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EMERGENCY ONCOLOGY ADMISSIONS DURING COVID-19 PANDEMIC: A MAJOR INSTITUTION EXPERIENCE FROM SAUDI ARABIA

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***Background*: The WHO has declared the coronavirus disease 2019 (COVID-19) pandemic in March 2020. Cancer patients are considered a highly susceptible group. The effect of this pandemic on cancer mortality is still unknown. *Aim*: Our aim is to know whether or not we need to postpone cancer treatment during viral pandemics in the future. *Materials and Methods*: A retrospective observational study from March 1, 2020 to June 1, 2020, included cancer patients on active treatment, who have been admitted to our oncology center through the emergency unit, and patients who received oncology treatment in the outpatient treatment unit. COVID-19 positive cases were identified based on polymerase chain reaction testing of nasopharyngeal swab. *Results*: A total of 1300 patients was included in the study, 1096 patients attended the outpatient clinics, 204 patients were admitted to our oncology floor for emergency care. The cancer diagnosis was mainly breast cancer, followed by colon cancer. The main cause of emergency room visit was mainly fever followed by pain. Admission diagnosis was mainly disease progression followed by symptom control, COVID-19 infection, and febrile neutropenia. 1288 cycles of anticancer therapy were provided to 513 patients in the outpatient treatment unit. Three out of the nineteen patients who had a confirmed COVID-19 infection (16%) died not only due to infection, but also disease progression. *Conclusion*: Cancer treatment is not a risk factor for COVID-19 infection or its complications. Cancer treatment should not be interrupted during viral pandemics and every effort should be made to give cancer patients the standard of care.**
***Key Words*: oncology admissions, COVID-19, anticancer treatment.**

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Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a newly discovered coronavirus — severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in Wuhan, China, in December 2019, and then two months later in Europe. The WHO has declared it a pandemic in March of 2020. Initially, all mortality reports were mainly in elderly people and people with co-morbidities. Cancer patients are considered a highly susceptible group in the current COVID-19 pandemic mainly due to cancer treatment that causes neutropenia in most cases. According to an analysis of Italian patients, 20% of those who died from COVID-19 in the country had active cancer in the last five years [1, 2]. The clinical characteristics of cancer patients who got infected with COVID-19 are unknown [3]. In our cancer center, the treatments of patients with chemotherapy or immunotherapy were not stopped since we assumed that the risks of infection were disparately lower than the risks of the sequela caused by treatment delaying of aggressive forms of cancer. We shifted some patients who are on a routine follow-up to limit exposure and avoid overcrowding in the waiting rooms. One of the theories about the causes of death from COVID-19 is the cytokine storm theory, on other hand, one of the lethal side effects of immunotherapy drugs is pneumonitis [4].

We need to know how the virus will affect the cancer mortality and if we need to hold these drugs during viral pandemics in the future.

MATERIALS AND METHODS

This was a retrospective observational study carried out from March 1, 2020 to June 1, 2020 at King Abdullah Medical City, Oncology Center in Makkah. The study included a total of 1300 patients including 1096 who attended the outpatient clinic and treatment unit in addition to 204 patients who admitted to the oncology floor through the emergency unit during the study period. Patients were identified through a retrospective review of medical records excluding patients on palliative care and those with no detailed clinical information.

The data collected were the characteristics of the patients who received anticancer therapy in the outpatient treatment unit and clinical data of the patients admitted to the oncology floor including date, cause, and outcome of admission. The data also included patients' age, gender, diagnosis, and treatment data. The treatment data including type of anticancer treatment, date of last chemotherapy cycle and date of the latest radiotherapy.

We identified the COVID-19 positive cases based on polymerase chain reaction (PCR) testing of na-

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Abbreviations used: COVID-19 – coronavirus disease 2019; ER – emergency room; PCR – polymerase chain reaction; SARS-CoV-2 – severe acute respiratory syndrome-related coronavirus 2.

sopharyngeal swab and reviewed their clinical data in detail.

Moreover, this research protocol was approved by the Institutional Review Board Committee. Since the study performed is retrospective, we obtained a waiver of informed consent from IRB.

RESULTS AND DISCUSSION

From March 1st to June 1st, we treated 1096 patients in outpatient clinics, 845 females and 251 males with age range from 14 to 95 years. The most common diagnosis was breast cancer 58% followed by colorectal 11% then lymphoma 6%. Chemotherapy was the active oncology treatment in 44% followed by hormonal therapy in 39% then targeted therapy in 13% and immunotherapy in 3%. Comorbidities, mainly diabetes and hypertension were reported in 62% of cases. Most of the patients in the outpatient setting were in good performance status I followed by II and nearly half of them were in stage IV of their disease (Table 1). Out of those patients, 513 received intravenous anti-cancer treatment either chemotherapy, immunotherapy, target therapy, or anti-angiogenesis. A total of 1288 cycles were administered; names of protocols are presented in Figure.

