Original Research Article

Influence of Covid-19 pandemic on safe and timely delivery of Systemic anti-cancer therapy, Dubai hospital experience

Abstract:

Aims:

~~Aim of this study is t~~To analyze the effect of COVID-19 pandemic on timely delivery of systemic anti-cancer treatment including chemotherapy, biological therapy and immunotherapy ~~in our institution~~ and assess complication rate.

Place and Duration of Study:

Department of Oncology, Dubai Hospital, Dubai, UAE from January 2020 to July 2020.

Methods:

~~We identified~~ This is a retrospective review of electronic medical records and infusion Centre log of the number of chemotherapy sessions administered in the infusion therapy Centre, Dubai hospital from January 2020 to July 2020 ~~through a retrospective review of electronic medical records and infusion Centre log~~. Data regarding treatment delays, treatment interruption or discontinuation and adverse events including febrile neutropenia was collected ~~retrospectively~~and analysed.

Results:

A total of 1553 systemic treatment sessions were recorded ~~in the oncology infusion therapy center, Dubai Hospital from~~between January 2020 to July 2020,with an average of 222 treatment sessions per month. Physician recorded delays were observed in ninety (5.79%) treatment sessions ~~over a 7 months period~~. Average duration of treatment delay was 7 (2-13) days. Overall treatment and disease related factors

(toxicities, disease progression) were the common reasons for delays. Highest number of treatment delays (n=23,10.2%) were recorded in the month of April at the peak of Covid 19 pandemic likely representing implementation of extreme precautionary measures. There were no treatment interruptions or discontinuations.

Fourteen (<1%) patients developed febrile neutropenia~~. and fully recovered after treatment~~With treatment, all of them recovered fully. ~~We did not observe any~~No significant change in systemic treatment related complications were observed during the pandemic.

Conclusion:

This study did not show any significant increase in systemic anticancer treatment delays or complication rate during COVID-19 pandemic. ~~Our~~ This experience suggests that systemic chemotherapy may be administered safely with infection control and precautionary measures during pandemic. However, further studies with larger sample size are required for better guidance in ~~this~~ such situations.

Keywords:

COVID-19 infection, Pandemic, Systemic anticancer therapy, Neutropenia

Introduction:

In March 2020, the World Health Organization (WHO) declared the novel coronavirus (COVID-19) outbreak as global pandemic. Since then, over 600 million people have been infected with over 6 million confirmed deaths globally[1]. ~~[1]~~ Governments were advised by WHO to introduce public health measures including social distancing, use of face masks, isolation and quarantine to reduce the risk of viral transmission. This resulted in disruption of diagnostics and treatment services due to reallocation of resources to prioritize emergency care to combat the ~~covid~~Covid-19 pandemic. Cancer services globally are resource dependent and require a multidisciplinary team approach.

Due to limited access to routine medical services, concerns were raised about continuation and safe delivery of systemic anti-cancer therapy (SACT). Oncology Physicians had to weigh the risks and benefits of administering SACT versus the risk of developing COVID 19 infection as cancer patients can be severely immunocompromised due to cancer and its treatment. Furthermore, many cancer patients are elderly and may require frequent visits to healthcare facilities for treatment, increasing the risk of infection transmission[2]. ~~[2]~~ Whether the cancer diagnosis or anti-cancer treatment leads to increased risk of complications in COVID-19 infection is unclear.

High rates of intensive care unit admission and deaths due to the COVID-19 infection in cancer patients have been reported in many studies[3]. ~~[3]~~ Data from a retrospective study suggested higher risk of complications if cancer treatment administered within 2 weeks of developing COVID-19 infection[4]. ~~[4]~~ However, data from the UK Coronavirus Cancer Monitoring Project (UKCCMP) did not report any evidence of a higher risk of mortality from the COVID-19 infection in cancer patients[5]. ~~[5]~~

The United Arab Emirates reported the first case of COVID-19 in January 2020. Being a major international transit hub, the government of the UAE took strict measures to contain viral spread. Dubai Health Authority (DHA) is one of the leading governmental entities providing medical care in the Emirate of Dubai. The oncology department of the Dubai Hospital (DH) manages approximately 20% of the UAE cancer population. ~~Cancer care is often complex, requiring input from other healthcare specialties.~~ Owing to the requirements of COVID-19 pandemic to reduce social contact and implement social distancing, the oncology department in Dubai hospital carried out several practical measures to ensure a safe and effective delivery of service. This included implementation of telemedicine service, laboratory tests and subcutaneous treatments in the community to reduce hospital visits, oral chemotherapeutic agents where possible, colony stimulating factors to reduce immunosuppression following chemotherapy, early treatment dose modifications and less frequent use of dose dense schedules. In this article,~~we share our~~the experience of the use of SACT during COVID-

19 pandemic is described. To the best of our knowledge, this ~~is the only study~~may be the first report on this subject from the Arabian Gulf ~~region~~.

