COVID and cancer

COVID-19 and Cancer: A Comparison of the Two Important Pandemic Waves in an Indian Cancer Patients' Cohort

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Abstract

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It is well known that patients with cancer are at an increased risk of severe COVID-19. There are no reports that depict the differences in outcomes in cancer patients between the two waves of the pandemic. This is a real-world experience aimed at characterizing the differences in demographics, clinical features, treatment details, and outcomes in COVID-19-positive cancer patients between the two pandemic waves. This was a prospective study of all COVID-19-positive cancer patients attending our specialty out-patient department at Rajiv Gandhi Cancer Institute and Research Centre between March 2020 and November 2020 (1st wave) and April 2021 and June 2021 (second wave). All patients diagnosed to have COVID-19 by real-time polymerase chain reaction (RT-PCR) with a biopsy-proven solid organ malignancy attending the medical oncology out-patient department were included during both the waves. A total of 300 patients with proven SARS-CoV-2 infection by either RT-PCR or cartridge based nucleic acid amplification test were encountered, of which 123 were encountered during the first wave of the pandemic and 177 during the second wave. The case fatality rate of the first wave was 9.8%, with a 15-day case fatality rate of 5.6%, whereas for the second wave, it was 13% and 7.2%, respectively. Twelve patients succumbed to COVID-19 disease in the first wave and 23 succumbed in the second. There were no statistically significant correlations; however, the death in the second wave tended to occur more in younger male patients, with comorbidities and history of smoking. There was no relation with ongoing cancer-directed treatment or chemotherapy. Our study is unique in comparing characteristics of the two most important COVID-19 waves and treatment patterns in cancer patients from a single center. The second wave showed a higher CFR, hospital admission rate, and higher frequency of respiratory complications; however, there was no relation to cancer-directed therapy and COVID-19, thus reiterating the fact that cancer treatment should not be halted in the event of a COVID-19 infection.

Keywords

- 1st two waves
- cancer
- comparison
- COVID
- India

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Introduction

Coronavirus disease-19 (COVID-19) that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared as a global pandemic in March 2020 by the World Health Organization (WHO).[1] Ever since, regional and global efforts have been underway to control this disease using both pharmaceutical and non-pharmaceutical measures.

It is well known that patients with cancer are at an increased risk of severe COVID-19, as evidenced by a retrospective study on 73 million patients in the United States, in which the adjusted odds ratio for COVID-19 infection in known patients of cancer was reported to be 7.[2] Although the overall case fatality rate (CFR) in India has been lower than that reported in the rest of the world,[3] the same cannot be extrapolated to the group of cancer-affected patients.[4] Additionally, the difference in CFR between the first and second pandemic waves differed. There have been studies from India as well as the rest of the world depicting the outcomes and mortality of cancer patients affected with COVID-19.[5,6] Roy et al reported 145 patients of solid organ malignancies, of which 22 (15%) patients succumbed,[7] whereas Mehta et al reported a glaringly high CFR of 28% in cancer patients when compared to match noncancer population (14%).[8]

With the vaccine roll-out drives in full swing across the world, the glaring truth is that this subgroup of patients were excluded from all vaccine trials; hence, the efficacy in the setting of malignancy remained elusive.[9,10] We have previously reported the vaccination status in cancer affected patients from our center in a cohort of 752 cancer patients, of which only 29.1% were vaccinated.[11] The knowledge and attitude toward vaccination was reported in a contemporary study by Noronha et al in 435 cancer patients, in which they demonstrated that fear of side effects and fear of effect on cancer therapy were the most common factors leading to vaccine hesitancy in cancer patients.[12]

Although some studies have reported clinical features as well as molecular mechanisms of increased risk of mortality and morbidity in COVID-infected cancer patients, there are none that depict the differences in outcomes between the two waves of the pandemic.[13,14]

This is a real-world study aimed at characterizing the differences in demographics, clinical features, treatment details, and outcomes in COVID-19-positive cancer (solid organ malignancies) patients between the two pandemic waves. This is relevant as the second wave was associated with higher infectivity and mortality rates, and knowledge of differences between the two waves may help disaster-preparedness programs and policy making, especially for the cancer affected subgroup of patients, who have been excluded from all drug and vaccine trials.

Materials and Methods

Study Design and Patient Accrual

This was a prospective study of all COVID-19-positive cancer patients (solid organ malignancies) attending our specialty outpatient department at Rajiv Gandhi Cancer Institute and Research Centre between March 2020 and November 2020 (1st wave) and April 2021 and June 2021 (second wave). All patients diagnosed to have COVID-19 by real-time polymerase chain reaction (RT-PCR) with a biopsy proven solid organ malignancy attending the medical oncology out-patient department were included during both the waves. Patients with suspected COVID-19 without a laboratory confirmation were excluded, irrespective of COVID-19-like symptoms. The clinical features, treatment details, and outcomes were retrieved from the medical record archives of the hospital. All consecutive cases presenting to the OPD, irrespective of age, gender, and type of malignancy were included in this study, and hence, no formal sample size calculation was done. This study has been carried out in accordance with the Declaration of Helsinki and has received approval from the Institutional Ethics Committee and Review Board.

