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Original Article

Internal Medicine Section

Clinical Profile and Outcomes of COVID-19 Patients with Malignancy: A Cross-sectional Study

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ABSTRACT

Introduction: Patients with history of past or active malignancy are at increased risk of contracting the virus and developing Coronavirus Disease-2019 (COVID-19) related complications. With the global prevalence of cancer and the high transmissibility of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), an understanding of the disease course of COVID-19 and factors influencing clinical outcomes in patients with cancer is necessary and is largely unknown.

Aim: To study the laboratory characteristics of patients with malignancy and COVID-19 infection and to evaluate the outcomes in terms of clinical features, severity of infection and mortality of patients with malignancy and COVID-19 infection.

Materials and Methods: The present study was a cross-sectional study conducted at Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India, involving 72 subjects with COVID-19 infection. The duration of the study was from April 2020 to November 2020. Demographic details and data were collected in patients with active or previous malignancy and COVID-19 illness based on Indian Council of Medical Research (ICMR) criteria. Clinical outcome of the patients was measured based on need for Intensive Care Unit (ICU) admission, oxygen therapy and mortality. Descriptive statistics of the explanatory and outcome variables were calculated as mean, Standard Deviation (SD), median and Interquartile Range (IQR) for quantitative variables, frequency and proportions for qualitative variables. Inferential statistics like Chi-square test was applied for qualitative variables.

Results: The mean age of the subjects was 52.10±14.512 years with 29 males and 43 females. Among 72 patients with malignancy, patients were classified as mild (23), moderate (22) and severe (27) according to ICMR case type, respectively. Among the total patients, 21 (29.2%) were asymptomatic and 51 (70.8%) were symptomatic with 26 (36.1%) symptomatic patients having severe disease. Also, 30 (41.7%) had requirement of Oxygen (O_2) and 28 (38.9%) were admitted to ICU. Most common was solid organ malignancy (66), lung carcinoma (13), breast (10), compared to haematological malignancies (6). A total of 22 (30.6%) patients had mortality with most common complication being Acute Respiratory Distress Syndrome (ARDS) (20.8%) followed by sepsis (4.2%).

Conclusion: The results of present study revealed higher mortality and increased inflammatory markers in patients with severe COVID-19 infection and malignancy.

Keywords: Cancer, Inflammatory markers, Severe acute respiratory syndrome coronavirus-2

INTRODUCTION

The novel coronavirus, also known as SARS-CoV-2 or COVID-19 is a non segmented positive stranded Ribonucleic Acid (RNA) virus with a protein envelope. COVID-19 has become a worldwide threat and international health concern. The rapid human to human transmission of the virus occurs through direct contact with an infected patient by respiratory droplets in the form of coughing or sneezing or indirect contact with fomites in the environment [1,2]. Patients with co-morbid conditions are more susceptible to manifest complications of the viral infections [3]. Studies suggest that patients with a history of or active malignancy might be at an increased risk of contracting the virus and developing COVID-19 related complications [4,5]. These patients are immunocompromised by the effects of antineoplastic therapy, medications such as steroids, augmented immune response to infection secondary to immunomodulatory drugs and the immunosuppressive properties of malignancy itself. Furthermore, older patients with cancer often have one or more co-morbidities, thereby increasing the risk for COVID-19 related morbidity and mortality [5].

With the global prevalence of cancer and the high transmissibility of SARS-CoV-2, understanding of the disease course of COVID-19 and factors influencing clinical outcomes in patients with cancer is necessary. Higher mortality in this population of patients, with the potential to receive curative treatment, has important practical implications for healthcare systems. The present aimed to study the laboratory characteristics of patients with COVID-19 infection and malignancy. To evaluate the outcomes in terms of severity of infection and mortality of patients with COVID-19 infection and malignancy.

