

IMPACT OF COVID-19 PANDEMIC ON MANAGEMENT OF STAGE I, II, AND III BREAST CANCER IN FEMALE EGYPTIAN PATIENTS: A SINGLE INSTITUTIONAL STUDY

Mohamed Ali Abdel Daiem, Hany M. Abdel Aziz, Mohamed Y. Moustafa, Ahmed S. Ibrahim Abdelmotal, Mona Quenawy

ABSTRACT:

Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University Cairo, Egypt.

Corresponding author

Mohamed Ali Abdel Daiem

Mobile: +201004299380

E.mail:

m7amd1993@hotmail.com

Received: 18/3/2022

Accepted: 7/4/2022

Online ISSN: 2735-3540

Background: Corona virus disease 2019 has stressed regular healthcare worldwide. Measures to alleviate the burden on healthcare systems were implemented. This posed a challenge to breast cancer care which is the most prevalent cancer and the leading cause of cancer death in women worldwide. Multiple studies showed the impact of pandemic on management of breast cancer.

Aim of the Work: To evaluate the impact of the COVID-19 pandemic on the management of non-metastatic breast cancer.

Patients and Methods: This is a retrospective study which included total 196 non-metastatic breast cancer female patients attending the breast clinic at the Clinical Oncology Department, Ain Shams University during 2 periods from March 1st, 2020, to end of July 2020 for recruitment of study group (GROUP A) and from March 1st, 2019, to end of July 2019 for the recruitment of comparative group (GROUP B).

Result: There was a statistical difference between the 2 groups regarding number of patients attending (55 in Group A vs 141 in Group B); in referral route (42.9% of patients referred in Group A was due to transforming the treating hospital to become quarantine hospital while none in Group B with majority of patients were referred as there was for radiotherapy); in details of treatment protocols and time delay between decisions taken and start of the treatment including total interrupted time with no treatment with more delay before receiving any treatment (neoadjuvant, adjuvant or surgery) in the study 2020 group

Conclusion: The impact of the COVID-19 pandemic over different health care systems around the globe was remarked, Cancer care was affected due to need of multidisciplinary teams to formulate the best plan of management and breast cancer care were among those affected.

Key Words: Non-metastatic, breast cancer, COVID-19 pandemic, Delay of treatment, cancer management during pandemic.

INTRODUCTION:

Corona virus disease 2019 (COVID-19) is a highly infectious disease caused by acute respiratory syndrome corona virus 2 (SARS-CoV-2) and responsible for the

ongoing pandemic¹. SARS-CoV-2 can mostly be detected with polymerase chain reaction from oropharyngeal swabs². At the beginning of January 2022, there are more than 298,194,606 cases and more than 5,468,069 deaths had been confirmed

worldwide³. Corona virus disease 2019 has had enormous effects on healthcare systems worldwide.

Breast cancer is the most common cancer and the leading cause of cancer death in women worldwide⁴. Early-stage breast cancer is defined as disease confined to the breast with or without regional lymph node involvement, and the absence of distant metastatic disease. This is since early-stage breast cancer is potentially curable. In developed countries more than 80% of patients with early-stage breast cancer have long-term survival after surgery, and in some cases systemic therapy as chemotherapy, hormone therapy, and targeted therapy, and local radiation⁵.

Surgery alone will result in long-term survival for some patients. Systemic therapy and local radiation can significantly improve the chances for long term survival, depending on the stage of disease, and biologic subtype of breast cancer. Therefore, the benefit of systemic therapy should be viewed as incremental benefit above surgery alone^{6&7}. The measures required to alleviate the burden on healthcare systems due to COVID-19 have strongly affected patients with breast cancer, especially the postponed surgeries⁸.

AIM OF THE WORK:

To evaluate the impact of the COVID-19 pandemic on the management of stage I, II, and III breast cancer according to 8th edition AJCC breast cancer staging.

PATIENTS AND METHODS:

For our study, it is a descriptive single institutional study, we used Breast Unit files at the Clinical oncology department, Ain Shams University Hospitals, Cairo, Egypt, to review differences in management of cancer breast between 2 different groups. One

group was managed during COVID-19 pandemic (Group A) from the start of March 1st, 2020, to end of July 2020 while the other group was seen before the pandemic (Group B), from the start of March 1st, 2019, to end of July 2019. The study elaborated the impact of the pandemic on management decisions.

