



Letter to the Editor

Guidance for Facing Dilemmas of Hematopoietic Stem Cell Transplant Clinicians in the COVID-19 Pandemic: An Iranian Consensus

Keywords: COVID-19; Hematopoietic Stem Cell Transplant; Clinicians.

Published: July, 2020

Received: May 17, 2020

Accepted: June 19, 2020

Citation: Mousavi S.A., Rad S., Rostami T., Vaezi M., Kamranzadeh H., Babakhani D., Tavakoli S., Barkhordar M., Bahri T., Hedayatiasl A., Kiumarsi A., Janbabaei G.. Guidance for Facing Dilemmas of Hematopoietic Stem Cell Transplant Clinicians in the COVID-19 Pandemic: An Iranian Consensus. *Mediterr J Hematol Infect Dis* 2020, 12(1): e2020050, DOI: <http://dx.doi.org/10.4084/MJHID.2020.050>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

To the editor.

Coronavirus Disease 2019 (COVID-19) has been classified as a pandemic by the World Health Organization since March 2020.¹ The number of involved cases is increasing rapidly around the world, and its burden on the health care system is progressively growing. Most countries have restricted their gatherings, travels, and other aspects of life. These restrictions would undoubtedly impact transplant activities in many centers. Although all people are susceptible to this infection, hematopoietic stem cell transplant (HSCT) recipients are at increased risk and dissimilar to other respiratory viruses, little is known about the clinical significance of human coronavirus infection in this population. Therefore, in this paper, we have provided the adopted recommendations on managing HSCT recipients and donors in COVID-19 pandemic from experts in “Hematology, Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran. These recommendations were based on the proposed international guidelines but were modified considering the limitations of health care resources in our country. The recommendations were presented to the health authorities of Iran and were approved by the Deputy Minister for therapeutic services at Ministry of Health of Iran and were suggested and signified to all transplant centers in the country as a practical guideline. It is imperative to note that data about this disease and its impact on our patients is evolving and so our strategy is to repeatedly update the guidance as soon as new information becomes accessible.

Recommendations

- **In HSCT candidates:** In patients not known to have COVID-19 (asymptomatic - the significant considered symptoms are fever, cough, shortness of breath - AND no history of close contact with a diagnosed case of COVID-19):

We would recommend patients for home isolation 14 days before hospital admission, and we would check for CBC, Diff, CRP and COVID-19 test by RT-PCR before admission. A negative result of COVID-19 test (by RT-PCR), 48 hours before the initiation of conditioning regimen is demanded.

In patients known or suspected to have COVID-19 (symptomatic¹ OR history of close contact with a diagnosed case of COVID-19): we would check for CBC, Diff, CRP, COVID-19 test by RT-PCR and chest CT scan before admission:

If a patient who is considered high risk for disease progression (i.e. acute leukemia, high-grade lymphomas), would have a positive RT-PCR test for COVID-19 or chest CT scan suspicious of COVID-19, HSCT should be deferred until symptoms are resolved and two separate negative RT-PCR tests, at least one week apart, are obtained.

If a patient whose underlying disease is considered low risk, would have a positive RT-PCR test for COVID-19, HSCT should be deferred for at least three months.

In patients who have a history of close contact with a known case of COVID-19, but their RT-PCR test for COVID-19 is negative, and their chest CT scan is normal, the conditioning regimen should be deferred until 14 days after the mentioned contact, and one negative RT-PCR test should be obtained before the initiation of the conditioning regimen.

We recommend deferring the HSCTs until the risks associated with the COVID-19 pandemic have passed: non-urgent indications (i.e. Multiple Myeloma in first complete remission - As some novel agents like Ibrutinib or Daratumumab aren't easily available for multiple myeloma patients, we can only defer auto-HSCT for patients in their first complete remission -, low-grade lymphoproliferative diseases, and consolidative transplants for solid tumors such as germ cell tumors) and non-malignant indications.

We recommend deferring the following allogeneic HSCTs until the risks associated with the COVID-19 pandemic have passed: HSCTs from international unrelated donor and HSCTs for non-malignant disorders (i.e. Thalassemia, etc.)

- **In stem cell donors:** Few is known about the risk of COVID-19 transmission from donor to recipient. Attention to donor epidemiological risk factors may help to weaken the risk of donor transmitted infection.²

In donors not known to have COVID-19 (asymptomatic AND no history of close contact with a diagnosed case of COVID-19), we recommend to sustain good hygiene and avoid crowded residences for at least 28 days before donation, and we would test for COVID-19 by RT-PCR one day before the initiation of conditioning regimen in the recipient.

In donors suspected to have COVID-19 (symptomatic OR history of close contact with a diagnosed case of COVID-19), we would check for COVID-19 test by RT-PCR and chest CT scan.

In donors with a history of close contact with a diagnosed case of COVID-19, if the RT-PCR test for COVID-19 is negative and the chest CT scan is normal, the donor would be considered eligible for the donation if 14 days have passed from the mentioned last contact and one negative RT-PCR test obtained before starting conditioning regimen.