MATERIALS AND METHODS

This cross-sectional study was conducted on 72 patients with active or past history of malignancy admitted for COVID-19 illness between April 2020 to November 2020 in Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India. After obtaining ethical approval and clearance (IEC: BMCRI/PS/254/2020-21) from Institutional Ethics Committee (IEC), the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent.

Inclusion criteria: Patients of either sex with age >18 years diagnosed with COVID-19 infection by Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) technique or rapid antigen testing, willing to give informed consent, chest Computed Tomography (CT) findings meeting the standard for diagnosis of COVID-19 and history of current or cured malignancy within past one year were included in the study.

Exclusion criteria: Patients not willing to give informed consent and age less than 18 years were excluded from the study.

Case record was used to record the duration of COVID-19 disease, history of treatment for malignancy and type of malignancy was noted. Patients included those who underwent the following laboratory investigations- Complete Blood Count (CBC), quantitative C-Reactive Protein (CRP), Serum Lactate Dehydrogenase (LDH), D-dimer and serum ferritin. As per ICMR standard regimen guidelines, patients

were classified as mild, moderate and severe COVID-19 illness and followed the same treatment regimen [6]. These patients were further followed-up for outcome measures which included course in hospital, requirement of ICU admission, requirement of oxygen therapy and severity of disease was followed-up until discharge or death.

STATISTICAL ANALYSIS

Descriptive statistics of the explanatory and outcome variables were calculated by mean, SD, median and IQR (based on data distribution) for quantitative variables; frequency and proportions for qualitative variables. Inferential statistics like Chi-square test was applied for qualitative variables. The level of significances set at 5%.

RESULTS

Most of patients in the present study were in between 56-65 years age group i.e., 21 (29.2%). The youngest age encountered was 18 years whereas the oldest patient was 88 years, with mean age of 52.10±14.512 years. Of the 72 patients in the study, 43 (59.7%) patients of the study population were females and 29 (40.3%) were males. The female:male (F:M) ratio is 1.48:1. Co-morbidities associated with the diseases were: 23 patients (31.9%) had diabetes mellitus, followed by hypertension 12 (16.7%), ischaemic heart disease 4 (5.6%), Chronic Obstructive Pulmonary Disease (COPD) 5 (6.9%), 26 patients (36.1%) did not had any co-morbidities in the study [Table/Fig-1].

Variables	ICMR case type			Total n (%)
	Mild (n=23)	Moderate (n=22)	Severe (n=27)	
Age (years)				
18 to 25	0	1	2	3 (4.2)
26 to 35	2	3	2	7 (9.7)
36 to 45	5	2	4	11 (15.3)
46 to 55	7	6	7	20 (27.8)
56 to 65	6	7	8	21 (29.2)
>65	3	3	4	10 (13.8)
Gender				
Female	15	14	14	43 (59.7)
Male	8	8	13	29 (40.3)
Co-morbidities				
Diabetes mellitus	3	10	10	23 (31.9)
Hypertension	7	4	1	12 (16.7)
Ischaemic heart disease	2	0	2	4 (5.6)
COPD	1	3	1	5 (6.9)
Others	1	0	1	2 (2.8)
Nil	9	5	12	26 (36.1)

[Table/Fig-1]: Baseline and clinical characteristics of patients (N=72).

Among 72 patients with malignancy, 27 patients (37.5%) had COVID-19 severe disease, followed by COVID-19 mild disease in 23 patients (31.9%) and 22 patients (30.6%) had COVID-19 moderate disease. Out of 72 patients with malignancy, 21 (29.2%) were asymptomatic and 51 (70.8%) were symptomatic with 26 (36.1%) symptomatic patients having severe disease [Table/Fig-2]. Out of 72 patients with malignancy and COVID-19 infection, 30 patients (41.7%) required oxygen therapy, 28 patients (38.9%) were admitted to ICU and 22 patients (30.6%) expired [Table/Fig-3].

