ORIGINAL RESEARCH

Scenario of covid-19 in patients with malignancy attending a tertiary care centre in north eastern India

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ABSTRACT

Introduction: The coronavirus disease 2019 (COVID-19) pandemic caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has expanded rapidly worldwide**.** The sudden occurrence of this pandemic of coronavirus disease 2019 (COVID-19) has affected significantly the health-care system all over the country and has developed an unusual menace for the therapeutic management of these at risk group of cancer patients. **Materials and methods:** This retrospective observational hospital based study was done on malignant cases. Real -time Polymerase Chain Reaction was performed for SARS COV- 2 in all these patients. **Results:** Among 164 patients, 58% patients were women and 42% were men. The majority of cases (31.7%) were in the 51-60 years of age group. Co-morbidities like hypertension, hypothyroidism, diabetes mellitus were found in 91% patients. Most of the breast cancer patients suffered from COVID-19 (20.12%), followed by esophageal cancer patients (10.98%). The period of COVID-19 positivity in different types of cancer patients ranged from first week to thirteenth week. On investigating the period of COVID-19 positivity in cancer patients with co morbidities, statistically significant difference were found. **Discussion:** Cancer patients are particularly at higher risk of getting infected with respiratory pathogens because of the immunosuppressive state. Cancer associated elements also appears to play a crucial role in prognosis of patients with cancer. **Conclusion:** Both patient and cancer-related factors has a remarkable part in the course of this disease. All these factors needs to be considered in development of COVID-19 preventative as well as therapeutic strategies in cancer patients to improve the patient care.

Keywords: COVID -19, Malignancy, RT-PCR, SARS-CoV-2

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first identified in Chinese city of Wuhan in December 2019. It has expanded speedily involving many countries globally causing a remarkably disastrous pandemic.[1-3] India reported its first COVID-19 case from the state of Kerala on 30 January 2020.[4] On 31 March 2020, Assam (north-eastern state of India) reported the first case of this COVID-19 pandemic.[5] Generally, most of the COVID-19 patients presents with mild symptoms or with no symptoms over the entire period of this illness. An intermediary category of patients develop moderate symptoms necessitating hospital admission and noninvasive treatment. Another category of patients presents with a very severe form of this infection resulting to lethal sequel or loss of life.[6]

The sudden occurrence of this pandemic of coronavirus disease 2019 (COVID-19) has affected significantly the health-care system all over the country and has developed an unusual menace for the therapeutic management of these at risk group of cancer patients.[7,8] Cancer patients comprise a particular group with increased risks of contracting COVID-19, apparently showing extreme course of the disease and even loss of life.[9-11] These conditions could be associated with different factors like cytotoxic chemotherapy, radiotherapy, use of immunosuppressant drugs, corticosteroids use, aged patients, concurrent diseases and lung engrossment (primary or secondary).[12,13]

Few previously published literatures shows that, the data analyzing the effect of this viral infection in

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cancer patients in relation to the demography, cancer type, stage and the associated comorbidities are still very scarce, incomplete and with diverse sequel. There is also lack of sufficient data related to COVID-19 in malignancy in North Eastern Region of India. Herein, we aim to evaluate the demographic and clinical attributes of cancer patients with RT PCR confirmed COVID- 19 infection, to explore the clinical outcomes in such patients and to assess the relation of the co morbidities if any.

MATERIALS AND METHODS

This single centered, retrospective observational study was conducted in a tertiary care institute in the North eastern region of India for a period of five months from August 2020 to January 2021 after obtaining ethical clearance. The calculated sample size has been estimated to be 164.

All malignant cases with laboratory confirmed RT-PCR for COVID-19 with complete details who approached the hospital during the aforesaid five months were included in the study. Non malignant cases and malignant cases with incomplete details were excluded from the study.

Real -time Polymerase Chain Reaction for SARS COV-2 was done in all these patients from a combination of nasal and oropharyngeal swabs. Both the swab specimens were inoculated in a tube of viral transport medium (Biogenix, Uttar Pradesh, India). Patients who had tested negative in RAT test were further confirmed by the Real Time Polymerase Chain Reaction (RT-PCR).[14,15] We have repeated RT-PCR test until negative viral shedding. Clinical data, course of treatment and outcome were retrieved from the hospital medical records.

RNA EXTRACTION

Conventional manual RNA extraction method was used for extraction of viral RNA by QiagenQIAamp@Viral RNA kits.

Real-Time Reverse Transcription–Polymerase Chain Reaction Assay for SARS-CoV 2

The real-time RT-PCR assay was performed by two steps method for the accurate determination of SARS-CoV-2. In the first step RNA is extracted from the patient samples followed by RT-PCR of these extracted RNA. Appropriate implementation of the whole procedure is important for accurate diagnosis. After extraction of RNA, it is reverse transcribed into complementary DNA (cDNA). With each thermocycling, the number of copies of cDNA doubles. These new cDNA copies are tagged with fluorescent nucleotides and the number of new copies per cycle are detected by this fluorescence. Number of amplification cycles required for the fluorescent signal to exceed the basal threshold level is called the cycle threshold (Ct). Lower cycle threshold (Ct) values signify higher target RNA levels in the patient sample and vice versa.

It is necessary to use controls for ensuring accuracy of the whole procedure. Documenting the results of both control as well as test samples is of paramount importance for its correct diagnosis.

Real Time -PCR system used:

1. Biorad CFX96 Real Time PCR Machine

Real Time -PCR kit used:

1. COVID Sure

(This is a multiplex RT-PCR kit. For screening E gene was tested and for confirmation ORF gene was tested as per the kit's instruction.)

