



COVID-19 in Cancer Patients From New York City: A Comparative Single Center Retrospective Analysis

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Preethi Ramachandran, MD, MRCP, FRCPath¹ ,
Balachandar Kathirvelu, MBBS, PhD², Abhishek Chakraborti, MD³,
Mahesh Gajendran, MD, MPH, FACP⁴, Umar Zhahid, MD⁵,
Snigdha Ghanta, MD³, Ifeanyichkwu Onukogu, MD³, Joshua Tetteh Narh, MD³,
Jen C. Wang, MD⁶, and Faiz Anwer, MD, FACP⁷ 

Abstract

In this retrospective study we analyze and compare clinical characteristics and outcomes of patients with and without cancer history who were infected with novel coronavirus disease 19 (COVID-19). Medical records were reviewed and a comparative analysis of 53 cancer and 135 non-cancer patients with COVID-19 were summarized. Results: The median age for COVID-19 patients with and without cancer was 71.5 and 61.6 years, respectively. Patients aged 60 years and above were 86.8% and 60.7% in cancer and non-cancer groups, respectively. A high proportion of cases were seen in African Americans 73.6% (with cancer) and 75.6% (without cancer) followed by Hispanic patients. Male and female patients had a high percentage of prostate (39.3%) and breast (32%) cancer respectively. Prostate cancer (18.9%) and myeloma (11.3%) were common among solid and hematological cancers respectively. Hypertension and smoking were prevalent among cancer (83% and 41.5%) compared to non-cancer (67.4% and 9.6%) patients. The common symptoms in cancer patients were dyspnea (64.2%) followed by fever and cough (50.9%) compared to fever (68.1%) and cough (66.7%) in non-cancer patients. Cancer patients had higher levels of lactic acidosis, C-reactive protein, lactate dehydrogenase, and alkaline phosphatase than non-cancer patients ($p < 0.05$). Conclusions: Rapid clinical deterioration was seen in cancer patients who were aged 60 years and above. Higher mortality was seen in this subgroup, especially when they had associated hypertension and elevated levels of CRP and LDH.

Keywords

cancer, COVID-19, mortality, SARS-CoV-2, retrospective, risk factors

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¹ Department of Hematology and Oncology, Brookdale University Hospital and Medical Center, Brooklyn, NY, USA

² Rehabilitation Sciences, The University of Texas at El Paso, El Paso, TX, USA

³ Department of Internal Medicine, Brookdale University Hospital and Medical Center, Brooklyn, NY, USA

⁴ Department of Internal Medicine, Paul L. Foster School of Medicine, Texas Tech University, El Paso, TX, USA

⁵ Department of Nephrology, Brookdale University Hospital and Medical Center, Brooklyn, NY, USA

⁶ New York Medical College, Hematology/Oncology research laboratory, Brookdale University Hospital and Medical Center, Brooklyn, NY, USA

⁷ Tausig Cancer Center, Hematology/Oncology, Stem Cell Transplantation, Cleveland Clinic, Cleveland, OH, USA

Corresponding Author:

Preethi Ramachandran, MD, MRCP, FRCPath, Department of Hematology and Oncology, Brookdale University Hospital and Medical Center, Brooklyn, NY 11212, USA.

Email: drpreethiram@hotmail.com



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Introduction

The outbreak of coronavirus disease 2019 (COVID-19) arising from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection become a global health crisis unlike any in recent history. There have been 5,304,772 cases of SARS-CoV-2 virus cases as of May 25th, 2020 globally with 270,404 deaths of which 28,978 have been in New York state, the epicenter of coronavirus outbreak in the USA. The WHO declared this a public health emergency of international concern and the disease was named Coronavirus disease 2019 (COVID-19). COVID-19 has a high infectious rate and not much information is known on how this disease targets patients who have cancer and on immunosuppressants, information is especially scarce for local NY state patients. Few studies have shown the rate of spread of COVID-19 and its propensity to cause severe damage to a subpopulation.¹⁻³ We decided to analyze cancer patients admitted to our teaching hospital in Brooklyn, New York to estimate disease risk in cancer patients. Cancer patients, by the nature of the underlying disease and being on immunosuppressive therapies are often immunocompromised and are susceptible to infection.¹ A study from China of 28 patients with cancer and COVID-19 disease showed them to be at risk of severe disease and poor outcomes.² Similarly, a report investigating 72,314 cases from the Chinese center for disease control and prevention showed an overall case-fatality rate (CFR) of 2.3% among COVID-19 confirmed cases in comparison to CFR of 5.6% in patients with preexisting cancer, showing a high vulnerability in cancer patients.⁴ The current literature review shows a few case studies and reports on COVID-19 patients with cancer from NY with limited information on their clinical course, prognostic indicators, and their progress during the illness. We aim to analyze the clinical characteristics of cancer patients with COVID-19 and compare the differences with the non-cancer group to identify risk factors that will help stratify patients and potentially open doors for early and effective interventions for better outcomes in cancer patients.

