

## Changes in Cancer Treatment Practice During the COVID-19 Pandemic: An Egyptian Multi-Institution Study

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### Abstract

**Background:** In many countries, especially the lower-income ones, the COVID-19 pandemic had a significant negative impact on the services provided to cancer patients. This necessitated setting guidelines for the management of cancer during the pandemic and resulted in changes in its practice.

**Aim:** To explore the change in practice of cancer treatment in cancer centers during the COVID-19 pandemic in Egypt, a lower-income country.

**Methods:** Oncologists from six geographically-distributed Egyptian cancer centers were invited to complete a semi-structured questionnaire evaluating their cancer treatment practice changes. This included systemic anti-cancer treatment, radiotherapy, surgery and supportive and palliative care.

**Results:** Regarding systemic chemotherapy, there was a switch from weekly to 3-4 weekly schedules, from longer to shorter courses and from parenteral to oral administration whenever possible in the majority of centers. Single agents were encouraged and regimens more likely to cause neutropenia were avoided. Hormonal and palliative care treatments were prescribed for longer durations. For many indications, especially the palliative, a switch to hypofractionated radiotherapy regimens was adopted. Excluding emergencies, surgeries were postponed in many centers. The number of elective hospital admissions was minimized and the time interval of follow up visits was prolonged. The majority used phone calls to follow up patients.

**Conclusion:** The COVID-19 pandemic has been associated with many changes in cancer treatment practice in Egyptian cancer care facilities. These changes are likely to minimize the risk of exposure of patients and health care professionals and to utilize the limited resources in a better way.

**Keywords:** Cancer treatment, COVID-19, Egypt, Lower-income, Pandemic, Practice change

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### Introduction

The new coronavirus disease (COVID-19) pandemic started in Wuhan City - China in December 2019<sup>1</sup>. Since then and as of the end of July 2020, it has resulted in more than 17 million confirmed cases and more than 660 thousand

confirmed deaths in 216 countries, areas or territories<sup>2</sup>. In Egypt, a lower-income country, the number of cases exceeded 90,000 and the deaths 4,500<sup>2</sup>.

Worldwide, the COVID-19 pandemic has strained health care systems and resulted in a severe negative impact on non-communicable diseases

care including cancer, especially in lower income countries<sup>3</sup>. In the survey conducted by the World Health Organization (WHO) to assess the impact of the COVID-19 pandemic on the care provided to noncommunicable diseases, 56% of surveyed countries in the phase of community transmission of the pandemic reported disruption of services to treat cancer<sup>3</sup>. There are concerns that cancer patients are at higher risk to get infected with COVID-19 and to have worse outcomes<sup>4-6</sup>. One study found that cancer patients infected with COVID-19 are at higher risk to develop severe outcomes<sup>4</sup>. In another cohort study, the 30-day all-cause mortality was high among COVID-19 infected cancer patients<sup>5</sup>. The disruption of cancer care services and the concern that COVID-19 cancer patients are likely to develop severe consequences, in addition to other factors, have resulted in changes in cancer care practice. In response; international organizations, cancer care facilities and researchers suggested guidelines on how to optimize cancer care during the COVID-19 pandemic<sup>7-9</sup>.

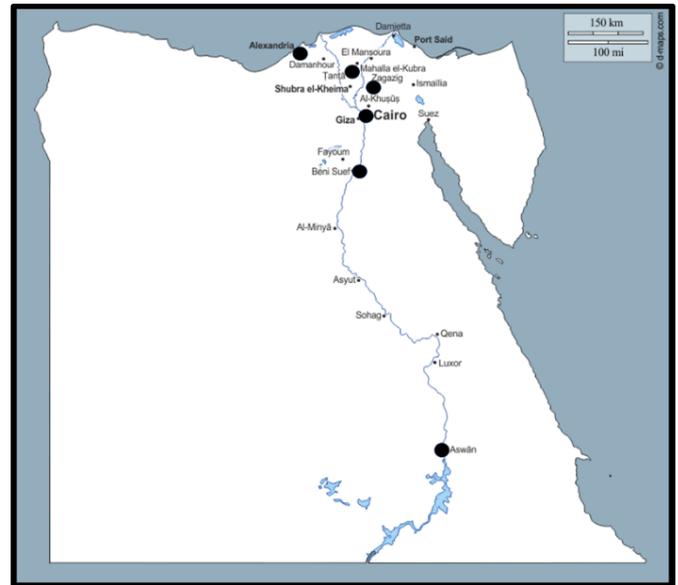
In Egypt with more than 100 million people and limited resources, cancer care is mainly provided by Ministry of Health and University hospitals. The aim of this study was to document the changes in oncology practice in Egyptian cancer centers during the COVID-19 pandemic. It was initiated before declaring it a pandemic by the WHO and the release of international guidelines for cancer care practice changes.