All cases were eligible for the study by the inclusion criteria for the recruitment of both comparative and study groups, so there was no sample method as all cases included. The study included females with Stage I, II, and III breast cancer above 18 years old with P.S. ECOG <3.

The study was approved by Ain Shams University research ethics committee and all our extracted data which included name, age, sex, pathological diagnosis, time of surgery & details of treatment were kept confidential and the patients were kept unidentified.

Statistical analysis: The quantitative data will be presented as mean, standard deviations and ranges when their distribution found parametric and median with inter quartile range when their distribution found nonparametric. Qualitative variables will be presented as number and percentages.

RESULTS:

In this study, data of 196 patients were collected and divided into 2 groups, Group A (study population during 2020 time period) 55 patients and group B (comparative population of during 2019 time period) 141 patients.

Demographic data: In (Table 1) there was a significant difference as regards residence (12.7 % of Group A were outside of Greater Cairo compared to 0.7% of Group B) due to referral from multiple centers converted to quarantine hospitals.

Table (1)

		Group A (N=55)		Group B (N=141)		t*	P Value
		Mean	SD	Mean	SD		
Age		51.84	13.59	53.95	11.31	1.02	0.31 NS
		N	%	N	%	X ^{2**}	P Value
Residence	Greater Cairo	48	87.3%	140	99.3%	13.60 FE	<0.001 HS
	Lower Egypt	4	7.3%	0	0.0%		
	Upper Egypt	2	3.6%	1	0.7%		
	Suez	1	1.8%	0	0.0%		

Route of referral: In (table 2) there was no statistical difference between 2 groups regarding number of patients referred (45.5% in Group A vs 55.3% in Group B) however there was significance in the reason of referral with 42.9% of patients referred to our center in Group A was due to

transforming the treating hospital to become quarantine hospital specialized to treat the increasing COVID cases while in Group B majority of patients were referred as there was no radiotherapy center at their treating hospital constituting 78.2 % of patients referred compared to 35.7% In Group A.

Table (2)

		Group A (N=55)		Group B (N=141)		X ^{2*}	P Value
		N	%	N	%		
Referred From Other Center	No	30	54.5%	63	44.7%	1.54	0.21 NS
	Yes	25	45.5%	78	55.3%		
Cause of Referral	Referring Hospital Became Quarantine	12	42.9%	0	0.0%	35.54 FE	<0.001 HS
	No RTH At Referring Hospital	10	35.7%	61	78.2%		
	Financial Issues	5	17.9%	15	19.2%		
	Other	1	3.6%	2	2.6%		

Details of treatment (A): In (Table 3) there was statistically significant difference between the 2 groups regarding time delay since decision till surgery with mean in Group A 7.8 weeks and in group B 4.6 weeks, same applies to start neoadjuvant or adjuvant treatment (3.14 weeks Group A vs

1.39 weeks Group B) and (3.66 weeks Group A vs 2.5 weeks Group B) respectively, with mean total interruption time delay without any type of treatment was much more evident in Group A 7.25 weeks vs 2.93 in Group B.

Table (3)

	Group A (N=55)		Group B (N=141)		t*	P Value
	Mean	SD	Mean	SD		
Number of weeks passed since decision of surgery and till it's done	7.83	3.64	4.64	1.82	2.87	0.01 HS
Time passed from decision to start neoadjuvant (weeks)	3.14	.36	1.39	.79	9.07	<0.001 HS
Weeks passed since decision till start adjuvant treatment	3.66	1.61	2.57	1.08	3.61	0.001 HS
Interruption time with no treatment weeks	7.25	4.63	2.93	3.39	6.30	<0.001 HS