In the same study period, we admitted 204 patients to our oncology floor. Out of them 88 were males, 116 females. 38% have additional comorbidities. The cancer diagnosis was mainly breast cancer followed by colon cancer. Ninety-nine patients have comorbidities in addition to the cancer diagnosis. Causes of emergency room (ER) visits were mainly fever followed by pain. Admission diagnosis was mainly disease progression followed by symptom control, followed by COVID-19 infection, followed by febrile neutropenia, and bacteremia. Admission was related to therapy in 19 cases mostly due to febrile neutropenia, two cases with drug-induced pancytopenia one case of drug-induced diarrhea, one case of erlotinib toxicity, and one case of pneumonitis related to immunotherapy. COVID-19 infection was suspected in 80 cases and COVID-19 swab was done for all of them. Neutropenia was observed in 20 cases. At admission, 10 patients were admitted to the ICU, 28 patients died. The cause of death was COVID-19 infection in three cases (Table 2).

Nineteen patients had confirmed COVID-19 infection with PCR testing. Most of them presented with fever, cough, shortness of breath (SOB), and two with diarrhea, 12 have comorbidities in addition to cancer. Out of them 3 died not only with infection but also with disease progression (see Table 2). Five of the COVID-19 infected patients received oncology treatment within 4 weeks. Four out of the five recovered from infection and one patient died due to disease progression in addition to COVID-19 infection, their clinical data are summarized in Table 3.

Makkah is the holy capital of Saudi Arabia, a place where people in millions from all over the world visit all over the year. On March 2, the first case of COVID-19 virus infection was reported in Saudi Arabia, then the number of cases progressively increased, despite the early and strictly enforced curfew. The number of cases was highest in Makkah [5, 6]. We assumed that patients with cancer are at increased risk of infection with COVID-19 and will most likely have adverse outcomes with this infection due to increased age, tendency to have more comorbidities, immunosuppression due to cancer

Table 1. Characteristics of patients attending oncology clinics for active cancer treatment

Number of patients	1096	%	Cancer		
Age			Breast	635	58%
range	14–95		Colorectal	120	11%
median	54		Lymphoma	62	6%
Gender			Lung	29	3%
female	845	77	Head and neck	31	3%
male	251	23	Liver	1	0.1%
BMI			Pancreatic-biliary	22	2%
range	13–58.9		Gastro-esophageal	9	1%
median	27.9		Kidney	13	1%
Comorbidity			Prostate	23	2%
no	675	62	Testis	0	0%
yes	421	38	Gynecological	74	7%
Most common comorbidities			Sarcoma	14	1%
asthma	7	1	CNS	6	1%
CKD	7	1	Neuroendocrine	5	0.5%
DM	135	12	Thyroid	1	0.1%
DVT	11	1	Other	25	2%
HTN	141	13	**Class**		
IHD	24	2	Chemotherapy	481	44%
other	72	7	Hormonal	431	39%
PE	14	1	Targeted	139	13%
ECOG			Immunotherapy	30	3%
1	606	55	**Number of Cycles**		
2	286	26	IV Chemotherapy/immunotherapy	1288	
3	65	6	Immunotherapy	77	
4	10	1			
Stage					
Stage I	79	7			
Stage II	209	19			
Stage III	325	30			
Stage IV	482	44			

Notes: PE – pulmonary embolism, DM – diabetes, DVT – deep venous thrombosis, HTN – hypertension, IHD – ischemic heart disease, CKD – chronic kidney disease.