Methods

Setting

Retrospective data from 725 consecutive admitted patients who were COVID-19 positive was collected from Brookdale University Hospital and Medical Center, New York, a regional tertiary care center covering the underserved population of East Brooklyn with the predominantly African American population. Data was collected from March 18 to April 30, 2020. All adult patients more than 18 years old, admitted to Brookdale Hospital with COVID-19 infection as evidenced by laboratory confirmation by RT-PCR were included in the study. We identified 53 patients with a history of cancer ($n = 53$) and included the first 135 non-cancer patients admitted with COVID-19 as a comparison group to investigate the clinical characteristics between cancer and non-cancer groups. We collected epidemiological, demographics, clinical presentation, laboratory

values, and outcome data in addition to their cancer history. The study was approved by the IRB Committee of Brookdale University Hospital and Medical Center.

Statistical Methods

Statistical analysis was performed using IBM SPSS software version 26 (SPSS Inc, Armonk, NY). Descriptive summary statistics are presented as means with standard deviation (SD) for normally distributed continuous variables, median with interquartile range (IQR) for non-normally distributed continuous variables, and frequencies with percentages for categorical variables. Categorical and continuous variables were tested for statistical significance using chi-square tests and t-tests or non-parametric tests, respectively. Multivariate analysis by Cox regression was performed to identify factors independently associated with inpatient mortality. The predictors were considered statistically significant in the multivariate model at $P < 0.05$.

Results

Demographic and Clinical Characteristics

The average age for COVID-19 patients with and without cancer was 71.5 and 61.6, respectively with a significant difference in the age group ($p \leq 0.001$). COVID-19 patients with and without cancer who were 60 years and above were 86.8% and 60.7%, respectively with a significant difference ($p = 0.001$). Irrespective of patients with or without cancer, the COVID-19 was seen more frequently in the population above 60 years. There is no significant difference in gender across COVID-19 patients irrespective of cancer status. In the inpatient cohort, high frequency was seen in African Americans 73.6% (with cancer) and 75.6% (without cancer) followed by the Hispanic population 13.2% (with cancer) and 8.9% (without cancer), respectively. The frequency was less than 5% in the Asian and Caucasians (Figure 1A and Table 1).

The most common COVID-19 presenting symptoms in cancer patients were dyspnea (64.2%) followed by fever and cough (50.9%), fatigue (34%), and myalgia (26.4%), whereas in patients without cancer symptoms were fever (68.1%), cough (66.7%), dyspnea (65.9%), fatigue (53.3%) and myalgia (40%). More COVID-19 patients without cancer showed symptoms of fever and fatigue compared to patients with cancer. Cough is the second most common symptom in both cancer and non-cancer patients, indicative of a clinical symptom that is the involved organ as well as in the mode of transmission.

Hypertension (HT) was the most frequently reported comorbidity in COVID-19 patients, documented in 83% and 67.4% in patients with and without cancer, respectively. Though HT was commonly seen in both groups, COVID-19 patients with cancer showed a significantly higher association with HT in comparison to patients without cancer ($p = 0.047$). Smoking history was frequent in COVID-19 patients with cancer (41.5%) in

