

COVID-19 and Hematology/Oncology Patients: Complications and Recommendations

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Abstract

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus causing a global pandemic and mainly characterized with respiratory symptoms, but a cytokine storm may occur. Hematology and Oncology patients are immunocompromised and laboratory data is altered in particularly the hematology parameters including a coagulopathy. In this review, the goal is emphasizing the complications and a consensus in recommendations on how to prevent further problems in patients with cancer and blood disorders and how to manage them.

Keywords: Complications; Covid-19; Hematology; Oncology; Patients; Recommendations

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Received Date: August 20, 2020

Accepted Date: August 25, 2020

Published Date: September 01, 2020

Citation: Morales-Borges RH (2020) COVID-19 and Hematology/Oncology Patients: Complications and Recommendations. J Hematol Hemother 5: 012.

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Introduction

COVID-19 also known as coronavirus disease and incorrectly as coronavirus pneumonia, is an infectious disease caused by the SARS-CoV-2 virus. Produces flu-like symptoms, including fever, dry cough, and shortness of breath, myalgia, and fatigue. Symptoms appear between two and fourteen days, an average of five days, after exposure to the virus. In severe cases, it is characterized by pneumonia, acute respiratory distress syndrome, sepsis, and septic shock leading to about 3.75% of those infected to death according to WHO. There is no specific treatment; the main therapeutic measures are to relieve symptoms and maintain vital functions [1].

There are 21,733,247 cases and 771,043 deaths globally with 25,695 cases and 329 deaths in Puerto Rico by August 16 of 2020 [2]. The outbreak of Coronavirus Disease 2019 (COVID-19) started back in December 2019 with a cluster of pneumonia cases in Wuhan, a city within the central part of China, and has rapidly evolved into a global pandemic [3]. After viremia, SARS-CoV-2 primarily affects tissues that express high levels of ACE2, including the lungs, heart, and gastrointestinal tract. Approximately 7 to 14 days from the onset of initial symptoms, there is an increase in clinical manifestations of the disease. This is with a pronounced systemic increase of inflammatory mediators and cytokines, which can even be characterized as a "cytokine storm" [1]. At this point, significant lymphopenia becomes apparent. Although further research on the underlying etiology is needed, several factors may contribute to COVID-19-associated lymphopenia. Lymphocytes have been shown to express the ACE2 receptor on its surface; therefore, SARS-CoV-2 can directly infect those cells and ultimately lead to their lysis [1]. Besides, cytokine storm is characterized by a noticeable increase in levels of interleukin (mainly IL-6, IL-2, IL-7, granulocyte colony-stimulating factor, interferon- γ inducible protein, MCP-1, MIP1- α) and Tumor Necrosis Factor (TNF)- α , which can promote lymphocyte apoptosis.

In oncology [4], the patient is more immunocompromised (3-5 times more). The reasons for being more immunocompromised are

Cancer, Surgery, Chemotherapy, Immunotherapy, Radiation Therapy, and Nutritional status. The main problem for these patients is limited access to health care (inability to receive the necessary services at an appropriate time). These patients become even more complicated when they are in the intensive and intubated units. Its most serious complications are Acute Respiratory Distress Syndrome (29%), Septic Shock (4%) Myocardial Infarction (4%).

In this review, I am emphasizing the complications and a consensus in recommendations on how to prevent further problems in patients with cancer and blood disorders and how to manage them.