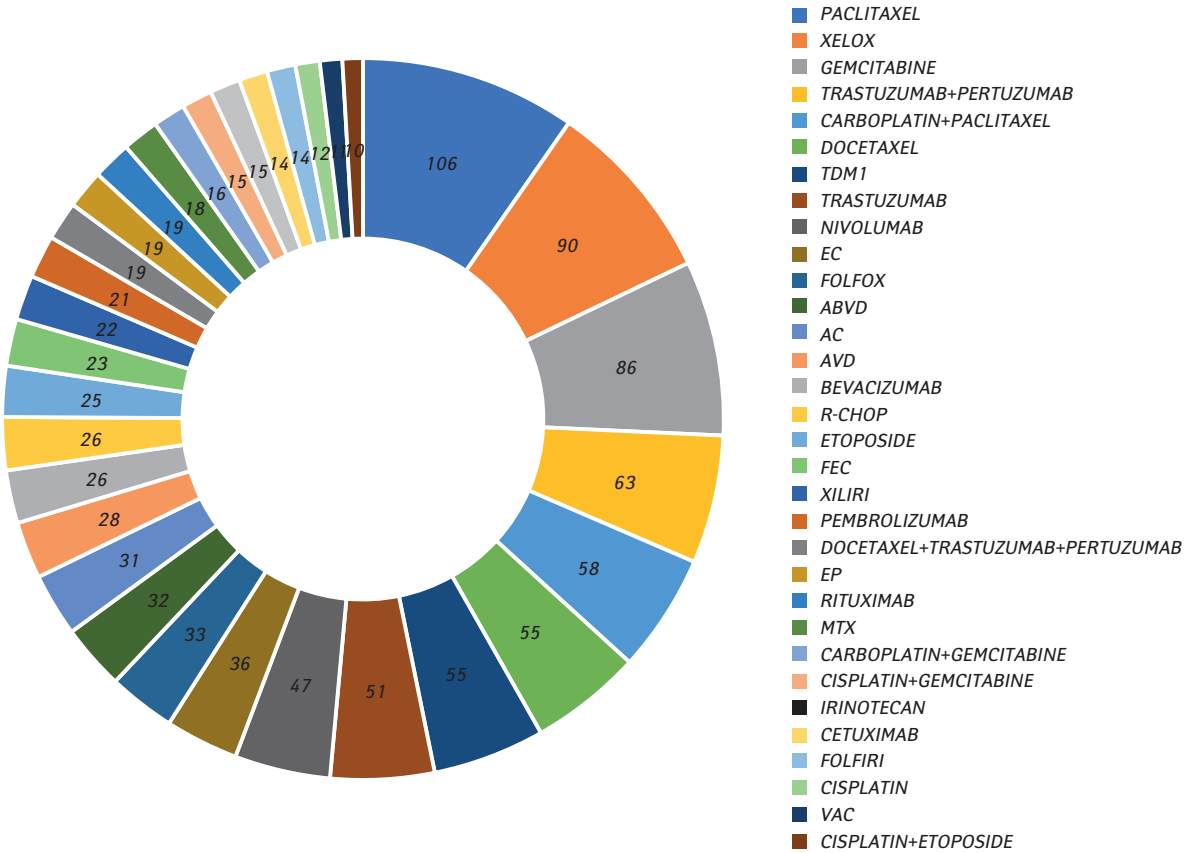

Figure. Outpatient anticancer protocols used to treat our patients during the pandemic. Only protocols with 10 or more counts are placed in the graph

Table 2. Characteristics of emergency oncology admissions

Total number of admissions	204	**COVID infected patients**	**Cause of ER visit**		**Neutropenia at presentation**		**COVID infected patients**
Age Range	17–90	43-84	Fever	66 (32%)	Yes	20 (10%)	1 (5%)
Median	55	55	Pain	56 (27%)	No	184 (90%)	18 (95%)
Male	88 (43%)	7 (37%)	SOB	36 (18%)	**COVID-19 suspected**		**COVID infected patients**
Female	116 (57%)	12 (63%)	Cough	27 (13%)	Yes	80 (39%)	19 (100%)
Diagnosis:		**COVID infected patients**	Diarrhoea	7 (3%)	No	124 (61%)	0
Breast cancer	45 (22%)	8 (4%)	Poor oral intake	6 (3%)	**Active oncology treatment within 4 weeks**		**COVID infected patients**
Colon/rectum	34 (17%)	4 (2%)	Dehydration	3 (1%)	Chemotherapy	54 (26%)	8(42%)
Lymphoma	21 (10%)	1 (0.5%)	Decreased level of consciousness	3 (1%)	Hormonal	26 (13%)	5(26%)
Lung cancer	18 (9%)	2 (1%)	Poor general condition	3 (1%)	Immunotherapy	11 (5%)	1 (5%)
Pancreatic cancer	13 (6%)	1 (0.5%)	Bleeding	1 (1%)	CD4/6 inhibitor	9 (4%)	-
Ovarian cancer	8 (4%)	-	**Admission diagnosis:**		TKI	2(1%)	-
Uterine cancer	7 (3%)	-	Disease progression	56 (27%)	**ICU admission**		**COVID infected patients**
Urinary bladder	6 (3%)	-	Pain and symptom control	21 (10%	Yes	10 (5%)	2 (11%)
Comorbidities:		**COVID infected patients**	COVID-19 infection	19 (9%)	No	194 (95%)	17 (89%)
Yes	99 (49%)	12 (63%)	Febrile neutropenia	14 (7%)	**Death**		**COVID infected patients**
No	105 (51%)	7 (37%)	Bacteraemia	11 (5%)	Yes	28 (14%)	3 (16%)
Metastatic disease		**COVID infected patients**	Pleural effusion	9 (4%)	No	176 (86%)	16 (84%)
Yes	140 (69%)	12 (63%)	Brain metastasis	6 (3%)	**Cause of death**		
No	64 (31%)	7 (37%)	Other	68 (33%)	COVID related	3 (1%)	3 (16%)
			Treatment related admission		Non COVID related	25 (12%)	
			Yes	19 (9%)			
			No	185 (90%)			