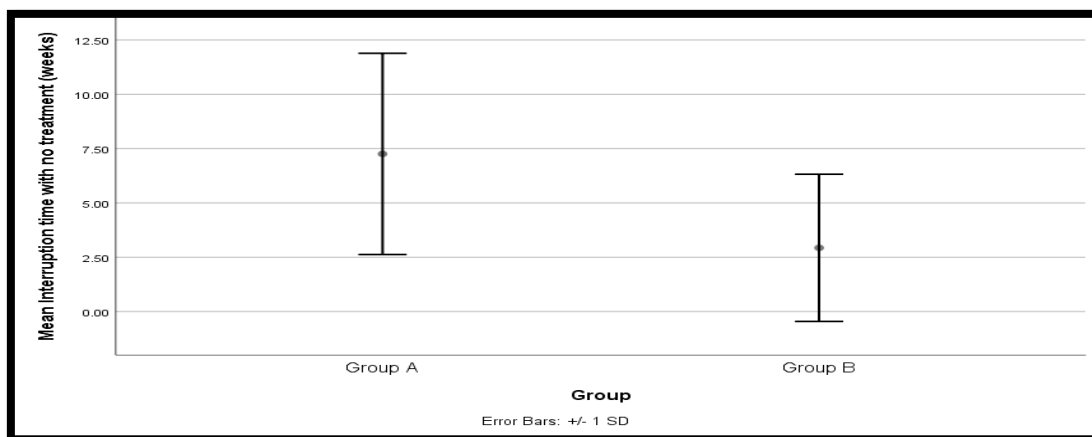


Diagram (1): details of treatment (A)

Details of treatment (B): In (Table 4) There was statistical difference between 2 groups regarding supportive bisphosphonates with adjuvant hormonal with no patients received at Group A, there was no Table (4):

statistical difference between 2 groups regarding fractionation in radiotherapy but there was not a single patient received conventional fractionation in Group A.

		Group A (N=55)		Group B (N=141)		X2*	P Value
		N	%	N	%		
Bisphosphonates / 6 months for osteopenia	No	45	100.0%	74	76.3%	12.73	<0.001 HS
	Yes	0	0.0%	23	23.7%		
Fractionation	conventional	0	0	6	4.6%	2.01 FE	0.34 NS
	hypofractionation	42	100%	124	95.4%		

Details of treatment (C): In (Table 5) In neoadjuvant setting as shows there was statistically difference between 2 groups regarding type of Taxans used, number of cycles used and duration between cycles with most common protocol in Group A was 3 cycles Taxol/21 days with only one patient received the weekly regimen and in Group B were Taxotere/21 days and 12 Taxol weekly were almost equal. Regarding anthracycline based chemotherapy there was no statistical difference between 2 groups however, triplet

regimen was less common than duplet regimens in Group A vs Group B (30% in Group a vs 41% in Group B) in Group A and 4 cycles protocol were more common in Group B than A (38% in Group A vs 59% in group B).

In adjuvant setting there was similar results to neoadjuvant setting regarding Taxans but with statistical difference in anthracycline based regimen were only 10% in Group A received triplet regimen vs 50% in Group B

Table (5):

		Group A		Group B		X2*	P Value
		N	%	N	%		
Protocol of taxans based chemotherapy in neoadjuvant setting	TAXOL	10	83.3%	11	50.0%	3.65	0.06
	TAXOTERE	2	16.7%	11	50.0%		
Duration between taxans based chemotherapy in neoadjuvant settings wks	1.00	1	8.3%	11	50.0%	5.90	0.02
	3.00	11	91.7%	11	50.0%		
Number of taxans based chemotherapy cycle in neoadjuvant setting	3.00	8	66.7%	8	36.4%	6.11 FE	0.05
	4.00	3	25.0%	3	13.6%		
	12.00	1	8.3%	11	50.0%		
Protocol of anthracyclin based chemotherapy in neoadjuvant	FEC	4	30.8%	9	40.9%	1.02 FE	0.66
	AC	7	53.8%	8	36.4%		
	EC	2	15.4%	5	22.7%		
Number of anthracyclin based chemotherapy cycle in neoadjuvant setting	1.00	1	7.7%	0	0.0%	2.55 FE	0.29
	3.00	7	53.8%	9	40.9%		
	4.00	5	38.5%	13	59.1%		
Protocol of taxans based chemotherapy in adjuvant setting	TAXOL	15	68.2%	12	33.3%	6.67	0.01
	TAXOTERE	7	31.8%	24	66.7%		
Duration between taxans based chemotherapy in adjuvant wks	1.00	2	9.1%	12	33.3%	4.38	0.04
	3.00	20	90.9%	24	66.7%		
Number of taxans based chemotherapy cycle in adjuvant	3.00	9	40.9%	19	52.8%	10.18	0.01
	4.00	11	50.0%	5	13.9%		
	12.00	2	9.1%	12	33.3%		
Protocol of anthracyclin based chemotherapy in adjuvant	FEC	2	10.5%	18	50.0%	15.29	<0.001
	AC	6	31.6%	14	38.9%		
	EC	11	57.9%	4	11.1%		
Number of anthracyclin based chemotherapy cycle in adjuvant	3.00	9	47.4%	19	51.4%	0.08	0.78
	4.00	10	52.6%	18	48.6%		
Type Of G-Csf Prophylaxis	primary	20	90.9%	26	72.3%	2.9	0.08
	secondary	2	9.1%	10	27.7%		

DISCUSSION:

The impact of the COVID-19 pandemic over different health care systems around the globe was remarked, and the significance of impact varies from a country to another.