Symptoms	ICMR case type			Total n (%)
	Mild	Moderate	Severe	
Asymptomatic	20	0	1	21 (29.2)
Symptomatic	3	22	26	51 (70.8)

[Table/Fig-2]: Distribution of the subjects based on ICMR case type.

Variables	ICMR case type			Total n (%)	p-value*
	Mild	Moderate	Severe		
O_2 requirement					
No	22	20	0	42 (58.3)	0.001
Yes	1	2	27	30 (41.7)	
ICU admission					
No	22	22	0	44 (61.1)	0.001
Yes	1	0	27	28 (38.9)	
Outcome					
Discharged	23	22	5	50 (69.4)	0.001
Death	0	0	22	22 (30.6)	

[Table/Fig-3]: ICMR case type with clinical outcome and mortality.
*Chi-square test; p-value <0.05 considered significant

[Table/Fig-4] shows the laboratory parameters based on ICMR case type. The mean haemoglobin (gm/dL) in mild, moderate and severe cases was 11.5, 11.2 and 10.33, respectively. The mean Total Leukocyte Count (TLC) (cells/mm^3) in mild, moderate and severe cases were 7017.39, 7963.64 and 13085.19, respectively. The mean neutophil:lymphocyte ratio in mild, moderate and severe cases was 3.3, 4.82 and 9.07, respectively. The mean Lactate Dehydrogenase (LDH) (IU/Litre) in mild, moderate and severe cases were 371.83, 368.55 and 462.78, respectively. The mean D-Dimer (µg/mL) in mild, moderate and severe cases was 1.13, 1.59 and 2.19, respectively. The mean CRP (mg/dL) levels in mild, moderate and severe cases were 19.04, 56.73 and 129.89, respectively. The mean ferritin (µg/L) levels in mild, moderate and severe cases were 555.09, 516.64 and 1348.0 respectively.

Laboratory parameters	Case type	Minimum	Maximum	Mean	Std. deviation
Haemogloin (gm/dL)	Mild	9.0	15.9	11.543	1.6337
	Moderate	8.0	15.0	11.273	1.5486
	Severe	8.0	13.4	10.333	1.7966
Total Leukocyte Count (TLC) (cells/mm^3)	Mild	2800	15900	7017.39	3130.445
	Moderate	3200	15900	7963.64	3904.033
	Severe	2500	25000	13085.19	7090.443
Neutrophils (%)	Mild	40	90	64.78	11.564
	Moderate	53	93	70.95	10.865
	Severe	40	97	75.70	12.892
Lymphocytes (%)	Mild	6	50	25.70	9.359
	Moderate	6	38	20.95	9.634
	Severe	3	50	16.07	11.475
N:L	Mild	1	15	3.30	2.803
	Moderate	1	16	4.82	3.554
	Severe	1	32	9.07	8.508
LDH (IU/L)	Mild	108	911	371.83	202.34
	Moderate	115	911	368.55	200.22
	Severe	139	875	462.78	192.06
D-Dimer (µg/mL)	Mild	0	9	1.13	1.938
	Moderate	0	9	1.59	2.039
	Severe	0	5	2.19	1.442
CRP (mg/dL)	Mild	0	68	19.04	17.35
	Moderate	0	291	56.73	77.53
	Severe	1	1097	129.89	208.83
Ferritin (µg/L)	Mild	10	2000	555.09	577.35
	Moderate	4	2000	516.64	473.68
	Severe	86	2000	1348.00	567.49

[Table/Fig-4]: Mean distribution of the laboratory parameters based on case type.