## Methods

This was an observational cross-sectional study to investigate the change in cancer treatment practice in Egyptian cancer centers during the COVID-19 pandemic. Six cancer care facilities representing different geographical areas of Egypt were included (Figure 1). The Clinical Oncology and Nuclear Medicine Department of Alexandria University represented the Northern Coast region, the Clinical Oncology Departments of Tanta and Zagazig Universities represented the Nile Delta, Kasr Al-Ainy Center of Clinical Oncology and Nuclear Medicine represented Greater Cairo and the Department of Clinical Oncology of Beni-Suef University and Aswan Cancer Center represented Upper Egypt.

A semi-structured questionnaire was developed for the purpose of this study and revised by twelve

oncologists. The questionnaire was divided into four sections covering different aspects of cancer treatment. The four section included questions related to systemic anti-cancer treatment (conventional chemotherapy, hormonal therapy and targeted therapy), radiotherapy, surgery and supportive/palliative care and organization of service; respectively.



**Figure 1: Geographical distribution of the six participating cancer care facilities** (Map available from: [https://d-maps.com/carte.php?num\\_car=34800&lang=en](https://d-maps.com/carte.php?num_car=34800&lang=en))

Oncologists from the selected six centers were invited to take part in the study and they consented to participate by completing the questionnaire.

Statistical analysis was performed using Microsoft Excel version 7 and the Statistical Package for the Social Science (SPSS) version 22 software.

The study was approved by the Research Ethics Committee of Kasr Al-Ainy School of Medicine, Cairo University on 4-February-2020.

## Results

The changes in practice related to systemic anti-cancer treatment are illustrated in Table 1. In the six included centers, tamoxifen was prescribed for a longer duration, LHRH analogue was administered every 3 months instead of monthly and weekly schedules of systemic chemotherapy were replaced by 3-4 weekly schedules. The majority switched to oral administration whenever possible and adhered to shorter chemotherapy courses.

Tamoxifen was prescribed for 4 months in 4 (66.6%) centers and for 6 months in 2 (33.3%). While aromatase inhibitors were prescribed for <3 months in 1 (16.6%) center, 3 months in 3 (50%) and 4 months in 2 (33.3%).

Minimizing chemotherapy combination and encouraging single and doublet regimens instead of triplet regimens was encouraged in only one (16.6%) center.

The choices and timing of treatment modalities

involving radiotherapy for selected indications are detailed in Table 2. For palliative radiotherapy indications, shorter courses were chosen in the majority of centers.

Adjuvant radiotherapy for low-risk breast cancer patient was more likely to be delayed when compared to radical radiotherapy for lung and prostate cancers. Hypofractionated schedules were preferred for glioblastoma multiforme and prostate cancer radical irradiation.

**Table 1: Change of practice related to systemic anti-cancer treatment**

Change	No.	%
Prescribed tamoxifen for longer duration ( $\geq 4$ months)	6	100
Switched from 4-weekly to 12-weekly LHRH analogue administration	6	100
Switched from weekly to 3-4 weekly chemotherapy schedules	6	100
Switched from parenteral to oral administration of chemotherapy	5	83.3
Switched from longer to shorter courses of chemotherapy	4	66.6
Avoided chemotherapy protocols that are more likely to cause neutropenia	3	50
Prescribed aromatase inhibitors for longer duration ( $\geq 4$ months)	2	33.3
Switched from 2-3 weekly to 4-6 weekly targeted therapy schedules	2	33.3
Stopped 3 <sup>rd</sup> line and further lines of palliative chemotherapy in advanced cancer patients	2	33.3
Stopped prescribing certain chemotherapeutic agents	1	16.6

