Prevalence and Infectivity of Asymptomatic COVID-19 Illness

Rudra Rajesh Nair, Abhishek Ingole*, Ashok Mehendale

Department of Community Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha, Maharashtra, India

ABSTRACT

The Severe Acute Respiratory Syndrome Corona Virus 2 is a novel coronavirus (SARS-CoV-2), triggered a coronavirus disease outbreak in December 2019. Acute respiratory distress syndrome, acute renal failure, acute respiratory injury, septic shock, and severe pneumonia are all manifestations of acute respiratory distress syndrome that have all been recorded in 33% of patients who have received COVID-19. COVID-19 has no specific medication or vaccine that has been approved, and several clinical trials are now studying potential COVID-19 treatments. Some carcinoma patients' immunosuppression (either induced by the disease or treatment) makes them more susceptible to infection. Presently, extensive studies and efforts are done to understand the how the infection occurs and how to treat covid, but risk factors, the prognosis and outcomes after treatment are yet to be understood and interpreted. Clinical focus is immense. Supportive interventions like supply of oxygen, fluid intake, and fever and pain control, as well as medications if a pre-existing bacterial is present, have been recommended so far. Remdesivir, immune globulins, arbidol hydrochloride integrated with interferon atomization, and ASC09F are all now being tested in clinical studies as potential COVID-19 therapies. As an effort made to curb covid by respective authorities, complications may arise or progression to severity can occur in such immune compromised patients. The severity varies from one patient to another covid infected cancer patient. Based on the latest literature and researches, risk factors, radiological and biochemical characteristics, the impact on diagnosis and treatment and treatment outcomes have been discussed. The challenging scenario of taking care of covid infected cancer patients has been discussed.

Key words: COVID-19, Cancer, Oncology, Radiological and biochemical characteristics, Treatment

INTRODUCTION

After the virus affected 4 million people worldwide and killed approximately 16000 people in 195 countries, Coronavirus disease was proclaimed or announced as a pandemic by World Health Organization in March 2020 (World Health Organization, 2020–WHO Director-opening General's remarks at the COVID-19 media briefing–March 11, 2020). As of February 8, 2021, the pandemic has impacted almost 105 million people world-wide, with instances continuing to rise at a disturbingly heightened rate (World Health Organization, 2021-COVID disease (COVID-19) pandemic 2021). COVID virus is a type of virus that can cause anything from a common cold to life-threatening infections. Coronavirus spreads from animals to person which is called zoonotic. A Cancer patient who has been infected with COVID, the virus that causes COVID-19, depicts an expansive array of symptoms. Some patients have little or no features, whereas others have striking symptoms and can progress into a serious clinical case with respiratory failure, cytokine release syndrome, and multi-organ failure. The capability of the virus to spread from one person to another through air is the primary cause of the pandemic. The risk of transmission is heightened when the virus transmits from single individual to another or from a single individual to 1000 people *i.e.* super spreader is transmitting by super spreading. Carcinoma is a disease or a collection of diseases marked by atypical cell proliferation that frequently results in death. Being predisposed to cancer can be genetic as well as a result of one's way of life. Majority of every bodily organ is susceptible to tumour formation; nevertheless, the incidence of organ-specific malignancies differs. According to Globocan, around 18.1 million individuals were confirmed with cancer in 2018, with 9.5 million dying as a result. COVID-19 individuals have been divided into subgroups that seem to be at a considerable probability of severe morbidity. The sickness has a huge impact on every element of life, but one of the most significant is its impact on cancer, which is related to human health and medical science. Prior to May 2020, over 2% of all COVID-19 patients had cancer, which is rather alarming because the patient can be described as extremely unfortunate to be diagnosed with cancer while also being infected with COVID. Because data on the

current situation is limited, this review will concentrate on the fatal pair of coronavirus and carcinoma (COVID-19). Patients with carcinoma diagnoses have been recognised as a particularly vulnerable section of the population when COVID-19 sickness began spreading all over the world in the beginning of 2020. Carcinoma patients have been found to have a more likelihood of getting coronavirus infection, as well as a considerably critical illness course, with a higher numbers requiring tremendous levels of intensive care, a faster-developing disease, and substantial chances of mortality. Tumour patients (of any age, gender, tumour subtype, or stage) have been categorised as considerable possibility for COVID disease as a result of a hypothesis of "COVID-19 vulnerable" cases, resulting in sweeping changes.

