

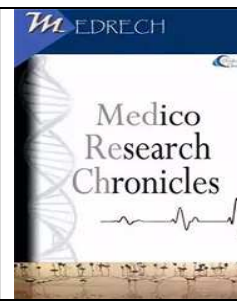


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Cancer Treatment Delay Due to COVID-19 Infection in Cancer Patients Attended in a Tertiary Hospital of Bangladesh

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ABSTRACT

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Introduction: The COVID-19 pandemic had a significant impact on health care systems worldwide. However, the brunt of this impact was on the cancer patients getting treatment in specialized oncology hospitals. **Objective:** to assess the cancer treatment delay due to covid-19 infection in cancer patients attended in a tertiary hospital of Bangladesh. **Methods:** It was a retrospective observational study and data of all patients dept. of Radiation Oncology, Combined Military Hospital (CMH), Dhaka, Bangladesh from July to December 2020 with cancer or history of cancer with COVID-19 was collected from interview of patient or attendant and medical records in a preformed data collection sheet and then analyzed. **Results:** Total 60 patients included were divided into two groups elderly population (>65 year) and younger population, the mean age of patient at diagnosis was 50 years, ranging from 28 to 72 years old, only 10 patients were aged 65 years or more. The most common co morbid condition associated was HTN followed by diabetes mellitus, IHD, bronchial asthma and cerebrovascular accident, patients with multiple co morbidities (26%) were also present in this study. Symptomatic analysis revealed most of the patient diagnosed asymptotically (32%) and among symptoms fever (28%), shortness of breath (13%) and cough (15%) were the most frequent ones, patients also presented with anosmia, loose motion or altered consciousness. Haematologic and biochemical finding of COVID-19 infected patients shows most of the patients had anaemia (45%) and lymphopaenia (50%) in CBC, hyponatraemia (65%) as electrolyte imbalance and also increased D dimer (85%), raised Ferritin (55%) and high CRP (65%) in biochemical parameter. The most prevailing cancers was breast cancer, Head neck region (larynx, pharynx, oral cavity), Gastrointestinal tract (GIT inc. esophagus,

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stomach, colorectal) followed by lung, gynecologic, central nervous system (CNS), genitourinary tract, lymphoma and carcinoma unknown primary (CUP). Most of the patients received combined modality treatment including surgery, radiotherapy and chemotherapy. Patients delay in attending oncologist, delay or gap in initiation and continuation of cancer treatment like surgery, radiotherapy or chemotherapy occurred in most of the patients, the average gap of treatment due to COVID-19 infection was 3 months with a minimum gap of 10 days to extending upto 8 months. **Conclusion:** In conclusion, COVID-19 positivity during the scheduled radiotherapy treatment course chemotherapy and surgery has caused treatment delays. Multiple patient factors, such as race and ethnicity, underlying primary malignant neoplasms, multimorbidity, geographic location, receipt of COVID-19 vaccine, severity of COVID-19, and timing of COVID-19 diagnosis, were associated with delays in cancer treatment.

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INTRODUCTION

The emergence of Coronavirus disease 2019 (COVID-19) has caused a global public health emergency. In December 2019 an outbreak of respiratory disease caused by a novel Corona virus was first detected in China and has now spread to more than 200 countries¹. As of December 2020, this virus has affected more than 200 countries and territories, infecting more than 63,747,751 people including 1,477,144 deaths. Case fatality rate is 0.6 to 11.2%² with the World Health Organization (WHO) declaring the novel Corona virus outbreak as a pandemic³. In Bangladesh Corona virus was first detected in March 2019 and till now about 4,67,225 cases detected including death of 6675 people⁴. With more than 18 million new case per year globally, cancer affects a significant portion of the population. Individuals affected by cancer are more susceptible to infections due to coexisting chronic diseases, overall poor health status and systemic immunosuppressive states caused by both cancer and anticancer treatments. As a consequence, patients with cancer who are infected by the SARS-CoV-2 Corona virus may experience more difficult outcome than other populations and a recent small case