STATISTICAL ANALYSIS

For analyzing the data Minitab version 17.1.0 package (Minitab, LLC, USA) and Rstudio version 1.3.959 (Rstudio, Boston, USA) were used. For comparing the dissimilarity of means among the groups in a univariate analysis, Kruskal-Wallis H test and One-way analysis of variance (ANOVA) were used. The population variation was considered significant at p value <0.05. To check the equality of variances, Levene's test (homogeneity variance test) was done after the ANOVA test. With a view to reach the expectation of homogeneity of variance, the p-value was considered below 0.05 for the Levene's test. Non-metric multidimensional scaling (nMDS) based on Bray-Curtis dissimilarities was constructed for finding the dissimilarities between period of COVID-19 infectivity in different types of cancer patients and in different types of treatments given to the cancer patients.

RESULTS

Demographic details and clinical characteristics

We identified a total of 164 patients with a history of malignancy who were also tested positive for COVID-19 during August 2020 to January 2021. The symptoms included fever, bodyache & generalised weakness, cough, sore throat, diarrhoea, dyspnoea, and respiratory distress (Fig. 1).

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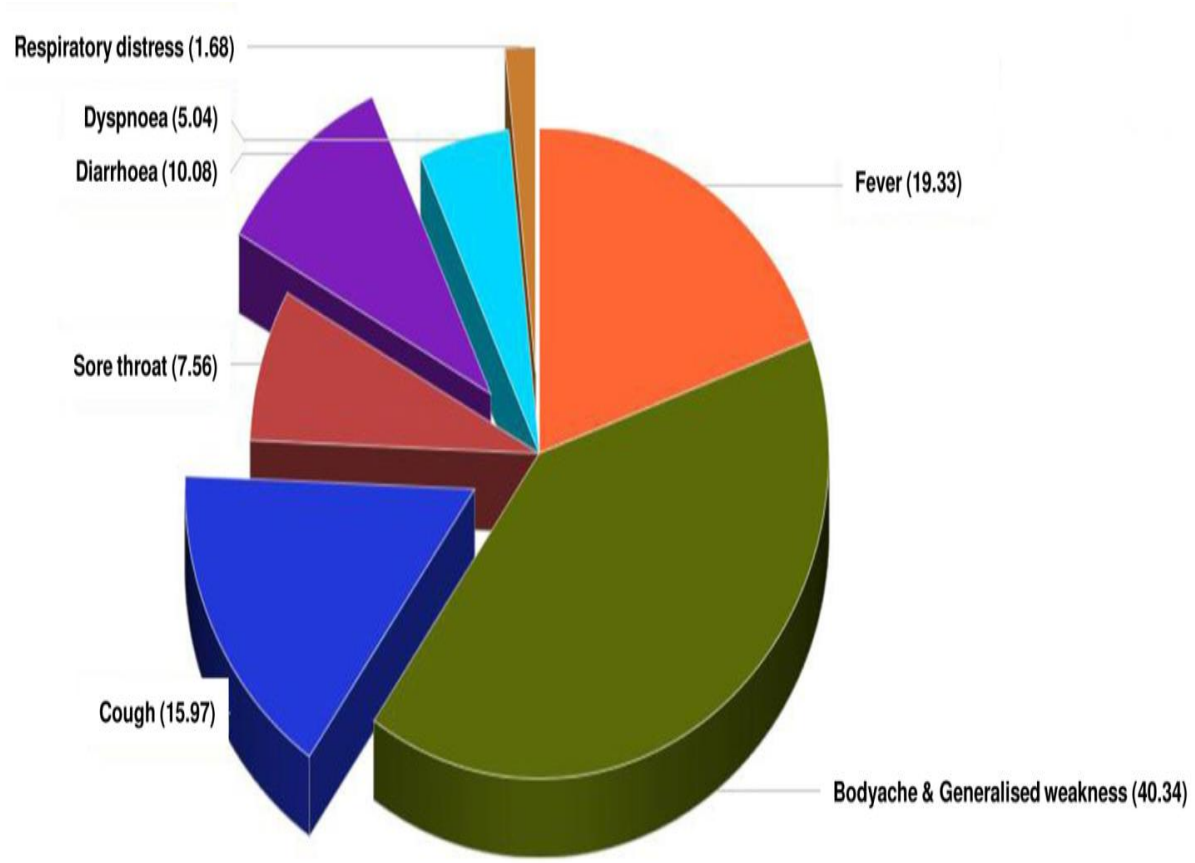

Figure:1 Pie chart displaying the different symptoms of COVID-19 in cancer patients.

Among which, 58% patients were women and 42% were men. The majority of cases (31.7%) were in the age range of 51-60 years, following that was 31% in the 41-50 years of age range; 20.1% belonging to the age group >60 years; 10.9% belonging to the 31-40 years of age range, 5.48% belonging to the age group 21-30 years and 0.61% belonging to 11-20 years of age group. Amidst these COVID-19 infected cancer patients, 91% patients also had co-morbidities like hypertension, hypothyroidism, diabetes mellitus. Of which 42% patients had hypertension; 32 had diabetes mellitus; 1 had hypothyroidism; 15 had both hypertension and diabetes mellitus; 1 had diabetes mellitus and hypothyroidism (Table S1). Total 6 cases (3.65%) of the cancer patients developed severe events among which 3 cases (1.82%) died.