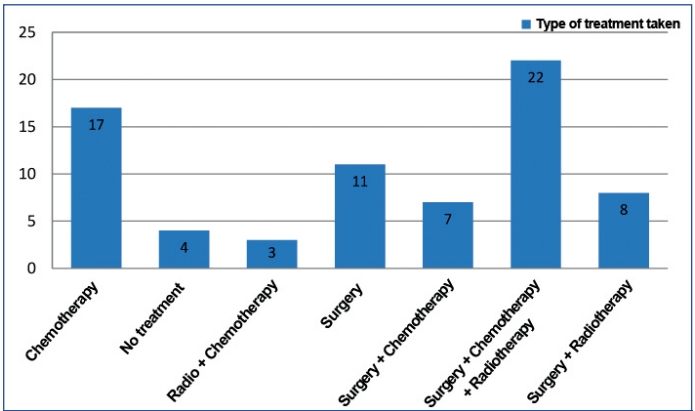
The most common type of malignancy was solid organ type. Of total 72 patients with malignancy, 66 patients (91.7%) had solid organ malignancies and 6 patients (8.3%) had haematological malignancies. Distribution into mild, moderate and severe is shown in [Table/Fig-5]. Most common malignancy in the present study was lung carcinoma (13), followed by breast carcinoma (10) other malignancies are shown in [Table/Fig-6]. Among the 72 patients, 22 patients underwent surgery, chemotherapy and radiotherapy. Seventeen patients were on chemotherapy alone and 11 patients had undergone surgery. Four patients were not currently on any treatment for malignancy [Table/Fig-7]. Among total of 72 patients with malignancy and COVID-19 infection, 22 patients died, with case fatality of 30.6%. The most common cause of death was ARDS 15 (20.8%) followed by sepsis 3 (4.2%) [Table/Fig-8].

Malignancy type	Case type			Total	p-value
	Mild	Moderate	Severe		
Haematological	1 (1.4%)	1 (1.4%)	4 (5.5%)	6 (8.3%)	0.30
Solid organ	22 (30.6%)	21 (29.2%)	23 (31.9%)	66 (91.7%)	

[Table/Fig-5]: Type of malignancy with case type.

Type of solid organ malignancy	Total
Lung	13
Breast	10
Cervix	8
Stomach and colon	6
Ovary	5
Oral	4
Brain	4
Thyroid	3
Larynx	2
Uterine	2
Renal cell carcinoma	2
Others	7

[Table/Fig-6]: Type of solid organ malignancy.



[Table/Fig-7]: Type of treatment taken by patients with malignancy.

Cause of death	Frequency	Percent
Acute coronary syndrome	1	1.4
ARDS	15	20.8
ARDS, MODS	1	1.4
Sepsis	3	4.2
Sepsis, MODS	2	2.8
Total	22	30.6

[Table/Fig-8]: Cause of death of cases.
MODS: Multiorgan dysfunction syndrome

DISCUSSION

This tertiary care hospital-based cross-sectional study was undertaken to study the clinical profile of patients with COVID-19 infection and malignancy. Patients diagnosed with COVID-19 infection by RT-PCR technique or rapid antigen testing or chest CT findings meeting the standard for diagnosis of COVID-19 were included. Other objective was to evaluate in terms of laboratory features, severity of infection and mortality of patients with malignancy and COVID-19 infection.

In the present study, it was observed that 21 (29.2%) patients belonged to 56-65 years of age. Among these patients, severe COVID-19 infection as per ICMR category was seen in eight patients. In a study done by Borah P et al., it was seen that elderly patients with haematological malignancy and severe COVID-19 had worst outcomes [7]. Older patients often have one or more major co-morbidities, putting them at increased risk for COVID-19 related morbidity and mortality. In this study, 43 patients (59.7%) of the study population were females and 29 patients (40.3%) were males. The female:male (F:M) ratio was 1.48:1.

In the present study, 23 patients (31.9%) had diabetes mellitus as the most common co-morbidity, followed by hypertension in 12 patients (16.7%), ischaemic heart disease in four patients (5.6%), COPD in five patients (6.9%). A total of 12 (36.1%) cases had no co-morbidities in present study. In a study done by Kuderer NM et al., higher numbers of co-morbidities were significantly associated with increased mortality [8].Specific co-morbidities are associated with a strong Angiotensin Converting Enzyme-2 (ACE-2) receptor expression and higher release of proprotein convertase thereby enhancing the viral entry into the host cells. The co-morbidities leads to increased risk of infection in COVID-19 patient and are substantially associated with significant morbidity and mortality [9].