series study supports this hypothesis. So, focus is needed on the impact of this rapidly spreading viral infection in cancer patients⁴. The risk of morbidity and mortality from cancer patients as a consequence of severe acute respiratory syndrome Corona virus 2 (SARS-CoV-2) infection is not uniform. Patients with cancer have been generally assumed to be at more risk of complications. This led to widespread global changes to patterns of prescribing chemotherapy and radiotherapy. As a global health emergency, oncologists must secure evidence from dataset, which can then inform their risk-benefit analyses for individual patients of cancer with COVID-19. This will help to plan for choosing the treatment, follow up and management of complications⁵. With the WHO declaring the novel Corona virus outbreak a pandemic, there is an urgent need to address the impact of such a pandemic on cancer patients¹. In Bangladesh there is no available data regarding prevalence of Corona in cancer patient, their outcome, treatment difficulties, delay in cancer treatment or modalities of cancer treatment. We aimed to describe the clinical and pathologic characteristics and outcomes of COVID-19 infection in this cohort of patients with cancer

and diagnosed COVID-19 and attempted to assess how the presence of COVID-19 disease delays the treatment of cancer patients.

MATERIALS AND METHODS

It was a retrospective observational study and data of all patients dept. of Radiation Oncology, Combined Military Hospital (CMH), Dhaka, Bangladesh from July to December 2020 with cancer or history of cancer with COVID-19 was collected from interview of patient or attendant and medical records in a preformed data collection sheet and then analyzed.

Results

Eligibility criteria for enrolment on the registry were as follows: adult patients (aged ≥ 18 years); active cancer and a positive SARS-CoV-2 RT-PCR test from a nose or throat swab. Patients with active cancer were defined as those with metastatic cancer or those undergoing anticancer treatment in any setting (curative, radical, adjuvant, or neoadjuvant) or those treated within the past 5 years with surgery, systemic anticancer therapy, or radiotherapy and now on follow up.

Table-I: Sociodemographic variables of the respondents (n=60)

Variables	Number	Percentage
Age		
Median	50	
<65 year	50	83
≥ 65 year	10	17
Gender		
Male	32	53
Female	28	47
Co morbidity		
<2 co morbidity	44	74
Diabetes	17	28
HTN	19	31
Bronchial asthma	5	8
CVD	4	6
IHD	7	12
≥ 2 co morbidity	16	26

Table-I shows sociodemographic variables, patients were divided into two groups elderly population (>65 year) and younger population, the mean age of patient at diagnosis was 50 years, ranging from 28 to 72 years old, only 10 patients were aged 65 years or more. The most common co morbid

condition associated was HTN followed by diabetes mellitus, IHD, bronchial asthma and cerebrovascular accident, patients with multiple co morbidities (26%) were also present in this study.

Symptomatic analysis revealed most of the patient diagnosed asymptotically (32%)

and among symptoms fever (28%), shortness of breath (13%) and cough (15%) were the most frequent ones, patients also presented

with anosmia, loose motion or altered consciousness (Fig-1).