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Supplementary materials

Table S1: Descriptive statistics of the malignant patients with COVID-19

Variables	No. of patients	Percentage of patients (%)
Malignant patients with COVID-19	164	
Gender		
Male	69	42
Female	95	58
Age group (years)		
0-10	0	0
11-20	1	0.61
21-30	9	5.48
31-40	18	10.9
41-50	51	31.0
51-60	52	31.7
>60	33	20.1
Co-morbidities	91	55.48
Hypertension	42	46.15
Diabetes mellitus	32	35.16
Hypothyroidism	1	1.09
Hypertension+Diabetes mellitus	15	16.48
Diabetes mellitus+ Hypothyroidism	1	1.09
Malignant patients with COVID-19 receiving treatment	101	61
Chemotherapy	43	42.57
Radiotherapy	11	10.89
Surgery	38	37.62
Chemotherapy+ Radiotherapy	2	1.98
Chemotherapy+ Surgery	6	5.94
Chemotherapy+ Radiotherapy+ Surgery	1	0.99

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Period of RT-PCR positivity of COVID-19 in cancer patients

It was observed that, most of the breast cancer patients suffered from COVID-19 (20.12%), followed by esophageal cancer patients (10.98%), base of tongue cancer patients (7.31%), ovarian cancer patients (6.7%), stomach cancer patients (5.45%) (Table1).

Table 1: Period of RT-PCR positivity in different types of cancer patients

Types of Malignancy	1week	2week	3week	4week	5week	6week	7week	8week	10week	13week
Ca Breast	0	13	6	5	2	4	1	1	1	0
Ca oesophagus	0	7	4	2	1	3	1	0	0	0
Ca Base of Tongue	2	4	2	1	0	1	0	2	0	0
Ca PFS	5	3	2	1	0	0	1	0	0	0
Ca ovary	0	2	4	1	1	1	0	1	1	0
Ca Stomach	1	3	2	1	0	0	0	0	1	1
Ca cervix	0	3	3	2	0	0	0	1	0	0
Ca GB	0	2	3	2	0	0	0	0	1	0
Ca Rectum	0	1	1	0	1	1	1	0	0	0
Ca submandibular region	0	3	1	1	0	0	0	0	0	0
Ca lung	0	0	0	1	0	1	0	1	1	0
Ca hypopharynx	0	0	2	1	0	0	0	0	0	0
multiple myeloma	1	1	0	0	0	0	0	0	0	0
Ca periampullary region	0	0	0	1	1	0	0	0	0	0
Ca oropharynx	0	1	1	0	0	0	0	0	0	0
Unknown primary	1	1	0	0	0	0	0	0	0	0
Hodgkin's lymphoma	1	0	1	0	0	0	0	0	0	0
Ca liver	0	0	1	0	0	0	0	0	1	0
Ca GIST	1	1	0	0	0	0	0	0	0	0
Ca Retrioperitoneum	0	0	0	0	1	1	0	0	0	0
RCC	0	0	0	0	0	0	1	0	0	1
Ca floor of mouth	0	0	1	0	0	0	0	0	0	0
Ca colon	0	0	0	1	0	0	0	0	0	0
Ca Knee	0	1	0	0	0	0	0	0	0	0
Ca thyroid	0	1	0	0	0	0	0	0	0	0
Ca arm	0	1	0	0	0	0	0	0	0	0
Ca CBD	0	0	1	0	0	0	0	0	0	0
Ca testes	0	1	0	0	0	0	0	0	0	0
Ca lip	0	1	0	0	0	0	0	0	0	0
Ca nasopharynx	0	0	1	0	0	0	0	0	0	0
Ca sigmoid colon	0	0	1	0	0	0	0	0	0	0
Ca maxilla	0	1	0	0	0	0	0	0	0	0
Ca transverse	0	0	1	0	0	0	0	0	0	0
Ca larynx	0	0	1	0	0	0	0	0	0	0
MVO with SNN	0	0	1	0	0	0	0	0	0	0
Ca supraglottis	0	1	0	0	0	0	0	0	0	0
Ca pancreas	0	0	1	0	0	0	0	0	0	0
Ca vagina	0	1	0	0	0	0	0	0	0	0

The period of COVID-19 positivity in different types of cancer patients ranged from first week to thirteenth week where maximum number of cancer patients had COVID-19 positivity upto second week and least upto thirteenth week. Importantly, One way ANOVA test and Levene's post hoc test infers a statistically significant difference in prevalence of infection across different types of cancer patients (F=4.13, p<0.001***). As depicted in figure 2a, most of the breast cancer patients had COVID-19 positivity upto second week and at least upto tenth week.

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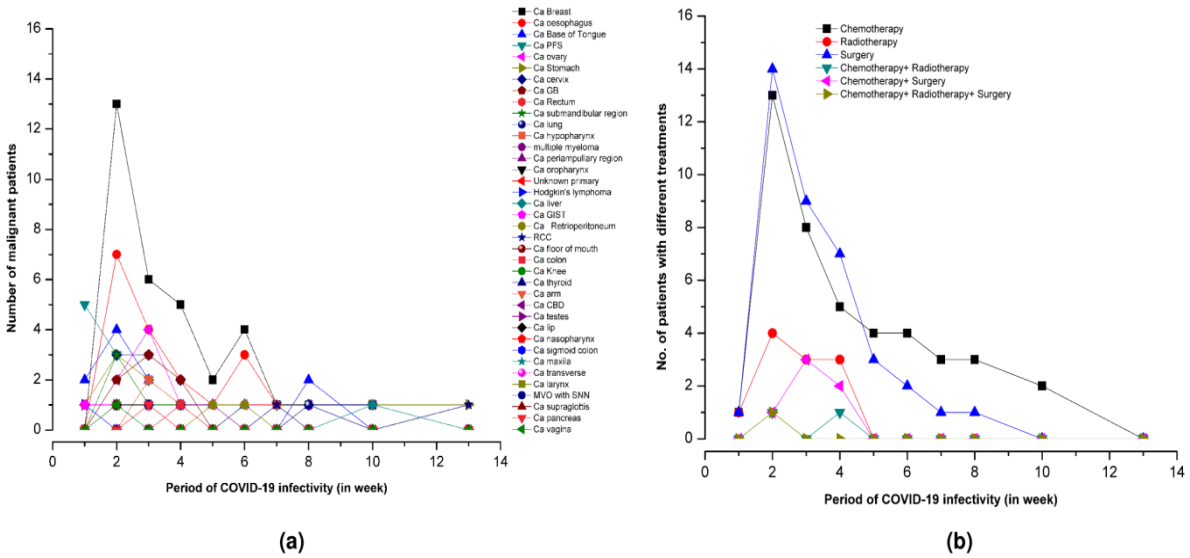