Out of the 72 cases, severe COVID-19 disease was most common comprising of 27 patient (37.5%), followed by mild disease in 23 patients (31.9%) and moderate disease in 22 patients (30.6%). It is observed that among 30 patients (41.7%) requiring oxygen therapy, 27 patients (90%) had severe COVID-19 infection. Among 28 patients (38.9%) who were admitted to ICU, 27 patients (96.4%) had severe COVID-19 infection at admission and one patient was admitted with mild COVID-19 infection. There was a statistically significant association between uses of oxygen therapy, ICU stay with severity of the disease ($p<0.001$). According to Salunke AA et al., presence of cancer in COVID-19 leads to higher risk of developing serious disease and has a significant impact on mortality rate in COVID-19 patients. Among a total of 3775 patients, there was a significant ICU requirement rates in cancer patient group compared with non cancer group- 40% versus 8.42%, respectively. The death rate in COVID-19 patients with and without cancer was 20.83% versus 7.82%, respectively [10].

In the present study, 50 (69.4%) patients were discharged and case fatality was seen in 30.6% of cases. In a study done by Zhang L et al., mortality rate was 28.6%, which was similar to the present study [11]. Patients suffering from cancer shows deteriorating conditions and poor outcomes from the COVID-19 infection.

In this study, 66 (91.7%) patients had solid organ malignancies and 6 (8.3%) patients had haematological malignancies. Among the patients with solid organ malignancies, 23 (31.9%) patients had severe COVID-19 infection, 21 patients (29.2%) had moderate COVID-19 infection, 22 patients (30.6%) mild COVID-19 infection respectively. In present study, lung carcinoma was found in 13 cases, followed by breast carcinoma (10), cervical carcinoma (8), stomach and colon malignancies (6). In a study done by Zhang L et al., among the cancer patients, lung cancer was the most frequent type of cancer, followed by oesophageal cancer and breast cancer, which was similar to this study [11].

Twenty two patients underwent surgery, chemotherapy and radiotherapy, 17 patients were on chemotherapy alone and 11 patients

had undergone surgery, whereas, four patients were not currently on any treatment for malignancy. Of these four patients not on treatment, three cases were of severe COVID-19 illness with requirement of ICU and died in the course of treatment due to ARDS. In a retrospective study done by Zhang L et al., six (21.4%) patients had received atleast one kind of antitumour therapy mainly chemotherapy (10.7%), targeted therapy (7.1%), radiotherapy (3.6%), immunotherapy (3.6%) [11]. There could be several reasons for these observations. The immunological disruption observed in patients with malignancies and the use of immunosuppressive treatment regimens might result in a combination of risk factor for COVID-19 infection. Increased susceptibility of these patients to infection and likelihood of severe consequences, such as cytokine storm and multiorgan failure thereby result in poor outcomes in these cases.

In the present study, consisting of 72 patients with malignancy and COVID-19 infection, with case fatality of 30.6%, ARDS was seen in 15 patients (20.8%) followed by sepsis in three patients (4.2%) and sepsis with Multiorgan Dysfunction Syndrome (MODS) in two patients (2.8%) with COVID-19 infection. This was similarly seen in a study done by Calles A et al., 39% of patients developed ARDS, and the case-fatality rate was 35% [12]. In a study done by Kumar R et al., a total of 231 COVID-19 patients were studied, with mean age of 39.8 years [13]. Co-morbidities were present in 21.2%, diabetes and hypertension being the most common. There were no deaths in that study.

In a hospital-based retrospective study done by Dasari D et al., among 299 COVID-19 cases, 55 patients died with case fatality rate was 18.4% [14]. Among the clinical variables, Saturated Oxygen (SpO_2) at the time of admission, having severe disease, oxygen dependency, requirement ofnasal cannula, requirement of Non Invasive Ventilation (NIV), requirement of intubation, and requirement of remdesivir treatment were found to be significantly associated with mortality.