Presentation

As China was the first epicenter for the pandemic, the Chinese epidemiologic knowledge constitutes most printed literature reportage COVID-19 infections. The first case series as well as a complete of three hundred COVID-19 patients identified a pair of cancer patients solely [5]. Later case series by Liang (18 cases), Zhang (28 cases) and Zhang (67 cases) reportable a better prevalence of cancer patients with COVID-19 infections compared with the population (1 vs 0.29%) [5], a better median age at identification (63-66 vs forty-nine years) [5-8], and a male predominance (61%) [6-8]. respiratory organ cancers (22-25%), channel cancers (14-16%), and breast cancers (11%) were the foremost encountered tumors [5-8]. The clinical options enclosed fever (80-82%), dry cough (75-81%), and symptom (50-66%) [5-8]. The symptom was noted at admission in severe cases (56.3 vs 11.4%) and in no survivors (66.7 vs 20.4%) whereas the opposite symptoms were similar between delicate and severe cases [6,8]. Laboratory tests showed symptoms (89%), lymphopenia (82%), inflated level of C-reactive protein (82%), and anemia (75%). as compared with patients while not cancer, cancer patients had a better risk of adverse events (39 vs 8%; $p=0.0003$) and deteriorated quicker (13vsforty-three days, HR=3.56; ninety-fifth CI: one.65-7.69) [5]. Severe events were reportable in 48-54% of cases (versus Sixteen Personality Factor

Questionnaire within the overall population), notably among patients receiving antineoplastic treatment among the previous a pair of weeks (OR=four.079; ninety-fifth CI: one.086-15.322) [5-8]. Compared with the delicate malady cluster, patients within the severe malady cluster were older (69 vs sixty-four years; $p<zero.001$) and had a lot of comorbidities (72 vs37%; $p=zero.004$) [6]. Serious complications enclosed acute metabolic process distress syndrome (20.9 vs3.4% within the overall population), heart condition (16.4%), and acute excretory organ injury (3 vs zero.5% within the overall population) [6-8]. Empirical antibiotics, antiviral agents, glucocorticoids, and intravenous immunoglobulins were administered in eighty-two, 71-85, forty-five, and 20-26%, severally. Chemical element medical aid, noninvasive ventilation, and invasive mechanical ventilation were needed in seventy-three, thirty, and 12-36%, severally [6-8]. Cancer patients had a better case-fatality rate (5.6-29 vs 1 Chronicle within the overall population) [6-8]. The median length to recovery and death was thirty-one and twenty days, severally [6].

Diagnosis

The role of clinical laboratory data in the differential diagnosis of the severe forms of COVID-19 has not been established. A retrospective study on COVID-19 patients from January 23, 2020, to February 2, 2020, in the Fuyang Second People's Hospital, was done to look for the warning index in severe COVID-19 patients [9]. They investigated 43 adult patients with COVID-19. The patients were classified into a mild group (28 patients) and severe group (15 patients). A comparison of the hematological parameters between the mild and severe groups showed significant differences in interleukin-6 (IL-6), d-dimer (d-D), glucose, thrombin time, fibrinogen, and C-reactive protein ($P < .05$). The optimal threshold and area under the Receiver Operator Characteristic Curve (ROC) of IL-6 were 24.3 and 0.795 $\mu\text{g/L}$, respectively, while those of d-D were 0.28 and 0.750 $\mu\text{g/L}$, respectively. The area under the ROC curve of IL-6 combined with d-D was 0.840. The specificity of predicting the severity of COVID-19 during IL-6 and d-D tandem testing was up to 93.3%, while the sensitivity of IL-6 and d-D by parallel test in the severe COVID-19 was 96.4%. IL-6 and d-D were closely related to the occurrence of severe COVID-19 in the adult patients, and their combined detection had the highest specificity and sensitivity for early prediction of the severity of COVID-19 patients, which has important clinical value [9].

The inflammatory response plays a critical role in coronavirus disease 2019 (COVID-19), an inflammatory cytokine storm increases the severity of COVID-19. A retrospective cohort study included 140 patients diagnosed with COVID-19 from January 18, 2020, to March 12, 2020, and they investigated the ability of interleukin-6 (IL-6), C-Reactive Protein (CRP), and Procalcitonin (PCT) to predict mild and severe cases of COVID-19 [10]. They found that patients with IL-6 >32.1 pg/mL or CRP >41.8 mg/L were more likely to have severe complications.