Methods:

In this retrospective study, ~~we reviewed~~the electronic medical records of patients with solid malignancies who received systemic anticancer therapy with either curative or palliative intent in Dubai Hospital during the first wave of COVID-19 pandemic from January 2020 to July 2020 were reviewed. Ethical approval was obtained from Dubai Scientific research ethics committee. Eligibility criteria included all adult patients who received one or more cycles of chemotherapy during the study period and had at least 6 weeks of follow up records available after the last session of chemotherapy. Patients with insufficient follow up documentations, incomplete toxicity assessment and previous history of COVID-19 infection as well as hematological malignancies were excluded from the study.

Patients were identified from the hospital cancer registry and chemotherapy infusion center log. Using electronic medical records and chemotherapy infusion center log, ~~we collected~~ data regarding, patients' demographics, cancer type, anticancer therapy, intention of treatment, use of colony stimulating factors, laboratory reports and relevant clinical information was collected. Data regarding the number of chemotherapy sessions administered, treatment interruption or discontinuation and adverse events including febrile neutropenia was also collected.

Any interruption or prolongation of treatment cycle of more than one day due to any cause including patient's choice was recorded and considered as ~~delayed~~ treatment delay. Chemotherapy toxicity was assessed using Common Terminology Criteria for Adverse Events (CTCAE v4.03). Data was analyzed using Microsoft Excel version 1808.

Results:

A total of 1553 systemic treatment sessions were recorded in the oncology infusion therapy center, Dubai Hospital, from January 2020 to July 2020 with an average of 222 treatment sessions per month.

Median age of the patients was 56 years and the majority of the patients were female (62 %).

Breast cancer was the most common diagnosis (40%) followed by Colon cancer (15%) and other malignancies (45%).

Sixty percent systemic anticancer treatment sessions were delivered in a curative setting and 40% with palliative intent.

Most commonly used antineoplastic agents were tTaxanes (dDocetaxel, paclitaxel) followed by aAnthracyclines (eEpirubicin,dDoxorubicin), platinum (cisplatin, carboplatin), and antimetabolites (capecitabine, ~~Gemcitabine~~gemcitabine).

Majority of the treatments were delivered in the month of July 2020 (n=308, 20%). Ninety (5.79%) treatment sessions were delayed by the Oncology Physicians over the 7 months study period. Average duration of treatment delay was 7 (2-13) days.

Common reasons for treatment delays included toxicities (n=58) and disease progression (n=17). Fifteen patients requested treatment deferral due to concerns of viral transmission.

Highest number of treatment delays (n=23, 10.2%) were recorded in the month of April at the peak of COVID-19 pandemic likely representing implementation of extreme precautionary measures. There were no treatment interruptions or discontinuations. (Table 1, Figure 1).

Fourteen (<1%) patients developed febrile neutropenia including seven patients with grade 4 febrile neutropenia. All patients received intravenous antibiotics within 1 hour of presentation to the Emergency department. Median duration of hospitalization was seven (4-17) days. All patients fully recovered after treatment with no complications. (Figure 2)

~~We did not observe any~~No significant change in systemic treatment related complications during the pandemic were observed.

Discussion:

Healthcare facilities globally underwent major changes to ensure safe and effective service delivery during COVID-19 pandemic. This included partial or complete closure of diagnostic services, cancellation of elective surgical procedures to increase capacity and conserve resources to deal with the emergent situation due to pandemic[6]. ~~[6]~~ The American College of Surgeons and Center for Medicare & Medicaid Services (CMS) recommended hospitals and surgeons to limit elective procedures to decrease viral exposure[7, 8]. ~~[7, 8]~~Cancer services were disrupted including reduction in any routine activity of cancer services, reduction in the number of cancer surgeries, delay in radiotherapy, and delay, reschedule, or cancellation of outpatient visits[9]. ~~[9]~~ Studies have shown that the risk of complications from COVID-19 infection is not uniform across the population[10]. ~~[10]~~ During pandemic, cancer patients receiving treatments were assumed to be at a higher risk of developing infection, however there is limited evidence to support this mainly in the form of retrospective case series involving a small number of patients[11]. ~~[11]~~ This hypothesis led to widespread changes to anticancer treatment prescriptions[12]. ~~[12] Our~~ Thisretrospective study looked at the practice of anticancer treatment prescriptions, delays, treatment dose modifications and adverse events in a 7 ~~month s~~month period during the first wave of the pandemic.