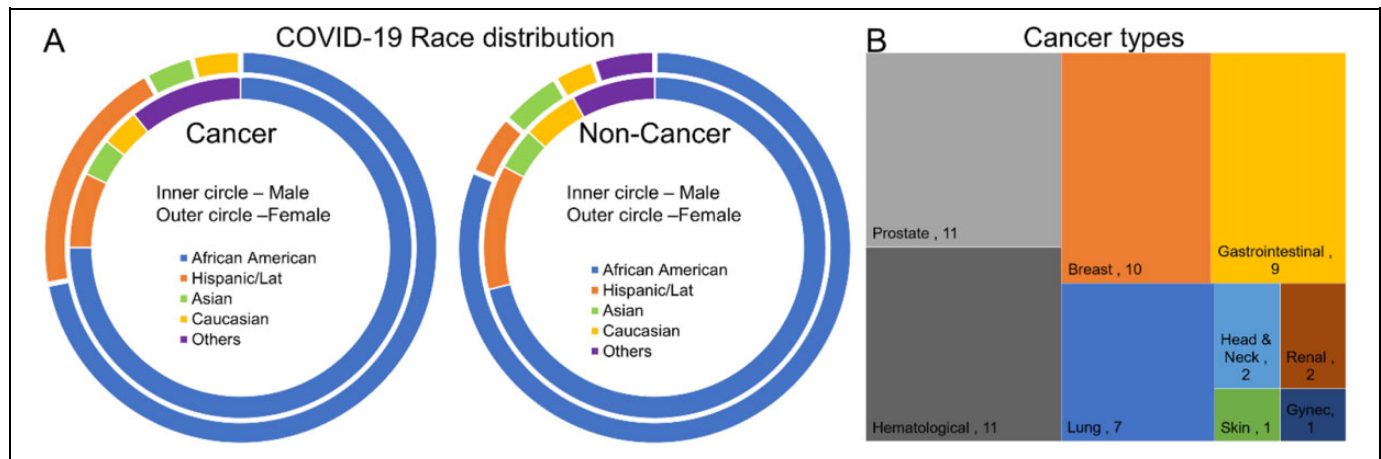


Figure 1. Race distribution in cancer and non-cancer patients (A) different types of cancer (B).

Table 1. Demographic and Baseline Clinical Characteristics of COVID-19 Patients With and Without Cancer.

Characteristic	COVID-19 patients without Cancer n = 135		COVID-19 patients with Cancer n = 53		P value
Age, mean (SD)	61.6	(15.5)	71.5	(10.0)	<0.001
Age, median (IQR)	63	(52, 73)	74	(63.5,77)	<0.001
Age >60 years	82	(60.7)	46	(86.8)	<0.001
Female gender	59	(43.7)	25	(47.2)	0.75
BMI, median (IQR)	29	(25.8, 34.9)	27.4	(24.2, 34.3)	0.46
Race	n	%	n	%	
White	6	4.4	2	3.8	
African American	102	75.6	39	73.6	
Hispanic	12	8.9	7	13.2	
Asian	6	4.4	2	1.1	
Unknown	9	6.7	3	5.7	
Comorbidities					
Hypertension	91	67.4	44	83.0	0.047
Dyslipidemia	48	35.6	11	20.8	0.056
CAD	26	19.3	10	18.9	1
DM	58	43.0	19	35.8	0.41
COPD	12	8.9	5	9.4	1
Smoker	13	9.6	22	41.5	<0.001
Medications					
ACEI/ARB	41	30.4	23	43.4	0.12
NSAID	32	23.7	5	9.4	0.03
Aspirin	45	33.3	19	35.8	0.74
Statin	63	46.7	18	34.0	0.14
Symptoms					
Cough	90	66.7	27	50.9	0.07
Fever	92	68.1	27	50.9	0.03
Dyspnea	89	65.9	34	64.2	0.87
Fatigue	72	53.3	18	34.0	0.02
Myalgia	54	40.0	14	26.4	0.09
GI symptom	27	20.0	6	11.3	0.2

SD = Standard deviation; IQR = interquartile range; BMI = Body mass index; CAD = Coronary artery disease; DM = Diabetes mellitus; COPD = Chronic obstructive pulmonary disease; ACEI = Angiotensin converting enzyme inhibitor; ARB = Angiotensin receptor blocking.

comparison to patients without cancer (9.6%). In terms of medication, NSAIDs was used significantly higher in COVID-19 patients without cancer (23.7%) in comparison with cancer patients (9.4%) (p = 0.03).

Cancer Characteristics

The percentage of COVID-19 infection in cancer patients above and below 60 years was 86.6% (n = 46) and 13.2% (n

Table 2. Blood Group Types and Mortality in COVID-19 Cancer Patients.