(a) (b)

Figure:2 Period of COVID-19 prevalence among (a) cancer patients (b) cancer patients with treatment

Similarly, maximum number of esophageal cancer patients had COVID-19 positivity upto second week and least upto seventh week. Most of the ovarian cancer patients suffered from COVID-19 upto third week of infection and least upto tenth week. COVID-19 positivity in patients with stomach cancer ranged from first week to thirteenth week; in lung cancer patients, it was from fourth week to tenth week. Additionally, NMDS based on Bray-Curtis dissimilarities showed the pattern of dissimilarities between periods of COVID-19 positivity in different types of cancer patients (Fig. S1) where periods of COVID-19 infectivity in breast cancer patients, esophageal cancer patients, stomach cancer patients were well separated from liver cancer patients, pancreatic cancer patients. The Empirical CDF plot analysis highlighted the empirical distribution follows the fitted distribution and the differences between different cancer patients (Fig. S2).

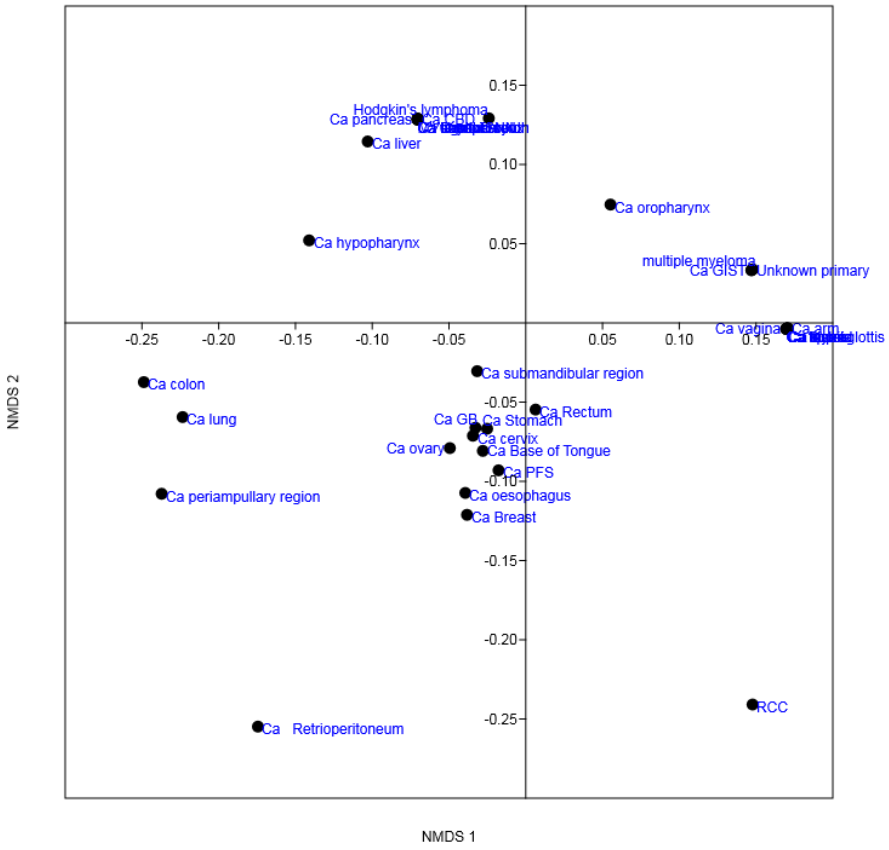

Figure S1: Non-metric multidimensional scaling (NMDS) plot based on dissimilarities calculated using the Bray-Curtis index of the period of COVID-19 infectivity in different types of cancer patients.