Liang *et al.*~~in his study~~ suggested that surgery or adjuvant chemotherapy should be postponed for stable patients during pandemic due to high risk of developing COVID-19 infection within 4 weeks after treatment[3]. ~~[3]~~ Another study by Zhang

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et al. reported vulnerability of cancer patients during the pandemic and suggested that cancer patients should receive anticancer therapy timely in the setting of vigorous screening for COVID-19 and extraordinary precautionary measures.

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Median age of patients in this study was 65 years and the majority (25%) of the patients had Lung cancer[4].

~~[4]~~ In contrast, ~~our~~ the study population reported in this study is younger and ~~Lung~~ lung cancer is less frequent. ~~In our study of~~ Amongst the 1553 chemotherapy sessions, the vast majority of treatments (94.21%) were delivered on time during the 7 months of study period with strict adherence to COVID-19 precautionary measures. This is consistent with the standard practice during non-pandemic situations.

Physicians documented treatment delay during ninety encounters (5.79%) with an average duration of delay of 7 days. Coinciding with the peak of the pandemic, 23 (10.2%) treatment sessions were delayed in the month of April 2020 ~~which coincided with the peak of the pandemic~~. ~~We believe t~~This was probably due to extreme restrictive precautionary measures and physician's perception of the overall situation.

Treatment related toxicities and disease progression were the common causes of chemotherapy delays.

Neutropenia is one of the common side effects of myelosuppressive chemotherapy and a major cause of treatment delays, dose modification, increased cost, reduced quality of life and infection related morbidity and mortality[13,14,15]. ~~[13,14,15]~~ Incidence of febrile neutropenia is 10-20 % in patients receiving chemotherapy for metastatic solid cancers and prophylactic use of ~~Granulocyte~~ granulocyte colony stimulating factors (G-CSF) can reduce

the severity and duration of febrile neutropenia[16, 17]. ~~[16, 17]~~. Toriumi R *et al* reported a significant reduction of febrile neutropenia rate in patients receiving inpatient chemotherapy for urological cancers during pandemic[18].~~[18]~~ This was suggested to be secondary to implementation of hygienic measures for healthcare professionals and patients. In ~~our~~ this study, the rate of febrile neutropenia was exceptionally low (n=14, <1%) as compared to pre pandemic data. ~~We believe t~~This ~~is~~ could be due to strict COVID-19 precautionary measures, adherence to infection prevention protocols and liberal use of G-CSF.

~~Our study concluded that~~In conclusion, it is safe to continue cancer treatment in a timely manner with low risk of febrile neutropenia during a pandemic with strict hygienic measures, adherence to infection prevention protocols, frequent use of growth factors and patient education. ~~Our study~~The results of this study may help ~~to~~ alleviate some concerns and assumptions for oncology clinicians facing the dilemma of choosing treatment or no treatment.

Findings of ~~our~~ this study are consistent with the other studies looking at the safety of SACT during pandemic. However, there are certain differences in patients' demographics ~~in our study~~. ~~Our~~ The study population in this report is younger and ~~Breast~~ breast cancer is the most common diagnosis as opposed to Lung cancer in other studies. This may have contributed to better treatment tolerance and immunity against infections. ~~Our~~ The results of this study provide~~d~~ important results for future comparative studies in the region and other parts of the world. ~~We believe our study provided a valuable contribution to the medical literature, however it has s~~Some limitations~~.~~ are:~~The data were collected retrospectively~~retrospective data from a single cancer center ~~in Dubai~~ and ~~the~~ a small sample size ~~was small~~. It may not fully reflect the feasibility and timely delivery of cancer therapy in other patient populations during pandemic situations in other geographical locations with entirely different logistic or healthcare situations.