According to a retrospective research, the most usual symptoms at presentation win cancer patients with covid were fever, dry cough and fatigue. In spite of normal and carcinoma patients with COVID-19 have alike clinical presentations, the latter appear to have higher fatigue and dyspnoea symptoms. COVID-19 individuals with lung metastasis or lung cancer were found to develop dyspnoea way sooner as compared to non-tumour patients and those who have other carcinoma types.

COVID-19 symptoms were more severe in cancer survivors infected with SARS-CoV-2 than in COVID-19 individuals who had never had cancer. The immune surveillance mechanisms in cancer patients may not fully recover, leading to an impaired defence against COVID-19 disease progression. In addition to illness and treatment related factors, advanced age is an unfavourable component for severe Covid disease in many tumour patients. Cancer patients developed COVID-19 major symptoms faster than individuals who did not have cancer regardless of the severity of the disease.

LITERATURE REVIEW

For infectivity, COVID virus interacts with the Renin Angiotensin Aldosterone System (RAAS) *via* Angiotensin Converting Enzyme-2 (ACE2) [1]. ACE-2 functions as a receptor for SARS-CoV-2 and counteracts RAAS activation physiologically. Although ACE-2 is demonstrated in an array of organs, it is thought to be most effective in lung alveolar epithelial cells. The host reaction is the critical feature for severity of pathogenesis once the virus obtains entry into the target cell. The bronchial mucosa is lined with Mucosal Associated Invariant T (MAIT) cells and T cells. By launching a cytokine cascade that is required for microbial death the innate-like lymphocytes quickly respond to pathogen invasion. Feature reported of patients who died indicate the importance of the host immune system in individuals with severe covid infection. Age, AC expression, and comorbidities are all factors that influence clinical outcomes. To eradicate CoV-2, a specific adaptive immune response is required after the initial innate response. Lympopenia (an independent unfavourable predictive sign in COVID positive patients) is predominant in carcinoma patients undergoing current treatment or even under proper supervision, disrupting the needed immune response. A

"cytokine storm" and substantial lung injury might result from consistent cytokine production (presumably driven by leukocytes other than T cells). Furthermore, a decreased specific immune response, especially in ACE-2 rich tissues, enhances viral multiplication, tissue damage, and development to severe stages. Reduced immunity or immune compromised and non lymphopenic cancer patients may be able to project enough response, with Cytotoxic T Lymphocytes (CTLs) and Natural Killer (NK) cells playing a critical role in viral infection treatment. Chronic adaptive immune activation that leads to lymphocyte depletion has been widely documented in cases of chronic infections, cancer, and as per reports, even covid infection. With CoV-2 infection, function of CTLs and NK cells are exhausted has been revealed, along with much increased levels of exhaustion markers [2].

Until March 30, 2020, the COVID-19 infection rate among tumour positive cases in a sole centre was projected to be 2.7% (37 of 1380 patients), which was 6 fold higher compared to in Wuhan (0.45%, 50,006 of 11,081,000). Cancer was found to be present in 54.1% of serious/critical COVID positive patients, which was significantly exceeded than the overall inhabitants.

The number of male patients was 20 (54.1%), and the mean age of these male patients was 62 years old. COVID-19 positive cancer patients, according to earlier research, were substantially older. 6 and 7 Fever (75.7%) and cough (56.8%) were the most prevalent start symptoms, which were often worsened by dyspnea (32.4%) or tiredness, diarrhoea, and myalgia [3].

Furthermore, COVID patients were divided into two categories based on the extremity of the disease: mild and serious/critical. Dyspnea was more common in the serious/critical group than in the mild class (50%). Thirteen of the 37 patients had had anti-cancer treatment within the previous month that included surgery, radiation, chemotherapy, targeted therapy, or immunotherapy; out of the thirteen, six patients were categorised in mild category and seven patients were from the severe/critical category. Nonetheless, as there was no significant difference between the two groups with or without a history of cancer therapy, implying that anti-cancer medication had no effect [4].

COVID-19-positive cancer patients' radiographic and laboratory findings: The most prevalent feature in chest CT imaging for both normal and tumour positive patients with COVID was ground-glass opacity, with patchy consolidation coming in second 5,23. In general COVID-19 patients, air bronchogram and interstitial aberrant findings were widespread, but not in cancer patients 5,23. It was reported that cancer patients suffering from COVID-19 had greater extent of bilateral lung involvement.

COVID-19 has biochemical characteristics in addition to radiographic observations. The cytokine release syndrome was found to be an indication of illness progression in one investigation. In COVID-19 patients, higher levels of IL-6 and IL-10, as well as lower levels of CD4+ and CD8+T cells, were associated to disease

severity. Carcinoma patients with covid had similar blood counts to COVID-19 patients having no tumour. COVID-19 cancer patients, on the other hand, were more likely to have anaemia. Due to the probable combination of deficiency in nutrition and immunosuppression, anemia is caused in such patients and therefore makes them more susceptible to respiratory infections.

Impact on diagnosis: In terms of health systems, particularly cancer care, such a dramatic effect has been felt worldwide. The first step to carcinoma treatment is diagnosis. Lag in the confirmation of diagnosis can have serious consequences for patients, as they delay everything from symptom management to cancer cure and monitoring. Due of the COVID-19 pandemic, various places have been recommended to postpone cancer treatment in order to reduce COVID-19 transmission, lowering cancer patients' quality of life. Additionally the necessity of frequent visits to the hospital is unsafe for healthcare professionals and family members, as well as when COVID-19 is transmitted in the community, making the decision to delay cancer detection imperative.

The fatal combination of SARS-CoV-2 and carcinoma makes diagnosis extremely challenging. The diagnosis of radiography in COVID-19 and cancer can look identical, deceiving the healthcare practitioner into making an incorrect diagnosis. CA125 and 153, Carcino Embryonic Antigens (CEA), Human Epididymis Protein 4 (HE4), C-Reactive Protein (CRP), and Cytokeratin-19 Fragment (CYFRA21-1) are frequent indicators in both COVID-19 and cancer. Unfortunately, it is difficult for the healthcare provider to ascertain if the increase in these prognostic indicators is because of COVID-19, cancer, or both together. The impact on diagnosis is critical, and it necessitates a thorough understanding of the pathologies of COVID-19 and cancer.

Effect on treatment: Treatment for cancer weakens as a result of the changes in cancer care. The parameters of cancer treatment are dramatically altered by a delay in diagnosis. The treatment must be conducted out while keeping in view the increased cancer risk factors linked with COVID-19. In order to eliminate cancer cells, various anti-oncological therapies may necessitate a suppression of immunity. The current status of the patient makes it vulnerable for the patient to acquire SARS-CoV-2. In the management of radiation, proper planning is required, and small sessions rather than a single session are not preferred. Also, the number of appointments of small sessions should be limited, and radiotherapy sessions should be correctly managed to mitigate the impacts of coronavirus infection during radiation therapy. Therapy with chemical substances that does not necessitate hospitalisation should be recommended. Oral antitumour therapy may be effective.

Antiviral therapy has been shown to influence anti-cancer treatment. Similarly, COVID treatment and oncology treatment may interact, but there isn't enough information to determine how chemotherapy interacts with COVID-19 treatment or other way round. The risk of reinfection is no less after the patient has recovered from

covid which is a unfavourable factor for anticancer treatment in such patients. Immunosuppressive drugs utilised as anti-cancer therapy may increases the likelihood of COVID-19 re-infection. Oncologists and cancer society's suggest delaying cytotoxic chemotherapy until the Corona virus is no longer present in the body to avoid further suffering for individuals suffering from the fatal pair of COVID-19 and cancer.

In reality, delaying cancer treatment has its own set of effects, ranging from the cancer's progression to the emergence of secondary issues such as anxiety. The decision to start the patient on chemotherapy and when to continue chemical agents depends on the individual's condition due to the immunosuppressive action of antitumour drugs causing revival of the virus. Chemotherapy patients are more susceptible to pneumonitis and neutropenia-like severe conditions compared to patients who have not received chemotherapy.

To prevent COVID-19, healthcare workers must work under increasing pressure and follow all precautions, as well as employ newer techniques like telemonitoring and artificial intelligence to improve cancer patient treatment timeliness and lower unfavourable factors connected with anti-tumour medication.

DISCUSSION

The factors that have a significant impact on oncological diagnosis and therapy options are inflammatory response, oxidative stress and other pathophysiological abnormalities which are all linked to coronavirus. In mild cases of COVID-19, there was dramatic increase in levels of many blood cancer indicators as compared to normal people, according to a retrospective investigation. In severe cases of COVID-19, these cancer biomarkers elevated far more. These alterations could influence the positive and negative predictive values of a multitude of tumor related biomarkers, making it very difficult to precisely evaluate and establish carcinoma diagnosis, disease progression, and treatment choices.

Immunosuppression (whether caused by the disease or treatment) raises the likelihood of infection in some cancer patients in contrast to the common population. Immunosuppression can also put cancer patients at risk of serious infection, leading to treatment delays and unnecessary hospitalizations, all of which can have a negative impact on the disease's prognosis. To handle carcinoma patients, healthcare professionals and healthcare centres on the accurate measures and recommendations on limiting the spread of this communicable disease and to increase the availability of resources in order to provide consistent cancer services, certain clinical resources have been published.

Despite the probability of COVID infection during antitumour therapy, it is generally suggested that individuals receiving healing cancer therapy carry on with their treatment. Delaying therapy for metastatic disease leads to a decline in performance, admission for symptom relief, and disease progression.

As a result, chemotherapy dose reduction may be considered. Surprisingly, tumour patients receiving radiation therapy did not have a greater risk of COVID-19 related serious events, which could be due to radiotherapy's activation of the immune system. However, to reduce the number of visits to treatment centres, radiation may need to be safely provided in a hypo fractionated method if possible. Patients who develop fever during targeted therapy should be tested for COVID-19 before continuing treatment.

CONCLUSION

SARS-CoV-2 infection rates were high in cancer patients, and it was easy for them to develop into debilitating cases, which should be actively supervised during the COVID-19 outbreak. Infection with covid has a significant impact on outcomes in the areas on diagnosis, prognosis and therapy of carcinoma. According to new research, cancer COVID-19 patients had a worse trend than covid positive patients having no tumour. Other studies, on the other hand, show that cancer patients do not have greater rates of COVID infection or severe episodes than the general population. As a result, more research is needed for greater insight in the association between COVID-19 and cancer. Extensive research into the cancer therapies being safe and effective must be looked into. To look into the complete demographics and unfavourable factors for acquiring covid in cancer patients, it is a necessity to facilitate various extensive multicentric retrospective studies.

For cancer patients, the current circumstance is rather alarming; if patients get exposed to COVID, handling the patient will be a struggle for healthcare systems all over the world. There is an increased risk of delivering symptomatic care to COVID oncological patients as the severity of the disease grows. The influence on cancer detection and treatment is deteriorating for patients and has even become uncontrollable, resulting in patient fatalities. Between tumours and COVID-19, the molecular process is pretty obvious, with ACE-2, cytokines, TMPRSS2, and coagulation all playing a role. Collaboration between the hospital system and oncological groups is critical and will save a lot of money.

Our current understanding of the comorbidities is limited due to the bulk of findings involving covid and tumour positive patients are cohort studies with limited sample size, poor clinical information, significant variation of tumour stages and oncological types, as well as a plethora of therapeutic options. The clinical effects and molecular basis for cancer COVID-19 comorbidity have yet to be explored. The possibility of coronavirus recurrence adds to the requirement of developing technologies to enhance the therapies and fostering of COVID-19 positive cancer patients.

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