When compared to the above studies without patients with malignancy, the present study had higher mortality rates. Patients with malignancy are immunocompromised by the effects of antineoplastic therapy, medications such as steroids, augmented immune response to infection secondary to immunomodulatory drugs and the immunosuppressive properties of malignancy itself, leading to adverse outcomes. Since, the study was done during first COVID-19 outbreak, protocols were yet to be setup and treatment of COVID-19 patients was a new set challenge.

Limitation(s)

Present study has also some limitations which includes the relatively small sample size that limited our power to draw formal conclusions in predictive factors of mortality. Also, other factors like tumour staging was not included in present study. There was no comparison made with patients without malignancy.

CONCLUSION(S)

This study evaluated the clinical features and outcome of COVID-19 patients with malignancy. With the ongoing pandemic wherein healthcare systems are engaged with the ongoing challenge of managing this infection effectively, patients with malignancy should be screened early for any minor symptoms of COVID-19 infection. Individualised treatment in terms of risk and benefit for active intervention in cancer patients should be considered.

REFERENCES

[1] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382(13):1199-207.
[2] Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, et al. Air, surface environmental, and personal protective equipment contamination by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) from a symptomatic patient. JAMA. 2020;323(16):1610-12.
[3] Guan W, Liang W, Zhao Y, Liang H, Chen Z, Li Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A nationwide analysis. Eur Respir J. 2020;55(5):2000547.
[4] Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. Lancet Oncol. 2020;21:335-37.
[5] Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: A multicenter study during the COVID-19 outbreak. Cancer Discov. 2020;10(6):783-91. Doi: 10.1158/2159–8290.CD-20-0422.
[6] Revised guidelines on management of COVID-19. Available from: https://www.mohfw.gov.in. [Accessed 31st March 2020].
[7] Borah P, Mirgh S, Sharma SK, Bansal S, Dixit A, Dolai TK, et al. Effect of age, comorbidity and remission status on outcome of COVID-19 in patients with hematological malignancies Blood Cells Mol Dis. 2021;87:102525. Available from: http://dx.doi.org/10.1016/j.bcmd.2020.102525.
[8] Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): A cohort study. The Lancet. Elsevier BV; 2020;395:1907-18. Available from: http://dx.doi.org/10.1016/S0140-6736(20)31187-9.
[9] Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K, Abdalla AE, et al. COVID-19 and comorbidities: Deleterious impact on infected patients. Journal of Infection and Public Health. Elsevier BV; 2020;13:1833-39.
[10] Salunke AA, Nandy K, Pathak SK, Shah J, Kamani M, Kottakota V, et al. Impact of COVID-19 in cancer patients on severity of disease and fatal outcomes: A systematic review and meta-analysis. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. Elsevier BV; 2020;14:1431-37. Available from: http://dx.doi.org/10.1016/j.dsx.2020.07.037.
[11] Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. Ann Oncol. 2020;31(7):894-901.
[12] Calles A, Aparicio MI, Alva M, Bringas M, Gutierrez N, Soto J, et al. Outcomes of COVID-19 in patients with lung cancer treated in a tertiary hospital in Madrid. Front Oncol. 2020;10:1777. Doi: 10.3389/fonc.2020.01777.
[13] Kumar R, Bhattacharya B, Meena VP, Aggarwal A, Tripathi M, Soneja M, et al. Characteristics and outcomes of 231 COVID-19 cases admitted at a tertiary facility in India: An observational cohort study. J Family Med Prim Care. 2020;9:6267-72.
[14] Dasari D, Pendurthi AK, Alam KC, Kodithyala PK. Risk factors of mortality among patients with COVID-19: A hospital-based retrospective study. Apollo Med. 2021;18:234-38.

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