Blood group	COVID-19 patients with cancer n = 53		Mortality (overall)	
	N	%	n	%
A+	14	26.4	9	17.0
O+	12	22.6	10	18.9
B+	5	9.4	2	3.8
AB+	2	3.8	1	1.9
A-	1	1.9	0	0.0
AB-	1	1.9	1	1.9
B-	1	1.9	0	0.0
Not known	17	32.1	9	17.0

= 7), respectively. Gender distribution showed a male preponderance (52.8%, n = 28). Blood group data from COVID-19 patients revealed a 26.4% of type A+ blood group with a mortality of 17% followed by O+ (22.6%) with mortality of 18.9%. Table 2. The percentage of solid organ and hematological cancers were 77% and 20%, respectively. Among those who had solid cancers, prostate cancer was the most common (n = 10, 18.9%) followed by breast cancer (n = 8, 15.1%). Myeloma was the most common type of malignancy (n = 6, 11.3%) among hematological cancer. The mortality rate in cancer patients were 60.4% with solid tumor patients contributing to 49% (n = 26) followed by hematological cancers (n = 6, 11.3%). The current and the past cancer treatment for each tumor type were summarized in Table 3. The mortality rate in cancer patients who have aged above and below 60 years were (n = 28, 52.8%) and (n = 4, 7.5%), respectively. Similarly, cancer remission (n = 14, 26.4%) is seen more in patients aged above 60 years whereas cancer non-remission (n = 3, 5.6%) was seen more in patients aged below 60 years. Older age was an important poor prognostic factor irrespective of cancer status, whereas active cancer status was a poor prognostic predictor in patients younger than 60 years old. Figure 1B and Table 3.

Laboratory Data

The median value for hemoglobin was 11.8 and 13.2 gm/dl in COVID-19 patients with and without cancer, respectively. The level of hemoglobin was significantly lower in cancer patients compared to patients without cancer (p = 0.04).

On comparing patients with cancer and COVID 19 and those without cancer, the other laboratory parameters which showed statistically significant differences were lactic acidosis [M 1.9 mmol/L (IQR 1.6-3.2) vs M 1.6 mmol/L (IQR 1.2-2); p < 0.05], elevated C-reactive protein(CRP) [M 20 mg/dL (IQR 7.3-26) vs M 7.4 mg/dL (IQR 4.3-18); p < 0.05] and elevated lactate dehydrogenase (LD) [M 1168 IU/L (IQR 888-1782) vs M 972 IU/L (IQR 734-1359); p < 0.05].

On analyzing liver enzyme levels, the difference in alkaline phosphatase levels (ALP) and alanine aminotransferase (ALT) levels between the 2 groups were noted to be statistically

significant [cancer vs non-cancer: (ALP) M 82.5 U/L (IQR 68-129) vs M 73 U/L (58.5-88); p < 0.05 and (ALT) M 32.5 U/L (IQR 23.3-47.8) vs M 40 U/L (IQR 28-58); p < 0.05]. Significant ALP elevation in cancer patients and ALT elevation in non-cancer patients may be due to the metastatic propensity of cancer in addition to the liver damage caused by COVID-19 disease. Other lab parameters were comparable between the 2 groups and details are listed in Table 4.

Outcome Data

COVID-19 cancer patients had a higher mortality rate (60.4%) in comparison to patients without cancer (36.3%) with statistical significance reaching a p = 0.02 Table 4. Multivariable cox regression analysis showed that the presence of cancer was significantly associated with increased risk of mortality when accounting for other variables including age (Hazard Ratio 2.3, 95% CI 1.2-4.5) Table 5. The median length of stay in cancer patients (5days) is significantly lower in comparison to patients without cancer (7days) (p ≤ 0.001). Similarly, the use of mechanical ventilation is significantly lower in cancer patients (9.4%) in comparison to non-cancer patients (26.7%) in Table 4.

Discussion

Cancer patients face unique challenges in terms of being susceptible to infections given their immunocompromised state attributed both due to cancer itself and from cancer therapies.^{5,6} Our study describes the clinical characteristics and outcomes of 53 cancer patients with COVID-19 and compared the differences with 135 non-cancer patients with COVID-19 infection.

Both cancer and non-cancer groups of patients with COVID-19 had a wide range of symptoms at presentation, including dyspnea, fever, cough, fatigue, myalgia, and gastrointestinal symptoms (nausea, vomiting, diarrhea). Based on data available so far, the most common presenting symptoms in patients likely to present with COVID-19 were fever and cough.⁷ Our data showed symptoms of fever and fatigue are significantly higher in non-cancer patients in comparison to cancer patients (p < 0.05) whereas cough and dyspnea showed no statistical difference in their presentation between the same group. This shows the clinical symptoms in cancer patients might be different compared to non-cancer patients, indicative of different requirements in the screening procedures. Also, effective screening methods may decrease viral transmission, particularly from asymptomatic COVID-19 patients.⁸ The mechanism of SARS-CoV-2 infection involves the virus binding with the cell membrane-bound (Angiotensin Converting Enzyme-2) ACE-2 receptor followed by internalization of the complex.⁹ The ACE-2 receptor is widely distributed in the lungs, heart, kidneys, brain, and gut, providing a rationale for the wide variety of symptomatology noted in our study population.