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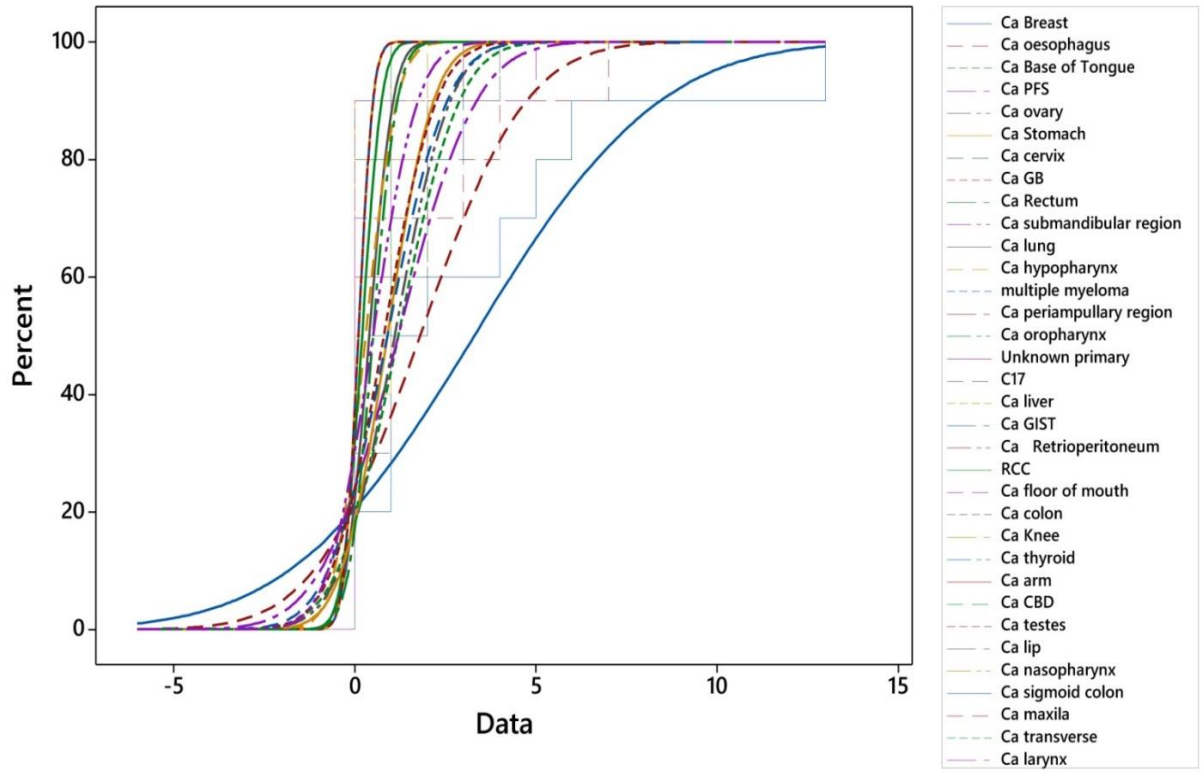

Figure S2: The Empirical CDF plot analysis highlighted the empirical distribution follows the fitted distribution and the differences between different cancer patients.

In the SARS-CoV-2-positive cohort, 101 (61%) of 164 patients received treatments. Among which, 43 patients received chemotherapy; 11 patients received radiotherapy; 38 patients had surgery, 2 cases treated with both chemotherapy and radiotherapy, 6 cases treated with surgery and chemotherapy; 1 case was treated with chemotherapy+radiotherapy+surgery. It was observed that, most of the patients received treatments had COVID-19 positivity upto second week, and least some upto tenth week (Fig. 2b). The majority of patients who had surgery (n=14), chemotherapy (n=13), radiotherapy (n=4), suffered from COVID-19 until the second week. However, patients receiving chemotherapy+surgery were infected with COVID-19 until the third week (Table 2).

Table 2: Period of positivity in different types of cancer patients receiving treatments

Treatment	1week	2week	3week	4week	5week	6week	7week	8week	10week	13week
Chemotherapy	1	13	8	5	4	4	3	3	2	0
Radiotherapy	1	4	3	3	0	0	0	0	0	0
Surgery	1	14	9	7	3	2	1	1	0	0
Chemotherapy+ Radiotherapy	0	1	0	1	0	0	0	0	0	0
Chemotherapy+ Surgery	0	1	3	2	0	0	0	0	0	0
Chemotherapy+ Radiotherapy+ Surgery	0	1	0	0	0	0	0	0	0	0

Significant variation was observed among periods of COVID-19 positivity in cancer patients under treatment (F=7.07, p<0.001***). The results are also supported by Levene's post-hoc test (F=7.11, p<0.001***). NMDS based on Bray-Curtis dissimilarities showed that period of COVID-19 positivity in cancer patients under chemotherapy+radiotherapy+surgery and chemotherapy+radiotherapy; chemotherapy and surgery were similar which differed from cancer patients under radiotherapy and chemotherapy+surgery (Fig. S3).