LHRH: Luteinizing hormone-releasing hormone

**Table 2: The choice / timing of treatment modality involving radiotherapy in selected indications**

Indication	Modality / Timing	No.	%
Palliative radiotherapy for bone metastases	Single fraction (600-800 cGy)	4	66.6
	Short course (500 cGy x 3 fractions or 400 cGy x 5 fractions)	2	33.3
	Conventional	0	0
Palliative radiotherapy for brain metastases	Short course (400 cGy x 5 fractions)	5	83.3
	Conventional	1	16.6
Palliative radiotherapy for lung cancer	Short course (300 cGy x 10-13 fractions)	6	100
	Conventional	0	0
Adjuvant radiotherapy for low-risk breast cancer	Delay	4	66.6
	No delay	2	33.3
Radical radiotherapy for glioblastoma multiforme	Hypofractionation (300 cGy x 15 fractions + temozolamide)	6	100
	Conventional	0	0
Radical radiotherapy for prostate cancer	Delay (if receiving hormonal treatment)	2	33.3
	Hypofractionation (300 cGy x 20 fractions using IMRT)	3	50
	Conventional	1	16.6
Neoadjuvant chemo-radiotherapy for rectal cancer	Short course (500 cGy x 5 fractions)	1	16.6
	Conventional	5	83.3
Radical radiotherapy for lung cancer	Delay	0	0
	Sequential chemo-radiotherapy (to delay radiotherapy)	3	50
	Concurrent chemo-radiotherapy	3	50

Table 3 shows the changes related to surgery, supportive / palliative care and organization of service. Surgeries for benign tumors and rehabilitation indications were postponed in all centers. The interval between follow up visits for palliative care patients was increased and they were referred to home care services whenever possible in the majority of centers. Granulocyte colony stimulating factors (GCSF) were adopted in one third (33.3%) of the centers. This was applied to all chemotherapy protocol in one center and to lymphoma regimens only in the other center.

All the centers postponed follow up appointments for patients who finished treatment and were disease free. The frequency of follow up visits for these patients was every 2 months in 3 (50%) centers, 3-4 months in 2 (33.3%) and 5-6 months in 1 (16.6%).

The follow up appointment was postponed for patients on hormonal treatment in 4 (66.6%) centers, hepatocellular carcinoma patients in 1 (16.6%) and patients with disease-free survival >2 years in 1 (16.6%). The majority of centers used phone call to follow up patients.

**Table 3: Practice changes related to surgery, supportive/palliative care and organization of service**

Domain	Change	No.	%
<b>Surgery</b>	Postponed surgeries for benign tumors	6	100
	Postponed rehabilitation surgeries	6	100
	Postponed major palliative surgeries	4	66.6
	Limited conservative surgeries	3	50
	Postponed all surgeries	1	16.6
<b>Supportive / palliative care</b>	Increased the interval between follow-up visits for palliative care patients	5	83.3
	Referred palliative care patients to a home care service whenever possible	5	83.3
	Dispensed larger amounts of palliative care drugs	4	66.6
	Postponed zoledronic acid / denosumab administration	4	66.6
<b>Organization of service</b>	Postponed follow up for patients who finished treatment and have no new symptoms	6	100
	Restricted the elective admission to inpatient wards	6	100
	Used phone calls to follow up patients (telemedicine)	5	83.3

## Discussion

During the COVID-19 pandemic, healthcare systems face a challenge to balance between maintaining adequate cancer patient care and minimizing the exposure of patients as well as healthcare staff to infection. Changes in healthcare policy and practice have evolved to achieve this balance. Practice changes included different aspects of cancer care; diagnosis, surgery, chemotherapy, radiotherapy, endocrine treatment and supportive and palliative care.

Egypt is a lower-income country with limited resources and considerable load on cancer care facilities. This study surveyed the common changes in cancer care practice in six Egyptian cancer care facilities representing different regions. In conjunction with the COVID-19 pandemic, all the surveyed centers adopted different practice changes to provide adequate cancer care while maintaining social distancing as much as possible

and minimizing the exposure of patients and healthcare professionals.

The main changes in practice in the surveyed cancer care facilities included the prolongation of the duration between chemotherapy cycles and avoiding regimens that are more likely to cause neutropenia. Although the use of granulocyte colony stimulating factors may have helped to achieve that aim, their use was limited, probably because of the limited resources. Single fraction or short courses of radiotherapy were used in the palliative setting and hypofractionated radiotherapy schedules were usually used for radical treatment. Admission to hospital was restricted and surgery was postponed for benign tumors and rehabilitative purposes. To prolong the outpatient follow up interval, medications (hormonal treatment and palliative care drugs) were dispensed for longer durations and patients were assessed by phone calls.