Analysis of comorbidities showed a striking prevalence of hypertension in patients with cancer and SARS-CoV-2

Table 4. Laboratory Values and Outcome in COVID-19 Patients With and Without Cancer.

Characteristic	COVID-19 patients without Cancer n = 135		COVID-19 patients with Cancer n = 53		P value
	Median	IQR	Median	IQR	
Hemoglobin	13.2	11.7, 14.3	11.8	10.3, 13.6	0.04
Ferritin	490	159, 1120	498	229, 1190	0.91
D-dimer	706	229, 3289	1680	339, 10367	0.23
WBC	6.4	5.1, 8.3	8.5	5.3, 12.4	0.11
Lymphocyte count	1	0.7, 1.3	0.9	0.6, 1.3	0.52
Creatinine	1.2	0.8, 1.8	1.2	0.8, 2.6	0.95
CPK	207	110.5, 464	188	53, 255	1
Lactate	1.6	1.2, 2	1.9	1.6, 3.2	0.003
LDH	972	734, 1359	1168	888, 1782	0.03
CRP	7.4	4.3, 18	20	7.3, 26	0.009
Bilirubin	0.6	0.4, 0.9	0.7	0.5, 1.1	0.42
Alkaline Phosphatase	73	58.5, 88	82.5	68, 129	0.02
AST	49	36, 77	43	34, 68	0.19
ALT	40	28, 58	32.5	23.3, 47.8	0.047
Platelets	193	155, 243	212	142.5, 271	0.87
Length of stay	Median	IQR	Median	IQR	
	7	5, 10	5	3, 7	0.001
	n	%	n	%	
Died	49	36.3	32	60.4	0.02
Mechanical Ventilation	36	26.7	5	9.4	0.01
Shock	39	28.9	12	22.6	0.47

IQR = Interquartile range; WBC = White Blood cells; CPK = Creatine phosphokinase; LDH = Lactate dehydrogenase; CRP = C-reactive protein; AST = Aspartate aminotransferase; ALT = Alanine aminotransferase.

Table 5. Association of Cancer and Other Variables With Mortality in COVID-19 Patients by Using Cox Regression Analysis.

Variable	Hazard Ratio	95% Confidence Interval		P value
		Lower	Upper	
Cancer	2.28	1.15	4.54	0.018
Age >60 years	1.18	0.51	2.73	0.705
Hypertension	0.90	0.44	1.82	0.766
Smoking	1.28	0.64	2.54	0.487
Hemoglobin (admission)	1.01	0.86	1.19	0.902
Lactate (admission)	0.97	0.84	1.13	0.731
C-reactive protein (admission)	1.02	0.97	1.06	0.456
Alkaline Phosphatase (admission)	1.00	1.00	1.01	0.666

infection compared to the non-cancer patients [44 (83%) vs 91 (67.4%); $p < 0.05$]. Studies have shown that among patients with COVID-19, patients with comorbidities had poorer clinical outcomes than patients without comorbidities.^{3,10-14} On analyzing specific comorbidities, research has shown that hypertension is most associated with the occurrence of severe disease in patients with COVID-19.¹⁵ The correlation between hypertension and ACE-2 receptor expression has been studied¹⁶ and provides clinical insight for patients with hypertension developing more severe disease. The difference in the

prevalence of smokers in the cancer group was higher compared to the non-cancer group [41.5% vs 9.6%; $p < 0.001$]. It is known that smoking upregulates the expression of ACE-2 receptors and novel methods of nicotine consumption including electronic cigarettes may do the same.¹⁷ The clinical significance of smoking status to outcomes in COVID 19 disease is poorly understood and requires further research.