COVID-19 RT-PCR Testing

COVID-19 was confirmed using real-time polymerase chain reaction (RT-PCR)/cartridge-based nucleic acid amplification (CBNAAT) on upper respiratory tract swab specimens (nasopharyngeal and nasal swabs) collected in viral transport media (Biogenix, Lucknow-226012, Uttar Pradesh, India). Samples for RT-PCR were tested using the TruPCR RT-PCR Kit (TRUPCR-3B BLACKBIO Biotech; Govindpura, Bhopal, Madhya Pradesh 462023, India) and were run on QuantStudioTM 5 Real-Time PCR System (Thermo-Fisher Scientific- Life Technologies Holdings Pvt. Ltd., Block 33, Marsiling Industrial Estate Road 3, Singapore 739256). The tests were done as per manufacturer recommendations and protocols and interpreted by expert personnel. The CBNAAT was performed using Cepheid, USA, Sunnyvale, CA 94089, United States (GeneXpert assay).

Study Duration and Follow-Up

The patients were followed up regularly (either via teleconsultation or telephonically), or in-person at the outpatient facility, at monthly intervals until December 31, 2021. The end points reported included case fatality rate, hospital admission frequency, and frequency of respiratory complications in both the cohorts.

Statistical Analysis

All statistical analysis were performed using the MedCalc Statistical Software version 19.4.0 (Ostend, Belgium). Continuous variables have been depicted using mean ± standard deviation (SD) and median wherever applicable. The categorical variables have been depicted in frequencies and percentages. Comparison of continuous variables was done using independent *t*-test, whereas for categorical variables Fisher's exact test and Chi-square tests were employed. Univariate and multivariate logistic regression were done to compute odds ratio after adjusting for confounding variables such as age and sex.

Results

A total of 300 patients of solid organ malignancies with proven SARS-CoV-2 infection by either RT-PCR or CBNAAT were encountered, of which 123 were encountered during

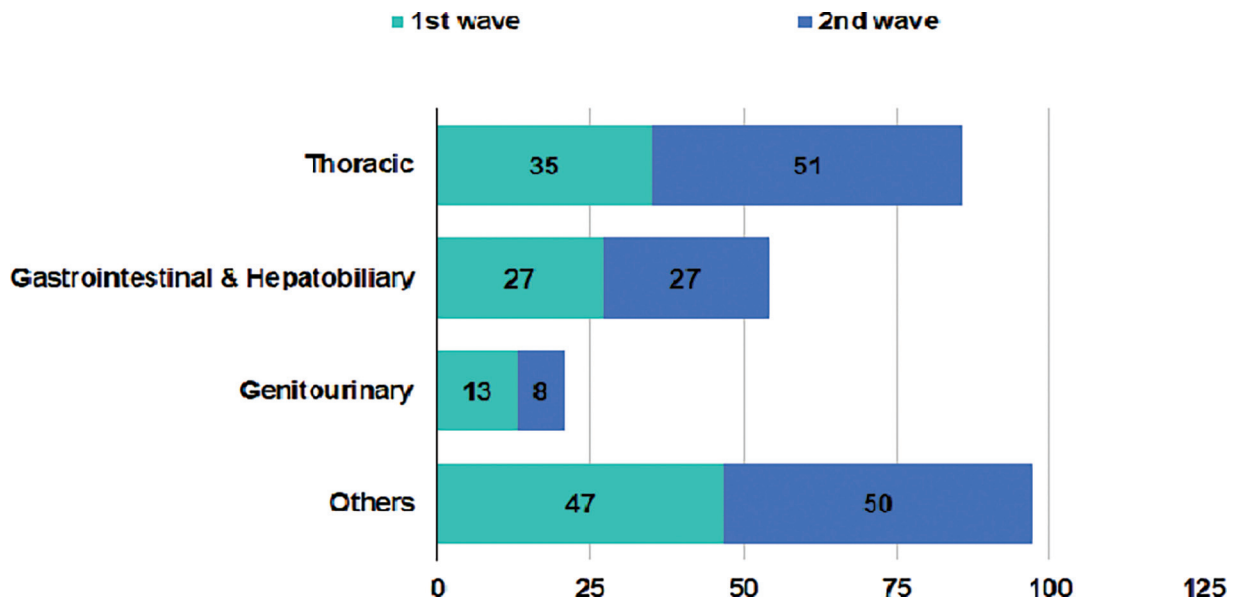

Fig. 1 Bar diagram depicting distribution of cancer types in 1st and 2nd waves.

the first wave of the pandemic and 177 during the second wave. The types of malignancies is depicted in ►Fig. 1.