Kutikov et al suggested a guidance to help in deciding whether to start cancer treatment

immediately or not during the COVID-19 pandemic<sup>9</sup>. Two factors were considered to develop that guidance, the risk of progression with cancer treatment delay and the risk of significant morbidity from COVID-19 infection. Patients were divided into three groups according to the risk of progression when treatment is delayed into low, intermediate and high risk. Then the patients were stratified according to their risk of significant morbidity from COVID-19 into also three groups according to age. Above 70 years was defined as high risk and below 50 as low risk. The decision of either to delay treatment or not was then taken<sup>9</sup>.

The priority to treat patients in a Canadian guideline (Cancer Care Ontario) was divided into three groups, "A", "B" and "C"<sup>10</sup>. Priority "A" was for critically ill individuals needing urgent treatment. Healthy individuals were classified as priority "C" where treatment delay will not affect their outcome. Lastly priority "B" included patients in need for treatment but not critically ill. The service is given according to the available resources. This classification is applied to chemotherapy, radiation therapy, surgery and palliative care. The screening program was priority "C" and was not advised. Those already screened with suspicious lesion were further investigated<sup>10</sup>.

The European Society for Medical Oncology (ESMO) has provided guidelines for cancer patients' management during the pandemic of COVID-19<sup>8</sup>. The guidelines defined three cancer care priority levels (high, medium and low) based on the criteria of Ontario Cancer Care, Huntsman Cancer Institute and ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS). For each of the common cancers, the three priority levels were applied for the different aspects of services provided including outpatient visits, imaging, surgery, systemic treatment and radiotherapy<sup>8</sup>. The American Society of Clinical Oncology (ASCO) also provided coronavirus resources including guide to cancer care delivery during the pandemic<sup>11</sup>.

Surgical delay for more than 6 months was shown to increase the 5-year mortality in all stages of cancer and was estimated to reach >30% in stage 3<sup>12</sup>. In breast cancer patients, and to avoid the negative impact of surgical delay, neoadjuvant chemotherapy is considered<sup>11</sup>.

Hypofractionated radiotherapy should be implemented whenever possible according to the American Society for Radiation Oncology (ASTRO) guidelines and the National Institute for Health and Care Excellence (NICE) rapid guidance<sup>13, 14</sup>. The

practice change in the current study is consistent with these recommendations.

In Italy, young oncologists have created their perspectives before the guidelines in March 2020<sup>15</sup>. They recommended continuing adjuvant treatment as well as chemotherapy for first line metastatic patients. Chemotherapy was advised to be delayed for second line treatment and further disease progression. In the present study, 3<sup>rd</sup> and further lines of palliative chemotherapy were deferred in one third of the centers surveyed.

In France, guidelines in oncology practice were proposed by a group of French experts<sup>16, 17</sup>. The screening program for breast cancer was withheld. Surgery was postponed in COVID-19 patients. Adjuvant radiotherapy was delayed and hypofractionation was favored. Adjuvant and neoadjuvant chemotherapy were given using the shortest protocols possible. Oral chemotherapy was preferred in metastatic cases. For cervical cancer patients, first line chemo-radiotherapy was preferred than surgery and neoadjuvant chemotherapy was given initially for locally advanced ovarian cancer<sup>18</sup>. For genitourinary cancers, it was recommended that curable treatment should be offered while surgery may be delayed<sup>19</sup>.

Many of the changes made to cancer treatment practice found in this study are similar to the above-mentioned international and national recommendations for cancer care during the pandemic.

### **Conclusion**

During the COVID-19 pandemic, the practice of cancer management in Egyptian cancer care facilities have changed in many aspects. This change aimed at continuing treatment of cancer patients using limited resources, while minimizing the risk of exposure whenever possible. In general, these changes were in agreement with the international recommendations for the management of cancer during the pandemic.

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None.

### **Author's Contribution**

Conception or design: MAA. and NYI; Acquisition, analysis or interpretation of data: AAMA, MA, MAE, RE, AH, AM and SMM; Drafting the manuscript: NYI; Revising the manuscript: MAA. AAMA, MA, MAE, RE, AH, AM and SMM; Approval of the manuscript version to be published: All authors; Agreement to be accountable for all aspects of the work: All authors.

**Conflict of Interest**

The authors declare that they have no conflict of interest to disclose.

**Data Availability**

Deidentified individual participant data used to produce the results of this study are available from the corresponding author (NYI) upon request.

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**Study Registration**

None.

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