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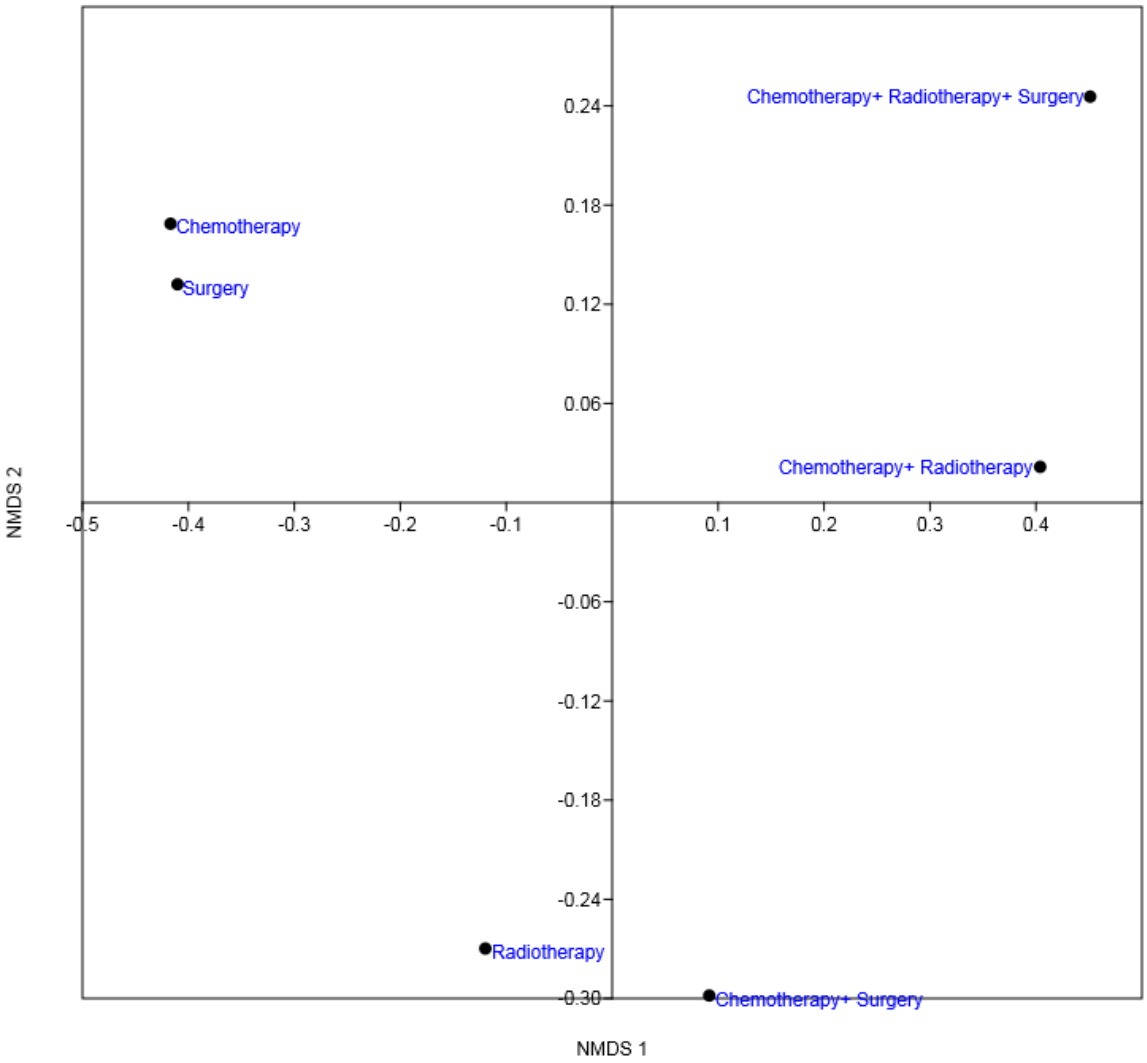

Figure S3: Non-metric multidimensional scaling (NMDS) plot based on dissimilarities calculated using the Bray-Curtis index of the period of COVID-19 infectivity in different types of cancer patients under different treatments.

On investigating the period of COVID-19 positivity in cancer patients with co morbidities, we observed statistically significant difference (F=6.33, p<0.001***). Levene's post hoc test also signifies significant variation among the period of COVID-19 positivity in cancer patients with co-morbidities (F=14.07, p<0.001***). Most of the cancer patients with hypertension (n=13) suffered from COVID-19 upto second week, followed by 9 patients upto third week, 8 patients each upto first week and third week, and 1 patient upto tenth week. Similarly, the majority of the cancer patients with diabetes mellitus (n=10) had COVID-19 up to the second week, followed by 7 patients up to the third week, 5 patients each up to the fourth and fifth weeks, and 1 patient up to the tenth week. But most of the cancer patients with both hypertension and diabetes mellitus (n=6) suffered from COVID-19 upto the fourth week (Fig. 3a).

We also evaluated the impact of cancer patients of different age-groups and genders on the period of COVID-19 positivity, which showed that the positivity period was significantly different among the age groups (F=4.91, p<0.001***). The result is also supported by Levene's test (F=7.17, p<0.001***). Cancer patients of age groups >60 years and 51 to 60 years suffered from COVID-19 ranges from first week to thirteenth week; 31-40 years and 41-50 years ranges from first week to tenth week, however, 21-30 years age groups patients had COVID-19 positivity period limited to first week to fourth week (Fig. 3b). Considering the gender on the period of COVID-19 positivity, it was not statistically different (F=0.54, p=0.341) (Fig. 3c).