First Wave Characteristics

The first wave of COVID-19 in India peaked from March 2020 to November 2020,[15] during which 123 known cancer patients were detected to be positive. The median age of these patients was 58 years (28–60 years), with a male predilection (male:female-1.2:1). The most common malignancy was of the lungs in 37 (30.1%) patients, followed by GIT in 27 (21.9%) and breast carcinoma in 23 (18.7%) patients. Other sites included head and neck, bone and soft tissue, female genital system, and others. The details of the same are depicted in ►Table 1. Of the 123 patients, 20 (16.3%) patients had diabetes mellitus and 28 (22.8%) had hypertension. With respect to cancer-directed therapy, 42 (34.1%) patients were being offered cytotoxic chemotherapy within 1 month of acquiring the COVID-19 infection. Of the 123 patients, 25 (20.3%) patients were admitted due to COVID-19 disease, of which 17 (68%) patients were admitted to the ward and 8 (32%) required intensive care. Respiratory complications in the form of acute respiratory distress syndrome (ARDS) and pneumonia were observed in eight and two patients, respectively, with only one patient of ARDS requiring mechanical ventilatory support. Cancer-directed therapy was therefore withheld in these patients, who later succumbed to COVID-19 disease.

Table 1 Characteristics of both waves

Patient characteristics	First wave ($n = 123$) (%)	Second wave ($n = 177$) (%)
Age-median (range)	58 (26-80)	55 (26-87)
Gender		
• Male • Female	66 (53.6) 57 (46.4)	95 (53.6) 82 (46.4)
Cancer site		
• Lung • Breast • GIT • Bone and soft tissue • Head and neck • FGT • Others	37 (30.1) 23 (18.7) 27 (21.9) 5 (4.1) 6 (4.9) 9 (7.3) 16 (13)	64 (36.2) 46 (26.1) 20 (11.2) 4 (2.3) 10 (5.6) 8 (4.5) 25 (14.1)
Co-morbidities		
• DM • HTN	20 (16.3) 28 (22.8)	35 (19.8) 28 (15.8)
Smoking		
• Yes	30 (24.4)	32 (18.1)

Abbreviations: DM, diabetes mellitus; FGT, female genital tract; GIT, gastrointestinal tract; HTN, hypertension.

Second Wave Characteristics

The second wave of COVID-19 in India peaked from April 2021 to June 2021,[15] during which 177 known cancer patients were detected to be positive. The median age was 55 years (26–87 years) with a male predilection (male: female-1.15:1). The most common malignancy was of the lungs in 64 (36.2%) cases, followed by carcinoma breast in 46 (26.1%) patients and GIT in 20 (11.2%) patients. Of the 177 patients, 35 (19.8%) had diabetes mellitus and 28 (15.8%) patients had hypertension. With respect to cancer-directed therapy, 70 (39.5%) patients were being offered cytotoxic chemotherapy within 1 month of acquiring the COVID-19 infection. Of the 177 patients, 44 (21.5%) patients were admitted due to COVID-19 disease, of which 34 (77.3%) patients were admitted to the ward and 10 (22.7%) required intensive care. Respiratory complications in the form of ARDS and pneumonia were observed in 19 and 8 patients, respectively, with 2 patients of ARDS and 1 patient of pneumonia requiring mechanical ventilation support. Cancer-directed therapy was therefore withheld in these patients, who later succumbed to the COVID-19 disease.

Table 2 Comparison of characteristics of both waves

Patient characteristics	First wave ($n = 123$) (%)	Second wave ($n = 177$) (%)	*P*-value
Age-median (range)	58 (26–80)	55 (26–87)	0.9
Gender			0.6
• Male • Female	66 (53.6) 57 (46.4)	95 (53.6) 82 (46.4)	
Co-morbidities			0.3
• DM • HTN	20 (16.3) 28 (22.8)	35 (19.8) 28 (15.8)	
Smoking			0.4
• Yes	30 (24.4)	32 (18.1)	
Chemotherapy			0.5
• Yes • No	42 (34.1) 81 (65.9)	70 (39.5) 107 (60.5)	
Death			0.08
• COVID • Cancer	12 (9.8) 5 (4.1)	23 (13.1) 11 (6.2)	

Abbreviations: DM, diabetes mellitus; HTN, hypertension.