A meta-analysis of 4,911 patients from 29 studies [11] demonstrated that severe patients tend to present with increased White Blood Cell (WBC) and neutrophil counts, Neutrophil-Lymphocyte Ratio (NLR), PCT, CRP, Erythrocyte Sedimentation Rate (ESR), and IL-6 and a decreased number of total lymphocyte and lymphocyte subtypes, such as CD4+ T lymphocyte and CD8+ T lymphocyte. They found that NLR, as a novel marker of a systemic inflammatory response, can also help predict clinical severity (OR=2.50, 95% CI: 2.04-3.06) in patients with COVID-19 [11].

A retrospective case study was carried out in three hospitals in Wuhan, China all affiliated with the Tongji Medical College of Huazhong University of Science and Technology with 28 hospitalized cancer patients diagnosed with COVID-9 infection were identified between 13 January 2020 and 26 February 2020 [12]. Low levels of serum albumin (31.1, 28.6e34.8 g/L) were observed in 25 (89.3%) patients and high levels of serum globulin (32.1, 27.9e37.1 g/L) in 11 (39.3%) patients. High levels of lactate dehydrogenase (262.9, 168.5e508.0 U/L) were found in 10 (50%) patients [12].

Coagulopathy in patients with COVID-19 is a common complication that jeopardizes the clinical course and is associated with poorer outcomes [13,14]. This COVID-19 coagulopathy presents mainly as a prothrombotic state, and there is evidence that anticoagulation may reduce mortality rates [15]. The Partial Thromboplastin Time (PTT) is prolonged in many patients with COVID-19 and may indicate the presence of LA [16]. Most patients with COVID-19 have elevated levels of C-Reactive Protein (CRP), and CRP is known to interfere with LA PTT-based tests, such as the hexagonal phase phospholipid neutralization assay STACLOT-LA [17]. One hundred eighty-seven patients had LA testing ordered from March 1 to April 30, 2020, at Montefiore Medical Center, a large tertiary center in the Bronx, New York. Of those, 119 were not tested or tested negative by COVID reverse transcriptase-polymerase chain reaction. The LA-positive rate by DRVVT in patients who tested negative for COVID-19 was 22% (27 of 119). In contrast, the LA-positive rate in patients who tested positive for COVID-19 was 44% (30 of 68) ($P=002$). Of the 30 COVID-19-positive patients who had a positive LA by DRVVT, 17 (59%) were also positive by hexagonal phospholipid neutralization STACLOT-LA test [17]. That cohort study found an increased incidence of LA positivity in patients with COVID-19 after adjusting for CRP levels. Besides, LA was associated with the incidence of thrombosis in patients with COVID-19. Limitations of this retrospective study include small sample size and inability to control the time of LA testing from admission to the outcome (mortality and thrombosis). LA-positive individuals have a marked risk of arterial and venous thrombosis, and therapeutic anticoagulation should be considered in these patients.

The coagulation changes associated with COVID-19 mimic other systemic coagulopathies that are regularly seen during severe infections, such as disseminated intravascular coagulation or thrombotic microangiopathy. However, at the same time, the clinical and laboratory characteristics of the coagulation changes in COVID are distinctly different from those in the common presentation of these conditions. Severe COVID-19 infections seem to cause a profound coagulation abnormality caused by inflammation-induced changes in coagulation in combination with severe endothelial cell injury, with a consequent massive release of von Willebrand factor and plasminogen activators [18]. This coagulopathy likely contributes to pulmonary microvascular thrombosis, bronchoalveolar fibrin deposition (which is a hallmark of adult respiratory distress syndrome), and thromboembolic complications [18]. So, the main laboratory tests in hematology should be monitored such as CBC, Peripheral smear, PT/PTT, Fibrinogen, and D-Dimer.

Regarding radiologic findings, in one study [12] the features on chest CT were: 78.6% with bilateral involvement, 21.4% of patients had unilateral focal involvement. Ground-glass opacity, the predominant CT imaging pattern, was observed in 75% of patients. Patchy consolidation was the second most common finding 46.3% of patients. Interstitial abnormalities, including reticular appearance,

fibrous strips, and interlobular septal thickening, were found in 14.3% of patients. Follow-up CT was carried out 7 to 14 days after admission and showed improvement in 46.4% of the patients.