There is a dearth of research data comparing laboratory parameters between COVID-19 patients with and without cancer. Our study was able to identify several key differences between the 2 groups. As described in Table 4, higher blood levels of lactic acid, LDH, CRP, and ALP were seen in patients with cancer compared to those without cancer. We also noted lower hemoglobin and ALT levels in cancer patients compared to their counterparts. The lower hemoglobin may be due to the myelosuppressive effects of cancer therapy and the significantly lower hemoglobin may be the reason why cancer patients showed dyspnea as the number one complaint, due to poor oxygenation. Multiple studies have shown that COVID 19 patients present with higher levels of LDH, CRP, AST, ALT, and lymphopenia.^{7,18,19} Higher LDH and CRP levels are associated with more severe forms of SARS-COV-2 infections and are harbingers of poor outcomes in terms of mortality and morbidity.^{15,20,21}

Given that our study showed patients with cancer and COVID-19 have 2.1 times the risk of mortality than patients

without cancer [HR 2.09; $p < 0.05$], we emphasize the necessity to trend levels of LDH and CRP on a daily basis to identify patients who require pre-emptive escalation of care to avoid negative outcomes. We echo the sentiment expressed by Liang et al that cancer patients with COVID-19 warrant more intensive care as they are at risk of rapid deterioration.¹ Notably, our study found that in our cancer patients, mortality was higher in those older than 60 years of age compared to those less than 60 [52.8% vs 7.5%]. The higher mortality in cancer patients might be due to several reasons but the laboratory data showed elevated levels of inflammatory and enzyme markers of tissue damage leading to poor oxygenation and outcome. Interestingly, 14 (26.4%) older patients had their cancer in remission compared to just 3 (5.6%) patients below 60 years of age. In older cancer patients, age appears to be a stronger indicator of mortality while active cancer and treatment status seems to play a bigger role in deciding outcomes for younger patients. These associations require further exploration in future studies. Although studies have shown patients with cancer have a higher risk of mechanical ventilation.¹ Our study noted a significantly lower incidence of mechanical ventilation [9.4% vs 26.7%; $p < 0.05$] and shorter hospital stay [Mn 5 days, IQR 3-7 vs Mn 7 days, IQR 5-10; $p < 0.05$] in COVID-19 cancer patients compared to non-cancer patients. We attribute this difference to the fact that a large proportion of cancer patients admitted during the study period decompensated rapidly (as indicated by the higher levels of LDH and CRP and a higher risk of mortality compared to their non-cancer counterparts) and several patients had advance directives reflecting no-intubation given the nature of their comorbidities.

There are many limitations to our study in that it was based on small sample size, retrospective in nature, the comparison group was arbitrarily selected and the study sample was non-randomized. Further studies with larger sample size, analysis stratified by types of malignancy, prospective studies with larger sample sizes will be needed to shed further light on the matter.

In summary, we recommend closer observation of patients with cancer who have COVID-19, particularly older patients with hypertension and higher levels of CRP and LDH as they are at risk of rapid deterioration and have increased risk of mortality. More extensive surveillance with broad community testing focused on cancer patients would help identify asymptomatic and mild cases who would benefit from regular follow up as outpatients and promote timely intervention prior to progression to more severe disease. We agree with Liang et al¹ and Zhang et al² that immunosuppressive treatment strategies should either be postponed for stable cancer patients or done under vigorous screening strategies for SARS-CoV-2, especially in younger patients in whom immunosuppression from active cancer or active antitumor treatment seems to play a major role in deciding outcomes. Pre-testing all patients with cancer, prior to elective surgeries and antitumor therapy should be explored. Special care should be taken to minimize community exposure to COVID-19 in patients with cancer, which could be accomplished by more stringent guidelines for

personal protective gear for these patients and people in close contact with them. In the early stages of a pandemic, where minimizing community spread is essential, it is imperative we take precautions to prevent our most vulnerable populations from being infected. These measures should result in a significant reduction in overall mortality from SARS-CoV-2 and in patients with cancer.

Authors' Note

IRB approved: Yes.

Author Contributions

Conceptualizations and methodology: PR, JCW. Statistical and data analysis: MG, UZ. Data collection & literature review: SG, IO, JTN, AC. Manuscript Writing, reviewing, and editing PR, BK, JCW, FA.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.


Ethical Approval and Consent

IRB of Brookdale University Hospital and Medical Center, NY approved this study. Reference Number: Protocol 20-12. IRB granted a waiver of informed consent due to the retrospective nature of the study.

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ORCID iDs

Preethi Ramachandran, MD, MRCP, FRCPath  <https://orcid.org/0000-0003-3032-8886>

Faiz Anwer, MD, FACP  <https://orcid.org/0000-0001-6914-7439>

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