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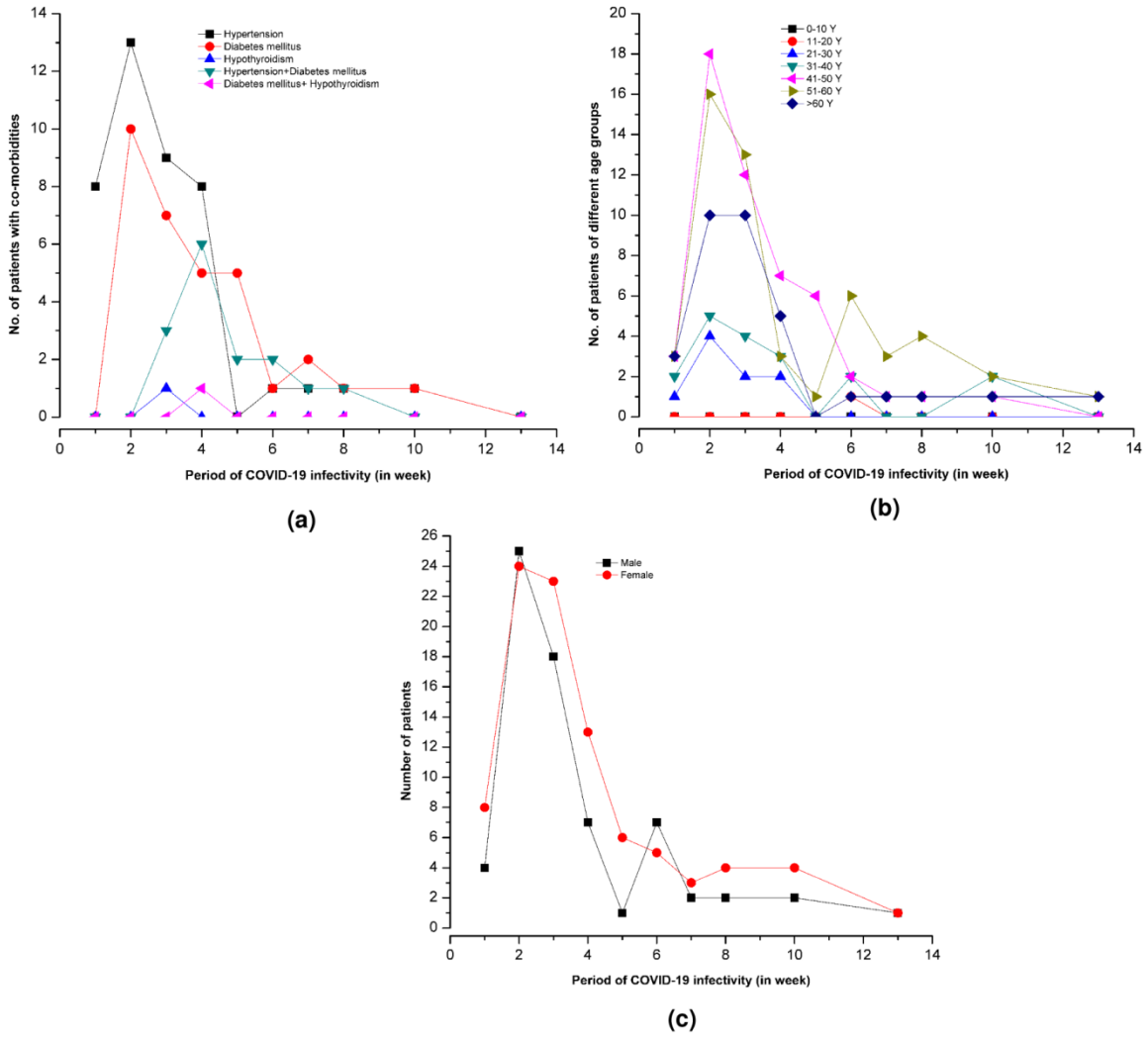

Figure:3 Period of COVID-19 infectivity among cancer patients (a) having co-morbidities (b) of different age groups (c) of different gender

DISCUSSION

Patients with cancer are specifically susceptible to respiratory tract infections mostly leading to severe form of pneumonia because of their immunocompromised condition owing to the malignancy and its treatment. Our study population manifested with symptoms of COVID-19 like fever, bodyache, sore throat, diarrhoea, dry cough, fatigue, generalised weakness, dyspnoea and respiratory distress. In our study population, 3.65% (6/164) of these patients exhibited serious consequences and 1.82% (3/164) of the patients faced fatal outcome. The three fatal cases were carcinoma breast, carcinoma stomach and carcinoma lung each. Cancer associated components are considered important for prognosis of these cancer patients. In COVID-19, some cancer types, most specifically lung cancer has been found to show terrible effects. This occurs because of the reduced respiratory reserve, immune suppressed state owing to the cancer itself and the immune-suppressive drug therapy which are mostly used for the treatment purpose.[16,17] The type along with the status of the tumor also influences the prognosis of these cancer patients. Poor prognosis in these patients may be associated with the general ill health and more advanced cancer disease also. Thus the causes of poor outcome in these patients remain unclear.

The period of these viral shedding is likely to be lenghthier in severely immunosuppressed patients.[18] Consequences of these sustained infection includes modification of the virus, therapy failure and virus transmission for an extended period of time. The duration of shedding of these replication competent virus has been found to range from 20 days to 2 months following the infection in these severely infected immunocompromised patients. [19-21] In immunocompetent persons, detection of live virus is rare after 11 day of infection, and its chances decreases with the increased time interval from onset of disease and more cycle threshold value.[22,23]

Casualty rates were dependent on cancer type and higher casualty in patients of COVID-19 with advanced age were coherent with other studies.[24-26]

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But some studies have reported older age as an independent factor of fatality in these viral respiratory infections like SARS, MERS, and COVID-19.[27-31]

In this study, sex was identified as an independent risk factor of fatality and this finding is coherent with other literature. [32-35] Factors like age and sex were no longer found to have significant effects in these patients with cancer.

There are various published studies concentrating the risk factors for fatality in COVID-19 patients. These studies have shown that comorbidities like hypertension, diabetes, CHD, cerebrovascular disease or COPD were dependent risk factors for mortality in hospitalised patients.[36-39] Contrary to our original assumption and previous studies findings, it was found that age, sex, cancer types and comorbidities were not associated with the fatality in these cancer patients.[40,41] These discordant findings might be due to the inter-institutional variation.

CONCLUSION

Both patient and cancer related factors have a crucial part in the course of this disease. These factors needs to be considered in development of COVID-19 preventative as well as therapeutic strategies in cancer patients to improve the patient care. It was also observed that SARS-COV-2 virus excretion is extended in patients with cancer. Decrease mortality due to COVID-19 in our study population recommend that this viral infection is not the end result for these immunocompromised cancer patients. Some patients have obtained this SARS CoV- 2 viral infection during hospitalization for anticancer therapy. Nonetheless, anticancer treatment should not be delayed due to SARS-CoV-2 infection. Overall, present data on the association between cancer and COVID-19 remains indecisive. Thus, more studies with bigger samples and prospective study designs are needed in future to analyze the different events in COVID19-infected cancer patients.

ACKNOWLEDGEMENTS

We would like to sincerely thank the technical staff of the COVID laboratory, SCI, Gauhati Medical College, Assam, India for their support and co-operation.