Complications

As much as 53.6% of the patients developed severe events, 21.4% were admitted to ICU, 35.7% had life-threatening complications, and 28.6% of the patients died [12]. Their results showed the following clinical features of COVID-19-infected cancer patients: typical symptoms of fever, dry cough, fatigue, and dyspnea, along with blood lymphocytopenia and high levels of highly sensitive C-reactive protein [12]. Cancer patients present with clinical features like those in the general population, except for anemia and hypoproteinemia, which were frequently found in this cohort. Anemia and hypoproteinemia were a major consequence of nutritional deterioration in cancer patients, which may adversely affect immunocompetence and increase the susceptibility to respiratory pathogens.

In respect to the pediatric cancer population, a study from New York, USA demonstrated that the total percentage of COVID-19-positive tests was low at 11% in their population and was consistent with the rates previously reported in pediatric patients [19]. Since social distancing to prevent infections is a well-established behavior in pediatric hematology, oncology, and HCT patients, this may not be reflective of the general pediatric population. Nevertheless, their data reinforced the impression that pediatric patients have a lower burden of COVID-19 disease compared to adults and that most of their COVID-19+ patients had relatively mild disease and could be treated outpatient or without the need for respiratory support [19]. A group from France (The French society of pediatric oncology) stated that although it's too quickly to share their small data, few of their patients required ICU and ventilator support [20]. COVID-19 in pediatric oncology patients appears to be rare, all stakeholders from physicians to patients and their families should be aware of a higher risk of severe forms compared to immunocompetent children [20].

Recommendations

Antiviral therapies like lopinavir-ritonavir and remdesivir square measure undergoing analysis, and the role of anti-cytokine therapies like tocilizumab for severe infections is below exploration [21]. Unfinished additional data, we advise that management of COVID-19 ought to be similar for patients with and while not cancer. Disorder patients with suspected or confirmed COVID-19 ought to be mentioned with an associate communicable disease or clinical biology specialist [21].

Temporary discontinuance of cancer therapies is secure for a few patients with cancer WHO develop symptoms of COVID-19, to reduce treatment-related immunological disorder, or to scale back the chance of drug interactions [21]. This could be undertaken in discussion with an associate specialist or specialist accustomed to the management of the malignancy, who will advise on the advantages and risks of pausing medical aid. Regarding adrenal cortical steroid, within the recovery trial, it was helpful for participants treated seven or a lot of days into the symptomatic part, with the onset of hypoxemia. Significantly, there was a non-significant trend ($P=0.14$) towards potential hurt moving participants while not hypoxemia and not on mechanical ventilation [22]. Recovery findings so support the use of adrenal cortical steroids just for patients with hypoxemia, not those with a milder malady. The info doesn't support the use of adrenal cortical steroid or alternative corticosteroids within the patient setting [22].

From a similar group of China [23], the primary prospective randomized controlled trials applying a High Dose offIntravenous Vitamin C (HIVC) to treat COVID-19 began. 'High-dose' antioxidant medical aid lacks a universal definition. A previous meta-analysis thought of high doses as capable as or larger than 10 g/day. During this trial, they're going to Vitamin C (VC) per day for seven days intravenously. HIVC has benefits in terms of stability, convenience, safety, and price compared with alternative treatments. The sample size was calculated in 2 stages to make sure the calculation is affordable, maximizes the likelihood of getting important results, and provides credible outcome knowledge. Because the length and distribution of infected cases square measure unpredictable geographically and temporally, the number of recruited patients at every center is additionally unpredictable, despite competitive ingress. As per Dr. Cheng [24], HIVC has conjointly been with success utilized in the treatment of fifty moderate to severe COVID-19 patients in China. The doses used varied between ten g and twenty grams per day, given over an amount of 8–10 h. further VC bolus could also be needed among patients in important conditions. The natural process index was up in real-time and every one of the patients eventually cured and were discharged [24]. HIVC has been clinically used for many decades and a recent NIH professional panel document states clearly that this program (1.5 g/kg body weight) is safe and while no major adverse events [24]. Regarding VC, [25] created a superb review regarding the renowned printed multiple mechanisms which has enhanced the operate of leukocytes as well as chemokinesis and taxis, body process, lysosomal protein production, generation of Reactive O Species (ROS) and microorganism killing, up-regulation of the protein response, and increasing antiviral. These effects, alongside increased leukocyte chemotactic action, are documented in humans receiving either endovenous (IV) ascorbic acid or taking gram doses orally. IV antioxidant encompasses a long diary of safety. It's been used traditionally within the management of infective agent infections and a lot of recently for infection. Current clinical trials within U. S. A., Canada, China, Italy, and alternative countries can hopefully support its widespread use for patients with COVID-19 infection within the larger medical profession [25].

