, and belief that breast cancer is untreatable. COVID-19 lockdown further added to this delay. Moreover, patients were not sure whether they would be entertained in hospitals for diagnostic services during the pandemic, so they postponed their medical check ups.

Table 1: Age Distribution

Sr. No.	Age group	Frequency	Percentage
1	<30	24	8%
2	31-40	78	26%
3	41-50	102	35%
4	51-60	78	26%
5	>60	15	5%



Graph 1: Stages of Breast Cancer



Graph 2: Nodal Stage

DISCUSSION

Breast cancer is a health issue of concern worldwide because of its high frequency. It is the third most common cancer after lung and stomach, and remains the most common female malignancy worldwide. Primary breast cancer, being the most common female malignancy, constitutes 30 % of total cancers[1]. It is the all-time feared malignancy among women owing to high mortality rate, being the second most common cause of death. The prime recognized cause of high mortality is late presentation. Outcome of breast cancer treatment highly depends upon the variation in stage at the time of presentation or diagnosis[9]. Probability of five years survival rate is calculated on the presenting stage. Breast cancer is staged by TNM, T1 (tumor size less than 2 cm), T2 (tumor size between 2 to 5 cm), T3 (Tumor size > 5), T4 (locally invaded to chest wall or skin or has distant metastasis[10,11].

Table 2: TNM Staging

T Stage Depends upon size of tumor	T1 <2 cm	39	13%
	T2 bet 2-5 cm	71	24%
	T3 > 5 cm	136	45.8%
	T4 Extend to skin or chest wall	51	17.2%
N Stage Depends upon involvement of lymph nodes	N0 No lymph node	208	70%
	N1 Ipsilateral moveable	22	7.4%
	N2 Ipsilateral fixed matted or IM	65	21.9%
	N3 Infra or supra clavicular or Bi/contralateral	2	0.7%
M Stage	M0 No distant mets	278	93.%
	M1 Distant mets present	39	13%

Combinations of TNM stages define group staging of invasive breast cancer[10].

Over all, 5 years survival rate in USA has been shown in a study to be up to 96.8% for localized lesions or early stage, while it is very poor, up to 10%, in stage IV patients[12]. Stage IV is taken as advanced stage and is considered to be incurable. Over all survival at this stage without treatment is less than 2.7 years. Stages I and II are defined as early stages[13,14]. Developing countries also show marked outcome variation by the differences in stage at diagnosis. Worldwide, efforts are being made to promote early diagnosis of breast cancer. Following the proven fact that breast cancer has high survival rate if diagnosed and treated at early stage, developed countries have reduced mortality rate to a great extent by enhancing early detection through mass screening and awareness programmes but it is still distressing in developing countries like ours[15,16]. Most prevalent reason is late presentation of patients by virtue of poverty, illiteracy, superstitions and lack of resources and infrastructure for early detection of breast cancer.

COVID-19 pandemic was the most urgent challenge worldwide in early 2020. It emerged in China and then spread in the whole world[17]. Millions of COVID-19 related deaths have been recorded[18]. It led to worse

Table 3: Clinical Course

Sr. No.	Features	Frequency of Positive	Percentage	Frequency of Negative	Percentage	Total
1	H/O Breast feeding	249	84%	48	16%	100%
2	H/O hormone therapy	95	32%	202	68%	100%
3	Family History	12	4%	285	96%	100%
4	Lymph nodes	89	30%	208	70%	100%
5	ER Estrogen receptors	50	17%	247	83%	100%
6	Progesterone receptors (PR)	57	19%	240	81%	100%
7	HER 2 Neu	30	10%	267	90%	100%

Table 4: Relevance of Stages

Features			Number of Patients	Percentage
Socioeconomic status	Early stage	Poor	6	5%
		Middle to high	103	95%
		Total	109	100%
	Late stage	Poor	173	92%
		Middle to high	15	8%
		Total	188	100%
Residence	Rural		267	90%
	Urban		30	10%
	Total (N)		297	100%
Education	Early stage	Literate	96	88%
		Illiterate	14	12%
		Total	109	100%
	Late stage	Literate	4	2%
		Illiterate	184	98%
		Total	188	100%

economic, physical, and psychological consequences[6]. It is a communicable viral disease that spreads through direct communication, coughing, and sneezing. In the absence of a definitive treatment or vaccine during the initial phase, the primary approach was to curb its spread by strictly adhering to social distancing and self-quarantine measures, along with employing additional protective measures such as wearing face masks and practicing frequent hand washing[19]. Lock down and priority shifting of health resources towards control of COVID-19 pandemic not only hindered effective screening but also created a gap between presentation and diagnosis of breast cancer, ultimately leading to failure of early detection of breast cancer.