SOURCE(S) OF SUPPORT

Nil

CONFLICT OF INTEREST (IF PRESENT, GIVE MORE DETAILS)

None

ETHICS STATEMENT

Ethical clearance was taken from Institutional Ethics Committee, Gauhati Medical College

REFERENCES

1. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395(10224):565–74.
2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W,et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270–3.
3. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020;579(7798):265–9.
4. Ministry of Health and Family Welfare, Government of India. COVID-19 India Update. Available from: https://www.mohfw.gov. in/. [Last accessed on 2020 Sep 29]
5. First Corona Case in Assam: 52 Year Tested Positive in Silchar Medical College. Barak Bulletin. Available at https://www.barakbulletin.com/ en_US/first-corona-case-in-assam-52-year-old-tested-positive-insilchar-medical-college/ [Last accessed April 30, 2021).
6. Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. Global Health Research and Policy. 2020; 5:6.
7. 7.Coles CE, Aristei C, Bliss J, Boersma L, Brunt AM, Chatterjee S, et al. International guidelines on radiation therapy for breast cancer during the COVID-19 pandemic. Clin Oncol (R Coll Radiol) 2020;32:279-81.
8. Curigliano G, Cardoso MJ, Poortmans P, Gentilini O, Pravettoni G, Mazzocco K, et al. Recommendations for triage, prioritization and treatment of breast cancer patients during the COVID-19 pandemic. Breast 2020;52:8-16.
9. Liang W., Guan W., Chen R., Wang W., Li J., Xu K., et al. (2020). Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 21, 335–337.
10. Garassino M.C., Whisenant J.G., Huang L.C., Trama A., Torri V., Agustoni F., et al. (2020). COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol. 21, 914–922.
11. Kuderer N.M., Choueiri T.K., Shah D.P., Shyr Y., Rubinstein S.M., Rivera D.R.,et al. (2020). Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 395, 1907–1918.
12. Xia Y., Jin R., Zhao J., Li W, Shen H. (2020). Risk of COVID-19 for patients with cancer. Lancet Oncol. 21:e180.
13. Yu J., Ouyang W., Chua M. L. K., Xie, C. (2020). SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. JAMA Oncol. 6, 1108–1110.
14. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020; 395(10223):507–13.
15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497-506
16. Dai M., Liu D., Liu M., Zhou F., Li G., Chen Z, et al. (2020). Patients with cancer appear more vulnerable to SARSCoV-2: a multicenter study during the COVID-19 outbreak.Cancer Discov. 10, 783.
17. Garassino M.C., Whisenant J.G., Huang L.C., Trama A., Torri V., Agustoni F., et al. (2020). COVID-19 in patients with thoracic malignancies (TERAVOLT):

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first results of an international, registry-based, cohort study. Lancet Oncol. 21, 914–922.
18. Richardson L, Brite J, Del Castillo M, et al. Comparison of respiratory virus shedding by conventional and molecular testing methods in patients with haematological malignancy. Clin Microbiol Infect 2016;22:380:e1–e7)
19. Aydillo T, Gonzalez-Reiche AS, Aslam S,, et al. Shedding of viable SARS CoV-2 after immunosuppressive therapy for cancer. N Engl J Med 2020;383:2586–2588.
20. Kampen JJA, Vijver D, Fraaij PLA,et al. Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19). Nat Commun 2021;12:267.
21. Choi B, Choudhary MC, Regan J, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host. N Engl J Med 2020;383:2291–2293.
22. 2Heinzerling A, Stuckey MJ, Scheuer T, et al. Transmission of COVID-19 to health care personnel during exposures to a hospitalized patient—Solano County, California, February 2020. Morb Mortal Wkly Rep 2020;69: 472–476.
23. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. N Engl J Med 2020 ;382:2081–2090.
24. Natale F, Ghio D, Tarchi D. COVID-19 cases and case fatality rate by age. European Commission 2020;52:154–64.
25. Ghisolfi S, Almås I, Sandefur JC, et al. Predicted COVID-19 fatality rates based on age, sex, comorbidities and health system capacity. BMJ Glob Health 2020;5:e003094.
26. Hoffmann C, Wolf E. Older age groups and country-specific case fatality rates of COVID-19 in Europe, USA and Canada. Infection 2021;49:111–6
27. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229): 1054–62.
28. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020;94:91–5. https://doi.org/10.1016/j.ijid.2020.03.017
29. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;13:e200994
30. Choi KW, Chau TN, Tsang O, Tso E, Chiu MC, Tong WL, et al. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. Ann Intern Med. 2003; 139(9):715–23.
31. Hong KH, Choi JP, Hong SH, Lee J, Kwon JS, Kim SM, et al. Predictors of mortality in Middle East respiratory syndrome (MERS). Thorax. 2018;73(3):286–9)
32. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J,et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020; 323(11):1061–9.
33. 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.
34. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020. https://doi.org/10. 1111/all.14238.
35. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al: Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. (2213-2619)
36. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229): 1054–62.
37. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;13:e200994
38. Garassino M.C., Whisenant J.G., Huang L.C., Trama A., Torri V., Agustoni F.,et al. (2020). COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol. 21, 914–922.
39. Kuderer N.M., Choueiri T.K., Shah D.P., Shyr Y., Rubinstein S.M., Rivera D.R.,et al. (2020). Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 395, 1907–1918
40. Mehta V, Goel S, Kabarriti R, et al. Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System. 2020. Cancer Discov. 2020;CD-20-0516. https://doi.org/10.1158/2159-8290.CD-20-0516.
41. Dai M, Liu D, Liu M, 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.

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