If the RT-PCR test for COVID-19 is positive OR the chest CT scan is suspicious of COVID-19, the donor would be considered ineligible to donate for at least three months after the complete resolution of symptoms.

If HSCT is urgent and there are no suitable alternative donors available, re-consider the donor's eligibility; if at least 28 days have passed from the complete resolution of symptoms AND there is no history of severe respiratory disease, and one negative RT-PCR test could be obtained before starting conditioning regimen, the donor would be considered eligible for donation.

As harvesting stem cells from bone marrow requires anaesthesia and referring the donor to the general operation room, in which the donor may be exposed to COVID-19, we prefer to choose peripheral blood as the source of stem cells, for the time being.

- **Recommendations for HSCT recipient's caregiver:** The patient should not have a caregiver if possible. If not possible to get admitted alone, the caregiver's COVID-19 RT-PCR test should be negative before entering HSCT ward. Caregivers with COVID-19 symptoms are ineligible and should be referred to a national guideline for diagnosis and management of COVID-19.

- **Recommendations for the HSCT unit:** SARS-CoV-2 is sensitive to ultraviolet rays and heat.

The virus can be effectively inactivated under conditions of 56 °C for 30 min, using ether, 75% alcohol, chlorine-containing disinfectant, and chloroform.³ Disinfection of HSCT wards should be performed with alcohol-containing disinfectants. People's commute in the HSCT unit should be restricted as much as possible, and non-essential staff & student contact with inpatients should be reduced.

The HSCT unit's workforce should be re-educated about hand hygiene practices, policies for respiratory virus isolation and the significantly associated symptoms of COVID-19. If employees of HSCT units are symptomatic or have a history of close contact with a diagnosed case of COVID-19, they should leave the unit immediately and should be referred to the national guideline of diagnosis and management of COVID-19.

- **Recommendations for recipients in the post-transplant phase:** Patients, after being discharged from the transplant unit should limit their contacts with potentially infected people and should adhere to national prevention guidelines recommendations such as hand hygiene, home isolation and social distancing.

Patients may use cyber network or telephone contact with healthcare providers to manage their non-emergent problems in order to reduce the frequency of travels to the hospital.

Prophylaxis after HSCT with hydroxychloroquine sulfate 400 mg as a single dose (Pediatric dose: 6.5 mg/kg, not to exceed 400 mg) every three weeks since engraftment until the COVID-19 pandemic has lapsed, is recommended.

- **Diagnosis and treatment of COVID-19 in HSCT patients:** For patients with upper or lower respiratory symptoms and for patients who have a history of close contact with a person diagnosed with COVID-19, RT-PCR test for COVID-19 and chest CT scan should be considered. Routine bronchoalveolar lavage (BAL) is not recommended if the patient has a positive RT-PCR test for COVID-19 unless a co-infection is suspected. If RT-PCR test for COVID-19 is positive or chest CT scan is suspicious of COVID-19, the patient should be managed and treated according to national COVID-19 guideline. Optimal management strategies have not been determined. Supportive care is the mainstay of therapy.

For prophylaxis and treatment of graft versus host disease, immunosuppressive therapy should be continued. Drug-drug interactions of anti-viral drugs with calcineurin inhibitors should be kept in mind.

Finally, the emergence of COVID-19 is a global crisis that the transplant community has been forced to face. We should learn from our experiences and implement the best possible strategies in order to protect our transplant recipients and also the healthcare providers.

Seied Asadollah Mousavi, Soroush Rad, Tahereh Rostami, Mohammad Vaezi, Hosein Kamranzadeh Fumani, Davood Babakhani, Sahar Tavakoli Shiraji, Maryam Barkhordar, Tanaz Bahri, Amirabas Hedayati Asl, Azadeh Kiumarsi and Ghasem Janbabaei.

Department of Adult HSCT, Hematology- Oncology and Stem Cell Transplantation Research Center, Shariati Hospital, Tehran University of Medical sciences, Tehran, Iran.

Competing interests: The authors declare no conflict of Interest.

Correspondence to: Tahereh Rostami, MD, Hematology- Oncology and Stem Cell Transplantation Research Center, Shariati Hospital, Kargar Shomali Street, Tehran, Iran, Postal Code:1411713131. Tel: +989123890394. Fax: +98 (21) 8802 9397, E-mail: trostami@sina.tums.ac.ir

Azadeh Kiumarsi, MD, Hematology- Oncology and Stem Cell Transplantation Research Center, Shariati Hospital, Kargar Shomali Street, Tehran, Iran, Postal Code:1411713131. Phone: +989121037104. Fax: +98 (21) 8802 9397, E-mail: raha1221@yahoo.com

References:

1. Branswell H, Joseph A. WHO declares the coronavirus outbreak a pandemic 2020. Available from: <https://www.statnews.com/2020/03/11/whodeclares-the-coronavirus-outbreak-a-pandemic>
2. Michaels MG, La Hoz RM, Danziger Isakov L, Blumberg EA, