A Mini Review on Covid-19 Infection and Severe Outcome on Cancer Patient

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Abstract

Introduction December 2019, the world witness a new strand of pathogen known as coronavirus-2 (SARS-CoV-2), later recognized as the novel coronavirus disease (COVID-19). By April 1st 2020, the confirmed cases were over 800,000 around the world with over 40,000 fatalities. Individuals with cancer are more vulnerable to COVID-19 impact because of compromised health-status.

Methods A comprehensive search method was applied by searching the google scholar using the keywords to select eligible studies to be included in the review

Results The findings showed that patients with cancer, especially thoracic malignancies that were infected with COVID-19 infection during the hospital stay developed severe cardiorespiratory symptoms that warranted use of a mechanical ventilator. The cancer patients with COVID-19 had increased rate of hospitalization and a poor outcome as well as a higher risk of mortality when compared to healthy individuals. It is recommended that cancer patients taking anti-tumour drugs should undergo early screening for COVID-19 because the anti-tumour drugs also suppress the immune system. Hence, their dosage should be regulated appropriately in case of COVID-19 co-infection.

Conclusion. In risk-mitigation pandemic scenario in COVID-19 period, efforts should be made not to compromise the prognosis of cancer in these patients by adhering to treatment guideline.

Key words: cancer patients, COVID-19 novel coronavirus, exercises.

Introduction

December 2019, the world was exposed to an unknown pathogen known as coronavirus-2 (SARS-CoV-2) which was later recognized as the novel coronavirus disease (COVID-19) (¹). By the 20th of March 2020, the number of infection has increased to 638,146 cases and 30,039 established deaths reported in more than 150 countries (²). By the 1st of April 2020, the confirmed cases were more than 800,000 patients around the world with more than 40,000 fatalities (³).

Toward mid of 2020, COVID-19 has infected nearly 2.9 million individuals in over 200 countries with more than 200,000 deaths (⁴).

COVID-19 is linked with manifestations ranging from an asymptomatic state to severe conditions of pneumonia, severe respiratory distress syndrome and fatality (¹). Individuals with cancer are more vulnerable to viral infections, especially if with concurrent history of chronic disease. Generally, poor health condition or immunocompromised status can mean poor treatment
outcome alongside with anticancer treatments (5). Dai, Liu (6) indicated that patients with cancer and infected by COVID-19 would experience a more unsatisfactory outcome than healthy populations. To the best of the researcher’s knowledge, there are insufficient data on the systematic assessment of COVID-19 on patients with cancer within a representative population. Another study conducted by Liang, Guan (7) showed in their study that cancer patients with superimposed COVID-19 infection had complex outcomes and complications, some of the patients requiring admission into ICU for mechanical respiratory assistance, this finding was also similar in the study by Zhang, Zhu (8). On the 10th of April, the city of New-York in the USA had reported a whopping number as high as 180,458 COVID-19 cases with acute respiratory distress syndrome, a severe complication that shorts down the respiratory system and recording about 9,385 deceased cancer patients, amounting to approximately 8.4% mortality figure (9).

During this sudden outbreak, the most vulnerable were the elderly especially those with the immunocompromised conditions such cancer, the rising death number was majorly among these age-groups, more so that, the health officers in Italy and the US were very concerned about the rising fatality in the nursing home because more deaths figure were reported during this short duration (10, 11). Although the exact cause of deaths could not be unravelled, a research gap was created concerning which particular marker could be used to trace or monitor which stage in the pathogenesis of cancer and its treatment confers the risk of severe COVID-19 to prompt quick medical response (12). Robilotti, Babady (13) showed in their study that having a profound knowledge or information about COVID-19 and cancer association is critical to be able to provide a standard and quality treatment to symptomatic cancer patient with confirmed COVID-19 infection. In their study, 40% (500 out of 2000 cases) were admitted for COVID-19, while 20 % developed acute respiratory disease with demand for mechanical ventilation while 12 % passed away within 30 days of confirmation of COVID-19. Generally, cancer patients with COVID-19 infection present with a significant rate of hospitalization and an acute outcome. Presently, the increasing incidence of COVID-19 in the United States is still at large, and there are still limited and comprehensive investigations or analysis to show that patients with cancer are at higher risk of severe condition (12, 14).

More so, there are few studies on the lasting adverse effects of COVID-19 in hospitalized patients with cancers especially haematological cancers, and because many these cancer patients would be treated with anticancer medications which suppress bone marrow function thus targeting the immune system and exposing them to a higher risk of public and hospital-contacted nosocomial infections and COVID-19 (15).

The Objective of the Review

There are many studies on COVID-19 pandemics in several countries. However, research on COVID-19 association and outcome on patients with cancer are still limited, and the address question is to understand whether cancer patients infected by COVID-19 have a higher risk and severe outcomes than the healthy population or whether these patients experience a worse prognosis and higher mortality.

Methodology

Selected studies were chosen by typing the keywords in google search wherein searched up till 2020 was obtained. Observational studies with retrospective studies, and comparative studies from various search-results included in the mini review. A total of 3000 studies and 89 full-text articles were assessed. Six studies met the inclusion criteria (COVID-19 impact and outcome on patient with cancer in 2020). The main outcomes of this review were overall survival, cancer-specific outcome and complication following COVID-19 infection on patients with cancer.
Table 1. Summary of selected studies on effect of COVID-19 infection and severe outcome on cancer

<table>
<thead>
<tr>
<th>Author/ Year</th>
<th>Title</th>
<th>Study Population</th>
<th>N</th>
<th>Methods</th>
<th>Results</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(16)</td>
<td>Thoracic Cancers International COVID-19 Collaboration (TERAVOLT): Impact of type of cancer therapy and COVID therapy on survival.</td>
<td>Cancer patients with COVID-19</td>
<td>295</td>
<td>Data from Global consortium from 59 different hospitals in 9 countries, Total of 295 patients with thoracic-malignancies infected with COVID-19 To determine the effect of COVID-19 on the cancer patients, provide information, direction and treatment outcome and identify the risk factors for the COVID-19 disease and fatality.</td>
<td>The result showed that COPD and HTN are the most recorded comorbidities The average age was 68, 31% female,69% male and total of 79% present/past smokers 73% NSCLC, 14% SCLC, 4% meso and thymic 49% of patients with stage IV disease 73% of patients require admission for cardiopulmonary features despite being on chemo or chemo-IO or RT and COVID-19 infection was treated with antibiotics 67%, antivirals 33%, and steroids 30%.</td>
<td>The study reported that patients with thoracic malignancies infected with COVID – 19 during the admitted time developed severe symptoms, more so are at higher risk of mortality</td>
</tr>
<tr>
<td>(4)</td>
<td>Case fatality rate of cancer patients with COVID-19 in a New York Hospital system</td>
<td>Cancer patients with COVID-19</td>
<td>218</td>
<td>Data on patients who tested positive for COVID-19 were selected from an electronic medical record in a single medical centre in New York from the 18th of March to the 8th of April, 2020 and correlated with an existing cancer database from a period of one month.</td>
<td>127 (58%) males and 91 (42%) females. HTN, DM and Chronic Lungs Disease are the most recorded comorbidities 164 (75%) patients have solid tumours, and 54 (25%) has hematologic Malignancies. COVID-19 related death on the cancer patient: Total of 61 (28%) death with a case mortality rate for 37% (20/54): hematologic malignancies 25% (41/164) for solid malignancies The number of fatalities was significantly higher among older age.</td>
<td>The Age-adjusted case mortality rate in cancer patients with COVID-19 contrasted with patients without cancer in the institution indicated a significant increase in the mortality rate among COVID-19 patients with cancer. Rates of ICU admission and ventilator use was slightly higher for the COVID-19 infected cancer patient</td>
</tr>
<tr>
<td>(15)</td>
<td>COVID-19 in persons with haematological cancers</td>
<td>Cancer patients with COVID-19</td>
<td>354</td>
<td>A cohort study conducted in China involving 128 patients hospitalized for haematological cancer (HC) and 226 healthcare-provider HCP 13 of 128 (10%) hospitalized-HC patients developed COVID-19 while, 16 of 226 of HCP had developed COVID-19, and 11 of whom were hospitalized Co-variates were contrasted with the 115 HC patients without COVID-19 with 11 hospitalized HCP with COVID-19 Most patients were adults over the age of 60 years (234, 56%) The median age of subjects with and without COVID-19 was 35 years (range, 23–53 years) and 49 years (range, 33–59 years; P = 0.082) Cardio- and cerebrovascular diseases were the most common comorbidities The result showed that there were no significant differences in baseline co-variates among patients who have HC positive or not-positive for COVID-19. The cases rate for COVID-19 was higher in hospitalized patients with HC: 10% (95% CI), 6, 17% compared with 7% (4, 12%; P = 0.322 in HCP. Case mortality rates were HC: 62% (32, 85%) and HCP: 0 (0, 32%; P = 0.002.</td>
<td>Admitted patients with HC had more severe presentations and at higher risk and mortality rate. The 13 patients with HC experienced more severe COVID-19 and more fatalities compared with HCP with COVID-19. However, the author was not able to detect the precise risk factors for COVID-19 in admitted patients with HC.</td>
<td></td>
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<tr>
<td>(13)</td>
<td>Determinants of COVID-19 disease severity in patients with cancer</td>
<td>Cancer patients with COVID-19</td>
<td>423</td>
<td>Record from the 10th of March to the 7th of April 2020 of 423 cases of symptomatic COVID-19 from 2,035 patients with confirmed cancer was diagnosed at Memorial Sloan Kettering Cancer Centre</td>
<td>The average age was 60, (234, 56%) Diabetes, hypertension, chronic kidney disease and cardiac disease were the most reported comorbidities 40% were admitted for COVID-19, of these: 20 % developed critical respiratory disease 9% of them needed mechanical ventilation 12 % passed away within 30 days.</td>
<td>The cancer patients with COVID – 19 had increased significant rate of hospitalization and a poor outcome</td>
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Cont... Table 1. Summary of selected studies on effect of COVID-19 infection and severe outcome on cancer

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Patients with cancer</th>
<th>Cancer patients with COVID-19</th>
<th>Study Details</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-control study</td>
<td>Cancer patients</td>
<td>28</td>
<td>A retrospective cohort study on cancer patients with COVID-19 was conducted. Data were collected through medical record over two months: Jan.13 to the 23rd of February, 2020. The results showed that lung cancer was the most common type of cancer reported.</td>
<td>The study outcome shows the vulnerability of cancer patients in the current pandemic. Poor treatment outcome and the possibility of mortality.</td>
</tr>
<tr>
<td>Case-control study</td>
<td>Cancer patients</td>
<td>641</td>
<td>A multicentre study on cancer patients with COVID-19 carried out in 14 hospitals over 2months in Hubei, China, among 105 cancer patients and 536 age-matched non-cancer patients tested positive with COVID-19. Four main outcomes analysed were death, admission into the ICU, development of severe/critical features, and requirement of mechanical ventilation.</td>
<td>The result indicated that cancer patients with COVID-19 had a higher risk than healthy individuals and at high risk of mortality and severe outcomes. More so, the result demonstrated that cancer patients appear more susceptible to COVID-19. Also, patients with COVID-19 who have non-metastatic cancer witnessed the same frequencies of severe health circumstances to those noticed in noncancerous patients.</td>
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**Discussion**

COVID-19 has dealt a massive setback on most of the countries around the world. The consequences of COVID-19 is fatal, and it created severe outcomes among people with an underlying health condition, especially cancers patients. COVID-19 has infected nearly 2.9 million individuals in over 200 countries, with the devastating number of deaths over 200,000, and the US has the highest fatality (4). With the ongoing risk of COVID-19 transmission and concurrent adverse outcomes, the long term psychological effect on cancer patients health will be heightened, and treatment safety on patients with these chronic diseases will be compromised. The six studies in the table demonstrated that patients with cancer especially thoracic malignancies that were infected with COVID-19 infection during the hospital stay developed severe cardiorespiratory symptoms that warranted admission into ICU and requirement of a mechanical ventilator and eventually higher mortality risk.

The age-adjusted case mortality rate in the cancer patients with COVID-19 in contrast with patients without cancer showed a significant increase in the rates of admission into intensive care unit ICU with mechanical ventilator use and more mortality among COVID-19 patients with cancer. Patients with haematological cancer HC was shown to have a devastating outcome, admitted patients with HC had increased severe presentations, higher risk and highest mortality. From the review analysis, it was shown that thoracic and haematological malignancies were the two with the most recorded severe COVID-19 infection and more fatalities.
among the cancers. According to Mehta, Goel (4), the number of fatalities was significantly higher among the older age, and the cancer patients with COVID–19 had increased significant rate of hospitalization and a poor outcome. Also, patients with COVID-19 who have non-metastatic cancer showed the same frequencies of severe health circumstances to those noticed in noncancerous patients. The study outcome shows the vulnerability and poor outcome of cancer patients in the current pandemic, illustrating that patients with cancer demonstrated more susceptibility to COVID-19, poor treatment outcome and possibility of increase mortality rate. However, a contrary outcome was noted by only one study which indicated that there were no significant differences in baseline co-variates among patients with HC positive and no-HC patients infected with COVID-19.

Cancer is regarded as a chronic illness that gradually causes a significant decrease in the strength of the immune system, thereby reducing the individual capability to ward off infections (17). A higher rate of severe outcomes and death were reported among the cancer patients with hematologic cancer (which included patients with lymphoma, myeloma, and leukaemia) thus recording the highest figure, followed by patients with lung cancer. (6). These poor and worsen outcomes were associated with down-grading and weakening of the immune system because of the malicious or dysfunctional state of the lymphocytes, white blood cells or plasma cells. Generally, hematologic malignancy reduces the capability of the immune system to fence-off virus and other infections, which perhaps, is the main synergistic cause of rapid and deteriorating effect of COVID–19-associated high mortality rate and severe outcomes in these patients (6, 18). Amongst solid tumours, patients with lung cancer have the utmost risk of contracting COVID–19 infections, because of the reduction in lungs function in lung cancer patients with superimposed acute COVID-19 infection, thus, contributing to the cardiorespiratory failure in this population (19).

It was indicated that the difference between the timeline in the hospitalization period and the severe events among cancer patient infected by COVID–19 and non-cancer patients infected by COVID–19 differs (6). Cancer patients with COVID–19 had a mean length of hospitalization of 27 days (SD 9.52) while non-cancer patients infected by COVID-19 had a mean length of hospitalization of 17.75 days (SD 8.64); which varies significantly (Wilcoxon test, $P < 0.01$). The severe medical events (composite endpoint) clearly defined as a circumstance demanding admission into an intensive care unit (ICU), the procedure of using mechanical ventilation, or mortality was very feasible and significant among the cancer patients infected with COVID-19 when compared to non-cancer patients with COVID-19 infection. In fact, the need for ICU intervention was seen to be 3-fold high among cancer patient infected with COVID-19 than when compare to the non-cancer patient with COVID-19 infection (20).

**Recommendations**

This review provides vital information on the vulnerability and outcome of COVID-19 on patients with cancer. Cancer patients infected by COVID –19 are linked with a significantly poor severe outcome and mortality rate, suggesting that the need for a dynamic and stringent approach is needed to decrease the spread of COVID-19 and to develop early accurate screening and pathogen identification in this susceptible population (4). It is recommended that healthcare provider in-charge should increase surveillance and increase medical equipment availability. Special attention on cancers patients, especially hematologic cancer on admission for COVID-19 infection should be monitored adequately and precisely if on bone marrow suppressing drugs as well as those with progressive cancer. Persistent preparedness is another vital approach needed for adequate cancer treatment, especially during the ongoing COVID-19 infection along with daily testing and screening of individuals for COVID-19. Cancer patients on anti-tumour drugs should have dynamic screening for COVID-19 because the chemotherapy drug are also associated with stiff adverse effects. Lastly, patient’s drugs dosages should be routinely reviewed in patients with immunocompromised status like cancer and other chronic medical comorbid diseases.

**The Benefit of Exercise For Cancer Patients.**

The treatment of cancer patients is a critical health matter that creates physical, emotional, mental health and discomfort. Cancer leads to a massive effect on patients with a high burden of disease. Cormie, Trevaskis (21) stated that exercise is harmless and effective adjunct therapy in cancer patients’ care. Exercise is significantly
essential in all the health centre around the world because integrating exercise as part therapy represents a standard practice of keeping patient mentally and physically fit (22, 23).

Several studies have shown that introducing exercise into the management of cancer patient is significantly effective in improving patients’ quality of life. If cancer patients perform moderate tolerable exercise frequently, they will have significantly immune boost, improve quality of life symptoms, possibly lengthening their survival, happiness, mental condition and physical status (24, 25). Experts explained that cancer patients who perform exercise regularly would reduce their manifestations by stimulating changes in the immune system, metabolism, systemic inflammation, angiogenesis and redox status. Exercise outcome on cancer patient had a positive effect when patients performed it on a routine of six metabolic equivalent task 6-METs or more (26). The American college of sports medicine (ACSM) admonishes the healthy person to perform twenty-sixty minutes of aerobic exercise at least 3-5 times/week and twenty repeated circle of resistance exercise with an intensity corresponding to 12-to-16 rate of exertion (20 is the maximum exertion rate) 2-to-3 times per week. Cancer patients can engage in 150 minutes of moderate-intensity aerobic exercise or aerobic combined to resistance exercise. The exercise-intensity is calculated using metabolic equivalent task (MET), 1-MET is equivalent to the expense-energy at rest. Moderate-intensity exercise is equivalent to 3-to-5.9 MET. High-intensity or vigorous exercise has a MET count of 6 and is referred to as an activity that produces perspiration and change in cardiac and breathing rates (26). An adjunct therapy such a high-quality exercise would significantly reduce the neuropathic pain level and improve functional quality of life QOL (27). High quality and regular aerobic exercise are highly advised for cancer patients or should be referred to an exercise physiotherapist: who has experience in cancer patients care (28, 29).

**Conclusion**

In a risk-mitigation pandemic scenario, efforts should be made not to compromise the prognosis of cancer in these patients by departing from guideline-recommended radiotherapy practice. If patients need for triage arise, important factors for triage such as potential for cure, relative benefit of radiation, life expectancy, and performance status should be employ in decision-making. The exposure and poor outcome of COVID-19 infection is increased in cancer patients as well as high mortality risk. Adequate and standard treatment procedures should be strictly followed. More so, exercise is a harmless and effective adjunct therapy in cancer patients’ care. Exercise will be significantly essential in all the centre around the world to integrate exercise as a portion of standard practice in cancer care because high-quality, regular and tolerable aerobic exercise would sufficiently boost the immune system and improve functional QOL.

**Conflict of Interest Declaration:** The research team declares that there is no conflict of interest in the course of this study

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**Ethical Approval:** The study was conducted in accordance with the guidelines of the institution, permission letter was obtained from office of the director of HUSM to conduct the study and ethical approval was obtained from the Universiti Sains Malaysia (USM) Human Research Ethics Committee (USM / JEPeM / 18120810).

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