Another difference that may be offered before long is that the immunizing agent. COVID-19 vaccine target product profile should address inoculating at-risk human populations as well as frontline care staff, people over the age of sixty, and people with underlying and enfeebling chronic conditions [26]. Among the immunizing agent technologies below analysis square measure whole virus vaccines, recombinant super molecule fractional monetary unit vaccines, and macromolecule vaccines [26]. Every current immunizing agent strategy has distinct benefits and drawbacks. Therefore, it's preponderating that multiple ways be advanced quickly and so evaluated for safety and effectively. Ultimately, the protection studies to reduce unwanted immunopotential can become the foremost important bottleneck in terms of your time. As a result of the event of efficacious vaccines and antiviral medicine takes time, VC and alternative antioxidants square measure among presently offered agents to mitigate COVID-19 associated respiratory disease.

Given the very fact that high-dose VC is safe, care professionals ought to take an in-depth exploration of this chance. Well-designed clinical studies square measure is completely required to develop commonplace protocols for side use. An interim management accord for hematology/oncology patients [21] within the COVID-19 pandemic was written and declared the following:

- In patients with cancer with fever and/or metabolism symptoms, consider causes additionally to COVID-19, as well as alternative infections and therapy-related inflammation.
- For suspected or confirmed COVID-19, discuss temporary stop of cancer medical aid with a relevant specialist.
- Offer data on COVID-19 for patients and their caregivers.
- Adopt measures inside cancer centers scale back to scale back to cut back} risk of healthcare facility SARS-CoV-2 acquisition; support population-wide social distancing; reduce demand on acute services; guarantee adequate staffing; and supply culturally safe care. Measures ought to be evenhanded, clear, and proportionate to the COVID-19 threat.
- Consider the risks and advantages of modifying cancer therapies thanks to COVID-19. Communicate treatment modifications, and review once health service capability permits.
- Take into account the potential impacts of COVID-19 on the blood offer and convenience of vegetative cell donors. • Discuss and document goals of care and involve palliative care services in contingency coming up with.

At last, the higher rate of cancer patients with COVID-19 could be biased and related to the closer medical follow-up of these patients and the higher mortality to delayed hospitalization while coping with the rapid influx of severe cases [8]. Several questions remain unanswered notably the risks of waiting for the COVID-19 epidemic to subside before treating cancer patients or the risks of exposure to this virus during admission for cancer treatment. This should be particularly assessed in patients that may be cured by oncologic treatments. Moreover, the risk of patients receiving hormonal therapy, immune checkpoint inhibitors, and targeted therapies should be assessed. Today, abiding by the old *primum non nocere* concept, clinicians may have to balance the risks of developing a COVID-19 infection against the risks of tumor progression, while taking into consideration the prevailing state of the healthcare system [8].

Conclusion

The COVID-19 pandemic is a challenge globally which is reaching us and causing a significant unprecedented trigger in the area of hematology and oncology. Our patients need attention in this new era. The present review makes a list of possible complications and how to assess and manage them inclusive of a consensus in management and prevention. This is a rapidly evolving situation, and I propose that oncologists and hematologists advocate for the timely application of public health measures, vaccines or treatments that might contain, delay or mitigate the spread of COVID -19 been cost-effective in our patients.

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