We conducted this study to find the damaging effects of COVID pandemic on clinical course, behaviour and stage of breast cancer at the time of presentation. Stage of disease at the time of presentation is most important predictive factor for 5 years survival[10]. The earlier the diagnosis, the better is the prognosis. Literature narrates different definitions for early stage of breast cancer but most accepted definition is Stage I and II elaborating tumor limited to breast with or without involvement of few (1-3 in numbers) axillary lymph nodes[20,21]. In developed countries, 70 % of breast cancer are diagnosed at early stages, while the figure is low in developing countries. In Pakistan, the figure is 60% for early stage (stage I and II) diagnosis and 40% for advanced stage (III and IV)[22]. Our study shows only 37% patients presented at early stage of I and II. Total 63% presented at advanced stages of III and IV, and 21.8% of our patients presented with distant metastasis. This indicates that the COVID pandemic crisis with lock-down badly affected the already compromised early diagnosis of breast cancer and might have enhanced the preexisting high mortality rate in our population.

Studies correlated variation in early diagnosis with age of the patient. Early diagnosis at younger age is better later[23]. Mean age of presentation in our study is 45.6 years with 59% of total patients presented being below the age of 40 years, while 70% patients diagnosed at early stage fell into age group below 40 years indicating good self-consciousness for health care.

A family history of breast cancer is a significant factor in early detection, as it provides firsthand insight into the challenges and consequences associated with delayed diagnosis. All this compels one to seek medical attention earlier in case of symptoms[24]. As many as 18.4 % patients were shown to have family history of breast cancer in a study conducted by A Tazzite, H Jouhadi in 2013[25]. But our study shows that only 4% had family history of breast cancer that does not correlate with literature.

Illiteracy and low socioeconomic status are recognized delaying factors. Higher education level is correlated with less delay. Less literate people have poor decision making abilities for their health issues. Many studies support this fact. Jasem et al noted the same in his study[26]. A study by Imran Majeed showed that low income status is highly correlated with delay in diagnosis and treatment as people with low income put health at the bottom level of priorities as compared to other basic necessities of life[23]. Our study also shows the same correlation. As many as 88% and 95% patients diagnosed at early stages were literate and belonged to middle to high socioeconomic status respectively. On the other hand, 98% and 92 % patients with late stage diagnosis corresponded to the low literacy and low socioeconomic status group. In our country, the costs of Mammography, Biopsy and Histopathology are high and the infrastructure for screening and diagnosis of breast cancer is deficient. People expect to have all medical services free from the Government and are not able to spend money for their healthcare.

Similarly, patients from rural areas neither have easy approach to health system nor are aware of the magnitude of this disease. Moreover, healthcare system in Pakistan is not built to provide medical cover at elementary level. More than 90% of our patients with advance stage diagnosis fall in this category. All of these factors contributed to a pervasive fear of contracting the deadly communicable disease, leading to widespread confinement at home. This not only impeded hospital visits but also significantly impacted businesses due to lockdown measures, resulting in a financial crisis for many.

This situation is alarming, possibly an aftermath of the COVID-19 pandemic, posing a significant barrier to screening and diagnosis, especially for symptomatic patients. This may contribute to an increase in the already high mortality rate of breast cancer in our population. Urgent efforts should be made to address this pressing concern.

The gist of all predisposing factors for delay in early diagnosis comes out to be a lack of awareness. Awareness campaigns are run in the month of October but are not very effective. Early detection of breast cancer should be encouraged through public awareness. Early diagnosis would ultimately bring about decrease in mortality rate. Moreover, there is an intense need to expand the diagnostic facilities for breast cancer at the level of basic health units.

CONCLUSION

The COVID-19 pandemic has significantly impacted the already high mortality rates from breast cancer by obstructing early diagnosis. This disruption has occurred not only due to hindrances in already insufficient screening programmes but also because of delays in diagnosing symptomatic patients caused by lockdowns and the reallocation of healthcare resources to pandemic control. In our population, which already suffers from a compromised healthcare system, it is crucial to implement effective public awareness and screening programmes to reduce the mortality rate to levels comparable to those in developed countries.

Limitation of Study: It is a single institute based study that does not represent whole population of country but only a part of a province.

Conflict of interest: Authors declare that there is no conflict of interest.

Authors' Contribution: RM led the manuscript writing and provided the primary idea; MAM, AK, NT, and SRH contributed to data recording, analysis, and manuscript writing, and provided critical review.

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