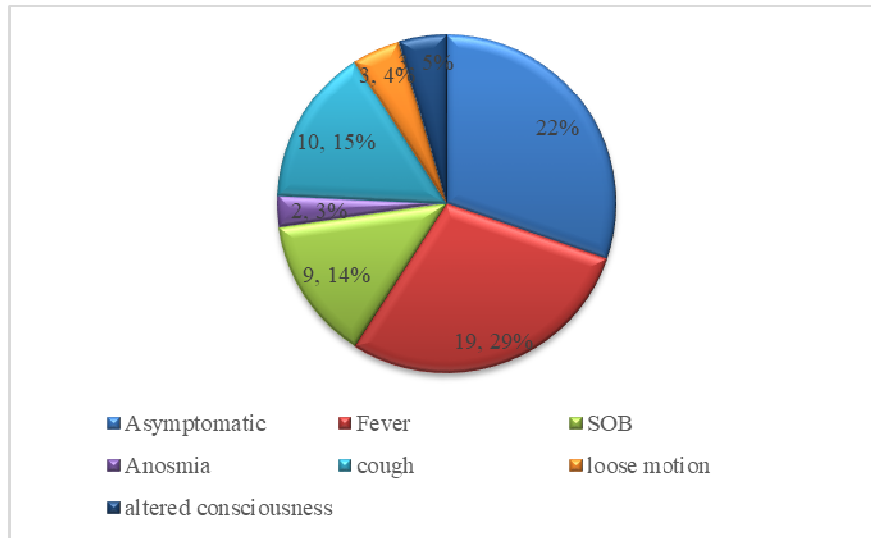


Fig-I: Distribution of respondents by symptoms of COVID (n=60)

Table-II: Haematologic and biochemical finding of COVID-19 infected patients (N=60)

Biochemical Parameter	N	%
Anaemia	27	45
Lymphopaenia	30	50
Hyponatraemia	39	65
Increased D dimer	51	85
Raised Ferritin	33	55
High CRP	39	65

Haematologic and biochemical finding of COVID-19 infected patients (Table-II) shows most of the patients had anaemia (45%) and lymphopaenia (50%) in CBC, hyponatraemia (65%) as electrolyte imbalance and also increased D dimer (85%), raised Ferritin (55%) and high CRP (65%) in biochemical parameter.

The most prevailing cancers was breast cancer, Head neck region (larynx, pharynx,

oral cavity), Gastrointestinal tract (GIT inc. esophagus, stomach, colorectal) followed by lung, gynecologic, central nervous system (CNS), genitourinary tract, lymphoma and carcinoma unknown primary (CUP). Most of the patients received combined modality treatment including surgery, radiotherapy and chemotherapy (Fig-II). Following figure showing frequency of cancer with treatment modalities received.