Similarly, A multicenter retrospective cohort study in Netherlands investigated the effects of COVID-19 on patients with breast cancer who had undergone surgery from March 9 to May 17, 2020, the primary endpoints were the number of surgical procedures performed during the study

period, tumor characteristics, surgery type, and route of referral. The results showed a total of 217 consecutive patients with breast cancer requiring surgery were included. An overall decrease in the number of patients with breast cancer who were undergoing surgery. The most significant decline was seen in surgery for T1-T2 and N0 tumors⁹.

Similarly, Veronesi et al stated, The COVID-19 viral pandemic responsible for the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) disease has dramatically impacted our work worldwide in the management of patients in terms of

diagnosis and surgical treatment of cancer - including breast cancer. It has led to a rapid and unprecedented reorganization of surgical units to ensure that those patients with respiratory distress disease received optimal care. From this global situation, we can observe two important consequences that affect clinical practice. In the short term, researchers and related resources have been reassigned to managing the test procedures of COVID-19 patients, and routine research activities have been suspended. Moreover, studies and clinical trials for COVID-19 have become a priority. In addition, travel restrictions have meant that several international conferences, audits, and student training have been cancelled. In the medium to longer term, recruitment delays resulting from the pandemic will negatively affect the early diagnosis of cancer and surgical procedures, with implications that are damaging not only financially, but also in terms of potential diagnosis of more advanced cancers, reducing possibilities of survival and optimal care delivery¹⁰.

Similarly, A retrospective multicentric study by Li J. et al, recently published in *E Clinical Medicine*, clearly demonstrated that the management of breast cancer patients suffered from a lack of care in terms of diagnosis and surgical procedures. They collected data on 8397 breast cancer patients from 97 Chinese cancer centers. In detail, Hubei province recorded the lowest incidence of early breast cancer (5.3%) in comparison to the other provinces (15.3%). Surgical procedures decreased dramatically from 16.4% (December 2019) to 2.6% (February 2020), and there was also a delay in timelines from surgery to adjuvant therapy¹¹.

In our study there were some statistically significant variables between the 2 groups studied regarding the flow and route of referral of the patients, treatment details and decisions. The noticed variation in number between the 2 study populations,

with only 55 patients in group A enrolled with the inclusion criteria compared to the comparative group in 141 patients, this maybe due to the halted screening programs, the occurrence of non-painful breast lump (most common presentation) is not an emergency during the national and international wide restrictions over hospital outpatient care and services with delayed presentation of cases, there was statistically significant results regarding residence with Group A more heterogenous population than group B with the documented reason of referral for those patients; where the treating district hospitals were transformed to quarantine hospitals.

The biggest difference between the 2 groups was in the details of treatment starting with delay to start any type of treatment, neoadjuvant, adjuvant or performing surgery with total interrupted time with no ongoing treatment was much higher in Group A, this is maybe due to the halted governmental services and financial paperwork to non-emergency medical services during the pandemic, regarding the surgical delay maybe also due to reservation of limited operating theaters to emergency surgeries, all the decision were made in an attempt to decrease the flow of the patients unless critically indicated. The vast majority of the patients who received Taxans either neoadjuvant or adjuvant was in form of Taxol/3 weeks regimen to avert weekly visits to the hospital, Taxol was preferred over Taxotere due to less risk of neutropenia, regarding Anthracyclins, the duplet regimens were more commonly used than the triplet ones with comparable side effects over all regimens. Regarding G-CSF prophylaxis, primary prophylaxis was more commonly used to avoid the need of hospital admission neutropenia.