Case Fatality Rate and Comparison of Characteristics of Deceased Patients of both Waves

The case fatality rate of the first wave was 9.8%, with a 15-day case fatality rate of 5.6%, whereas for the second wave, it was 13.1% and 7.2%, respectively. Twelve patients succumbed to the COVID-19 disease in the first wave and 23 succumbed in the second. A comparison of clinical characteristics of these is depicted in ►Table 2. There were no statistically significant correlations; however, the death in the second wave tended to occur more in younger male patients, with comorbidities and history of smoking (►Table 3). There was no relation with ongoing cancer-directed treatment or chemotherapy.

Discussion

This was a prospective single-center, single-specialty study characterizing the differences between the first wave of the COVID-19 pandemic and the dreadful second wave in cancer patients. The second wave showed a higher CFR, hospital admission rate, and higher frequency of respiratory complications. Nationwide lockdown and severity of COVID-19 disease reduced the number of patients opting for cancer-targeted therapies. Although guidelines and recommendations were laid for approach toward tumors with curative intent versus palliative; however, reduced patient attendance to the clinic

Table 3 Comparison of COVID-related deaths in both waves

Patient characteristics	First wave ($n = 12$) (%)	Second-wave ($n = 23$) (%)	*P*-value
Age-median	63	55	0.7
Gender			0.09
• Male • Female	7 (58.3) 5 (41.7)	18 (78.3) 5 (21.7)	
Co-morbidities			0.12
• DM • HTN	3 (25) 4 (33.3)	3 (13) 3 (13)	
Smoking			0.3
• Yes	2 (16.7)	6 (26.1)	
Chemotherapy			0.8
• Yes • No	5 (41.7) 7 (58.3)	8 (34.8) 15 (65.2)	
Other cancer therapy			0.7
• Yes • No	0 7 (58.3)	3 (13) 12 (52.2)	

Abbreviations: DM, diabetes mellitus; HTN, hypertension.

deferred therapy in many.[2] In our study, however, for those enrolled, therapy was not deferred except for those with severe COVID-19-related complications.

When compared with other real-world experiences of the COVID-19 disease in cancer patients, our study is unique in comparing the characteristics of both waves. The most common malignancy encountered in our study was of the lungs followed by GIT and breast, which conforms with contemporary studies by Roy et al and CCC-19 literature,[7,16] however differs from the UK Coronavirus Cancer Monitoring Project (UKCCMP) data.[17]

The case fatality rate in an unselected Indian population was 1.9%[8]; however, in cancer patients, it was reported to be 6.5% in the first wave from a study in cancer patients in India.[18] Another study from India on cancer patients reported a CFR of 14.5%.[8] Our study reported a CFR of 9.8% in the first wave and 13% in the second wave. This partly conforms to the contemporary studies from India, as well as that reported by Ma et al (CFR-13.5%),[19] whereas the CFR is substantially lower than reported literature from the UK CCMP data (28%) and published literature from the United States (25–28%).[20,21] The lower CFR may be attributed to exclusion of hematologic malignancies where reported CFR is the maximum,[22] racial disparities and majority of the patients had mild disease not requiring hospitalization. Similar to other contemporary reports, and MSKCC[20] and UKCCMP data,[23] there was no relation of mortality with cancer directed therapy in this study as well.

There have been many reports in the form of reviews and meta-analyses comparing both wave characteristics; however, there was only one real-world study from Reus, Spain, in unselected patients.[24] This study reported a higher incidence in babies and pregnant women in the second wave, and cancer patients were not analyzed separately. In our study, the CFR was distinctly higher in the second wave, in concordance with other real-world reported literature of Delta virus outbreak although our study could not analyze severity categories and treatment-related outcomes. The vaccination status of our patients has already been published and hence is not reiterated here.[11]

Our study is unique in comparing characteristics of the two most important COVID-19 waves and treatment patterns in cancer patients from a single center. However, there are a few limitations. Multivariate analyses and Cox's regression could not be performed owing to non-significant variables in the univariate analysis. The severity scoring of COVID-19 infection and COVID-19 directed therapy could not be performed owing to missing data points for severity scoring and very few numbers in remdesivir and immunological treatment groups ($n = 1$ each).

The third wave of the pandemic was not analyzed, owing to lesser hospital admissions, and attendance during the same, which would lead to underestimation of the cases. Additionally, this is a single center study with a small sample size, and does not represent a geographical area; therefore conclusions drawn should be interpreted cautiously. However, the information presented here is relevant for the oncology fraternity that despite differences in genomic variants of SARS-CoV-2, cancer-directed therapy had no relation to case fatality or mortality. This is important for treating oncologists to continue cancer-directed treatment even in concurrent COVID-19 infections.

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Conflict of Interest
None declared.

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