treatment, including steroids in addition to their lower performance status. Despite the current pandemic, we continued the standard cancer care as delaying cancer treatment can have an adverse outcome. Nevertheless, we managed to give more than one thousand chemotherapy cycles during this time without any major or unexpected complications.

Many cancer centers held their services in response to early reports from China. When a retrospective cohort study was reported, the study included cancer patients with confirmed COVID-19 infection. Twenty-eight patients were included. Fifteen (53.6%) patients had severe events and the mortality rate was 28.6%. If the last cancer treatment was within 14 days,

Table 3. Characteristics of COVID-19 infected patients who received chemotherapy within 4 weeks from infection

Patient	Age	Sex	Diagnosis	Metastasis	Comorbidities	Symptoms at presentation	Last oncology treatment	Interval from last cycle	ICU admission	Outcome and cause of death	Disease response
1	59	F	Breast cancer	No	Chronic cardiomyopathy, DM HTN	Cough, fever	Weekly paclitaxel	One week	No	Recovered	CR
2	59	M	Pancreatic cancer	Yes	DM HTN	Fever	Gemcitabine	One week	No	Death	PD
3	55	F	Mycosis fungoides	Yes	None	Diarrhea, nausea, generalized body aches	Gemcitabine /vinblastine	20 days	No	Recovered	PD
4	62	F	Breast cancer	No	None	Fever, cough	EC	Three weeks	No	Recovered	CR
5	54	M	Colorectal cancer	Yes	None	Fever, dry cough	Cetuximab/ irinotecan/ capecitabine	1 month	No	Recovered	PD

Notes: F – female; M – male; DM – diabetes; HTN – hypertension; CR – complete response; PD –progressive disease; EC – Epirubicin/cyclophosphamide.

the risk of developing severe events was significantly increased (HR = 4.079, 95% CI 1.086–15.322, $p = 0.037$). The authors recommended the avoidance of immunosuppressive medications [7]. Researchers also found that microvascular COVID-19 lung vessels obstructive thromboembolic syndrome causing micro clots is one of the main theories of the cause of death in COVID infection and it is well known that cancer patient is more prone to thrombosis not only by disease but also by medication like chemotherapy and antiangiogenic agents [8].

We collected all the oncology admissions during this pandemic aiming to identify major complications to our cancer management. Two hundred and four cases were admitted over three months. 19 admissions were treatment-related 56 admissions were related to disease progression. We are reporting here only 19 cases of COVID-19 infection occurred in three months period after the pandemic has been declared. All our COVID positive cases were hospitalized as per our policy and not due to the severity of their conditions.

The mortality rate among our COVID cases was 16%. Five of COVID infected cases received chemotherapy within the last 4 weeks before catching COVID-19 infection. Only one of them died and the others recovered. This is in agreement with a retrospective study from a Pakistan reported the outcome of cancer patients diagnosed with COVID-19 infection within 4 weeks of receiving anticancer treatment. This study concluded that mortality in cancer patients with COVID-19 is mainly driven by the advanced stage of disease and chemotherapy is not significant risk factor [9].

Multiple oncology centers reported high mortality from COVID-19 infection among cancer patients on active treatment. A large cancer center in Saudi Arabia published their data of 19 COVID-infected cancer patients and reported a very high mortality of 39% [10]. In the CCC-19 (COVID-19 and Cancer Consortium) one of the largest world datasets investigating the risk of death in cancer patients with COVID-19 infection was reported in the ASCO meeting 2020. The study reported 928 patients with cancer and confirmed COVID-19 infection by RT-PCR including 21% breast cancer, 16% prostate cancer, 12% gastrointestinal cancer, 11% lymphoma, and 10% thoracic malignancies. The CCC-19 study reported a 13% mortality rate and 14% ICU admission. Independent factors for mortality in CCC-19 were older age, poor performance, active chemotherapy and the presence of comorbidities. In China, the mortality rate was higher in cancer patients compared to a non-cancer patient and in New York mortality rate were significantly higher in cancer patients 25% to 14% in non-cancer patients [11–13].

The Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) study reported 400 thoracic cancer patients with confirmed COVID-19 RT-PCR, clinically suspected infection, and radiologically suspected cases. The authors concluded that patients on steroids and anticoagulation, prior to the diagnosis, were at increased risk of mortality from COVID-19, and prior administration of chemotherapy as a unique modality or in combination with immune checkpoint inhibitors was associated with increased risk of death while immunotherapy and tyrosine kinase inhibitors were not [14].

On the other hand, a recent study reported from the UK strongly supports our finding, they explored the effect of anticancer treatment during the COVID-19 pandemic and with multivariate analysis, they concluded that the administration of chemotherapy within 4 weeks before confirmed COVID-19 infection is not a significant factor to more severe disease or a predictor of death from COVID-19 infection. They observed the same for other therapies like immunotherapy and target therapy [15].

A little is known about the effect of immune checkpoint inhibitors on COVID-19 infection in patients with cancer. In our study a total of 1288 anti-cancer treatment cycles were successfully administered, including 77 cycles of immunotherapy without unexpected complications. Among thirty patients treated with immunotherapy, only one diagnosed with COVID infection and recovered without complications. This is in contrast to a study from New York found that COVID-19 infected cancer patients who received immune checkpoint inhibitors had a statistically significant increase in risk of hospitalization and this was based on the treatment of 31 patients [16].

Our study has limitations being a single center study with few cases of COVID-19 infection, however, the number of cases who received anticancer treatment is large and representing most of the protocols used in cancer treatment.

According to our data, cancer treatment is not a risk factor for COVID-19 infection or its complications. Cancer treatment should not be interrupted during pandemics and every effort should be made to give cancer patients the standard of care. In this study, most of the COVID-19 infected patients recovered completely without complications, and deaths were not only due to COVID-19 infection but also because of disease progression. Particularly during pandemics cancer treatment prioritization should balance interventions based on the magnitude of benefits. Treatment guidelines should be regularly updated to fulfill this concept. This requires active collaboration between experts.

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УРГЕНТНА ГОСПІТАЛІЗАЦІЯ ОНКОЛОГІЧНИХ ХВОРИХ ПІД ЧАС ПАНДЕМІЇ COVID-19: ДОСВІД ВЕЛИКОГО МЕДИЧНОГО ЦЕНТРУ САУДІВСЬКОЇ АРАВІЇ

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Стан питання: ВООЗ оголосила пандемію коронавірусної хвороби 2019 (COVID-19) у березні 2020 р. Вважається, що хворі на рак є дуже вразливими до цієї інфекції. До цього часу невідомо достеменно, чи впливає пандемія на показники смертності внаслідок онкологічних захворювань. ***Мета***: З'ясувати на майбутнє, чи слід відтерміновувати лікування онкологічних хворих під час вірусної пандемії. ***Матеріали та методи***: Ретроспективне обсерваційне дослідження, яке охоплювало період з 1 березня до 1 червня 2020 р., включало хворих на рак у фазі активної терапії, які надходили до нашого онкологічного центру у зв'язку з необхідністю у невідкладній допомозі або ж отримували лікування в амбулаторному відділенні. COVID-19-позитивних хворих виявляли за результатами полімеразної ланцюгової реакції в назофарингеальних мазках. ***Результати***: Усього в дослідження було включено 1300 хворих, з них 1096 лікувались амбулаторно, і 204 хворих було госпіталізовано у зв'язку з необхідністю невідкладної допомоги. Серед діагнозів переважав рак молочної залози, на другому місці був рак товстої кишки. Основною причиною звернення за невідкладною допомогою були лихоманка та біль. Основним діагнозом під час надходження до клініки було прогресування онкологічного захворювання. Далі серед причин звернення за допомогою були необхідність усунення симптомів, інфекція COVID-19 та фебрильна нейтропенія. Амбулаторно було проведено загалом 1288 циклів протипухлинної терапії 513 хворим. З з 19 хворих із підтвердженим COVID-19 (16%) померли, але не тільки через COVID-19, а також і через прогресування онкологічного захворювання. ***Висновок***: Протипухлинне лікування не є фактором ризику щодо COVID-19 або його ускладнення. Тому терапію онкологічного захворювання не слід переривати під час пандемії. Навпаки, слід робити все можливе, аби надавати онкологічним хворим у цій ситуації лікування згідно зі стандартами.

Ключові слова: госпіталізація онкологічних хворих, COVID-19, протипухлинна терапія.

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