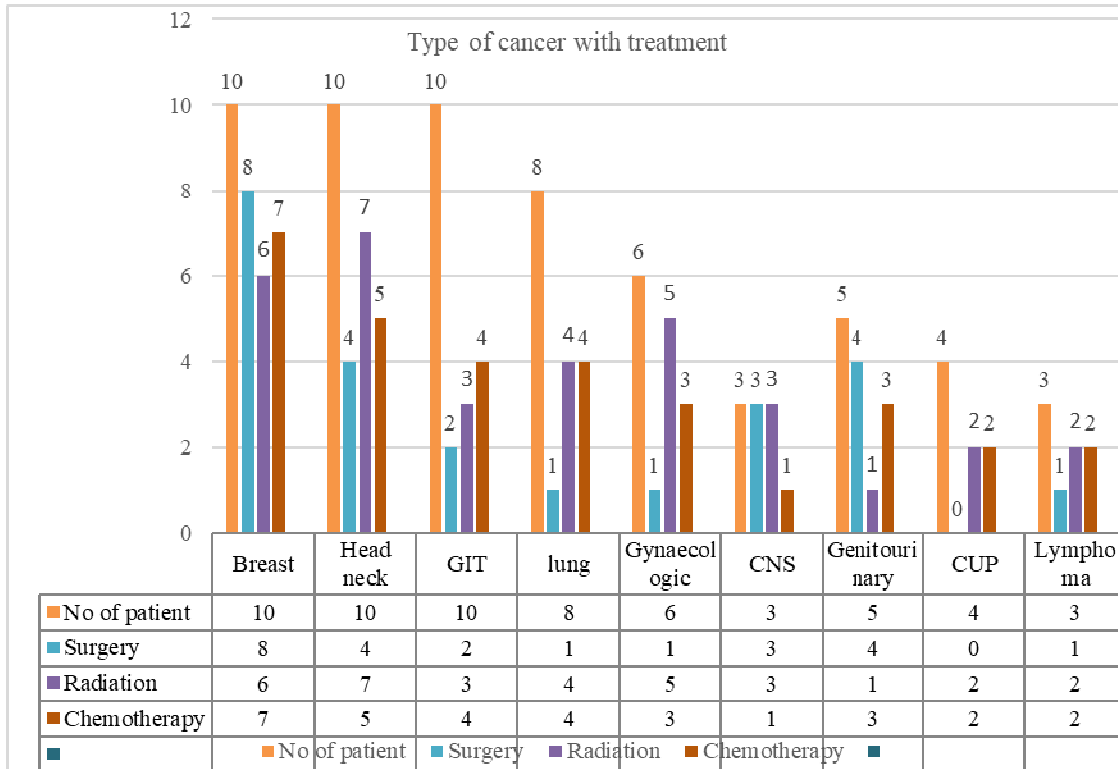


Fig-II: Types of cancer with treatment received among the respondents (n=60)

Table-III: Association between risk factors and mortality among the respondents (n=60)

Variables	Number (Percentage)	Number (Percentage)
	Cured 50(83)	Death 10(17)
Performance status ≥ 3	4(8)	6(60)
PS < 3	46 (92)	4 (40)
Older age ≥ 65	16(32)	3(30)
Age <65	34 (68)	7 (70)
Co morbidity ≥ 2	11(22)	5(50)
<2	39 (78)	5(50)
Advanced stage III or IV	9(18)	10(100)
Early stage	41(82)	0 (00)
On treatment	27(54)	8(80)
On follow up	9(18)	1(10)

Treatment delay due to COVID-19 infection radiotherapy, chemotherapy or surgery:

Due to COVID-19 infection, patients had to take treatment for Covid infection and

some patients recovered early from Covid and some developed complications. Patients delay in attending oncologist, delay or gap in initiation and continuation of cancer treatment like surgery, radiotherapy or chemotherapy occurred in most of the patients, the average gap of treatment due to COVID-19 infection was 3 months with a minimum gap of 10 days to extending upto 8 months. In this short period of time it is difficult to determine the detrimental effect of cancer due to this delay but in different studies it was proved that in some form of cancer 1-day gap of treatment causes 1% or more chance of cancer recurrence or decrease in cancer survival.

DISCUSSION

That multiple patient factors, such as race and ethnicity, underlying primary malignant neoplasms (ie, diagnosis and extent of spread), multimorbidity, geographic location, receipt of COVID-19 vaccine, severity of COVID-19, and timing of COVID-19 diagnosis, were associated with delays in cancer treatment. Interestingly, we only found associations between a few social determinants of health variables and likelihood of treatment delay. These findings provide insight into the state of cancer care during the most significant public health emergency of this era. Delay in radiation treatment results in poor treatment outcomes.^{6,7} Unplanned treatment interruptions have resulted in poor local control in many cancer subsites including, head and neck, cervix, urinary bladder, lung, and breast.^{8,9} Among all subsites, the most robust evidence is in head and neck cancers. A treatment delay of one day could decrease the local control rate by approximately 1.4%.^{5,6,10,11} In our analysis, the median treatment delay was 18 days. In order to compensate for the treatment delay, different approaches have been described in the literature.¹² The first method is to maintain the overall treatment time (OTT) by accelerated radiotherapy (treating the patients on weekends) and by hyper fractionation (giving