REFERENCES

1. Li H, Liu S-M, Yu X-H, et al.: Corona virus disease 2019 (COVID-19): current

- status and future perspectives. *Int J Antimicrob Agents* 2020; 55:105951.
2. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020; 25:2000045.
 3. Johns Hopkins Center for Systems Science and Engineering. Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available at: <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>.
 4. Bray F, Ferlay J, Soerjomataram I, et al.: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; 68:394-424.
 5. Coleman, M. P.: Cancer survival in five continents: a worldwide population-based study (CONCORD). *The Lancet Oncology*. 9(8):730-756 (2008).
 6. Burstein, H. J.: Adjuvant Endocrine Therapy for Women With Hormone Receptor–Positive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update. *Journal of Clinical Oncology* JCO-2013 (2014).
 7. Peto R, Davies C, Godwin J et al; Early Breast Cancer Trialists' Collaborative Group. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials. *The Lancet*. 379(9814):432-444 (2012).
 8. Dinmohamed AG, Visser O, Verhoeven RHA, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. *Lancet Oncol* 2020; 21:750-1.
 9. Filipe, MD, Désirée van Deukeren, Marijn Kip, et al.: Effect of the COVID-19 Pandemic on Surgical Breast Cancer Care in the Netherlands: A Multicenter Retrospective Cohort Study. 2020
 10. Veronesi P, Corso Ge. Impact of COVID-19 pandemic on clinical and surgical breast cancer management, *Clinical Medicine* (2020) 26.
 11. Li J, Wang H, Jiang Z, E. Suboptimal declines and delays in early breast cancer treatment after COVID-19 quarantine restrictions in China: A national survey of 8397 patients in the first quarter of 2020 *Clinical Medicine*.

تأثير جائحة COVID-19 على علاج المرحلة الأولى والثانية والثالثة من سرطان الثدي لدى
المريضات المصريات: دراسة في مؤسسة واحدة

محمد علي عبد الدايم علي , هاني محمد عبد العزيز, محمد يس مصطفى, احمد سعيد ابراهيم عبد المتعال

و منى قناوي

قسم علاج الأورام و الطب النووي، كلية الطب، جامعة عين شمس

الخلفية: شدد مرض فيروس كورونا ٢٠١٩ على الرعاية الصحية المنتظمة في جميع أنحاء العالم. تم تنفيذ تدابير لتخفيف العبء على أنظمة الرعاية الصحية. وقد شكل ذلك تحدياً لرعاية مرضى سرطان الثدي ، وهو أكثر أنواع السرطانات انتشاراً والسبب الرئيسي للوفاة بالسرطان لدى النساء في جميع أنحاء العالم. أظهرت دراسات متعددة تأثير الجائحة على إدارة سرطان الثدي.

هدف العمل: تقييم تأثير جائحة COVID-19 على إدارة سرطان الثدي غير المنتشر.

المرضى والطرق: هذه دراسة بأثر رجعي شملت ما مجموعه ١٩٦ مريضة بسرطان الثدي غير المنتشر في عيادة الثدي بقسم علاج الأورام بجامعة عين شمس خلال فترتين من ١ مارس ٢٠٢٠ حتى نهاية يوليو ٢٠٢٠ لادخال مجموعة الدراسة (المجموعة أ) ومن ١ مارس ٢٠١٩ إلى نهاية يوليو ٢٠١٩ لادخال المجموعة المقارنة (المجموعة ب).

النتيجة: كان هناك فرق إحصائي بين المجموعتين فيما يتعلق بعدد المرضى الذين حضروا (٥٥ في المجموعة أ مقابل ١٤١ في المجموعة ب) ؛ في مسار الإحالة (٤٢,٩٪ من المرضى المحولين في المجموعة أ كان بسبب تحويل المستشفى المعالج إلى مستشفى للحجر الصحي بينما لم يتم إحالة أي من المجموعة ب مع غالبية المرضى حيث كان هناك للعلاج الإشعاعي) ؛ في تفاصيل بروتوكولات العلاج والتأخير الزمني بين القرارات المتخذة وبدء العلاج بما في ذلك إجمالي وقت التوقف مع عدم وجود علاج مع مزيد من التأخير قبل تلقي أي علاج (مساعد أو مساعد أو جراحة) في مجموعة دراسة ٢٠٢٠

الاستنتاج: لوحظ تأثير جائحة COVID-19 على أنظمة الرعاية الصحية المختلفة في جميع أنحاء العالم وتأثرت رعاية مرضى السرطان بسبب الحاجة إلى فرق متعددة التخصصات لصياغة أفضل خطة للإدارة وكان رعاية سرطان الثدي من بين المتضررين.