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Conclusions:

Systemic anticancer therapy can be safely administered in a timely manner during pandemic with strict adherence to infection prevention measures~~. In our study, there were no significant anticancer~~without any treatment delays during COVID-19 pandemic~~. and~~The complication rate including incidence of febrile neutropenia was low. ~~However further studies with larger sample sizes are required for better guidance in this situation.~~

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Month	No of SACT sessions	No. of SACT delays	Percentage of delays	No of patients with FN

January	215	08	3.70%	0
February	207	10	4.80%	0
March	220	16	7.20%	02
April	213	23	10.70%	04
May	183	07	3.80%	01
June	207	10	4.80%	02
July	308	16	5.19%	05

Table 1: Details of treatment sessions, delays and incidence of febrile neutropenia (year 2020). SACT= Systemic anticancer therapy, FN=Febrile Neutropenia

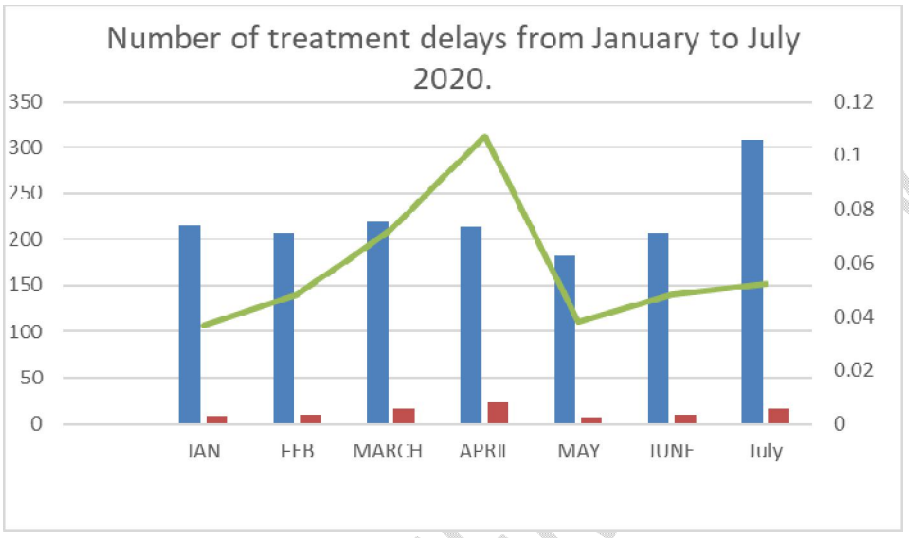

Figure 1: Anticancer therapy delays from January 2020 to July 2020

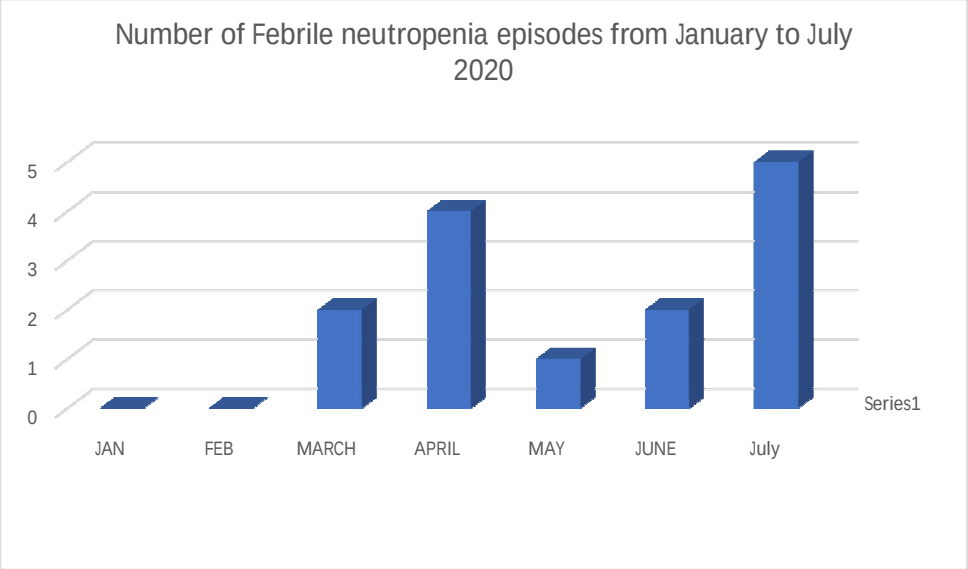

Figure 2: Episodes of Febrile Neutropenia from January to July 2020