multiple fractions a day with 6 hours gap between fractions). However, this method will be difficult to implement when the OTT is increased due to a gap near the end schedule of radiotherapy because there would not be many weekends left to compensate for the delay in OTT.¹³ Total 60 patients included in our study. The mean age of patient at diagnosis was 50 years, ranging from 28 to 72 years old, only 10 patients were aged 65 years or more. The most common co morbid condition associated was HTN followed by diabetes mellitus, IHD, bronchial asthma and cerebrovascular accident, patients with multiple co morbidities (26%) were also present in this study. Symptomatic analysis revealed most of the patient diagnosed asymptotically (32%) and among symptoms fever (28%), shortness of breath (13%) and cough (15%) were the most frequent ones, patients also presented with anosmia, loose motion or altered consciousness. Other studies have identified an increased risk for COVID-19 mortality among patients with hematologic malignant neoplasms, linking this to virus-specific properties, but not assessing the association with treatment delays.^{14,15} To the extent that treatment delays may be contributing to overall increased mortality in this subgroup, special attention must be paid to how treatment delay or discontinuation protocols developed by institutions may be inadvertently exacerbating adverse outcomes in a high-risk group. Haematologic and biochemical finding of COVID-19 infected patients (Table-II) shows most of the patients had anaemia (45%) and lymphopaenia (50%) in CBC, hyponatraemia (65%) as electrolyte imbalance and also increased D dimer (85%), raised Ferritin (55%) and high CRP (65%) in biochemical parameter. The most prevailing cancers was breast cancer, Head neck region (larynx, pharynx, oral cavity), Gastrointestinal tract (GIT inc. esophagus, stomach, colorectal) followed by lung, gynecologic, central nervous system (CNS), genitourinary tract, lymphoma

and carcinoma unknown primary (CUP). Most of the patients received combined modality treatment including surgery, radiotherapy and chemotherapy. In our study, we noted that compared with individuals who contracted COVID-19 during the initial outbreak of the pandemic from March to June 2020, contracting COVID-19 later in the pandemic was associated with a lower likelihood of treatment delay and reduction in delays. A 2022 analysis on the ASCO COVID-19 registry by Mileham *et al*¹⁶ found that before June 2020, the main reason for testing for SARS-CoV-2 was COVID-19 symptoms (74% of tests). Due to COVID-19 infection, patients had to take treatment for Covid infection and some patients recovered early from Covid and some developed complications. Patients delay in attending oncologist, delay or gap in initiation and continuation of cancer treatment like surgery, radiotherapy or chemotherapy occurred in most of the patients, the average gap of treatment due to COVID-19 infection was 3 months with a minimum gap of 10 days to extending upto 8 months. In this short period of time it is difficult to determine the detrimental effect of cancer due to this delay but in different studies it was proved that in some form of cancer 1-day gap of treatment causes 1% or more chance of cancer recurrence or decrease in cancer survival. One global systematic review that identified 38 different categories of delays and disruptions reported that clinician- or system-related variables, such as medicine stockouts or shortages of devices, personal protective equipment, and laboratorial or imaging tests, were the most frequently reported structural or process-related factors associated with delay.¹⁷ Several single-institution reports and surveys of physicians revealed that there were more treatment delays among patients infected with SARS-CoV-2 compared with patients who were not infected.^{18,19} Our analysis is the first study, to our knowledge, to identify

systemic delays or cancellations in cancer treatment for a cohort of patients who were all diagnosed with SARS-CoV-2 infection. To our knowledge, this is the first study that analyzed the oncology outcomes because of treatment delay due to COVID-19 infection. However, the study's median follow-up time is very short to draw any conclusions. Moreover, the results could be skewed due to the high number of lost to follow-up cases in the study.

CONCLUSION

In conclusion, COVID-19 positivity during the scheduled radiotherapy treatment course chemotherapy and surgery has caused treatment delays. Multiple patient factors, such as race and ethnicity, underlying primary malignant neoplasms, multimorbidity, geographic location, receipt of COVID-19 vaccine, severity of COVID-19, and timing of COVID-19 diagnosis, were associated with delays in cancer treatment. Even though compensated using the gap correction technique, this treatment delay could potentially cause adverse oncological outcomes. Of note, most patients had only mild or asymptomatic COVID-19 infection. At the same time, case fatality rate (CFR) due to the infection was significantly low. Therefore, it will remain debatable whether it was worth delaying radiotherapy for a significant time to cause a potential cancer treatment failure.

Conflict of Interest: None.

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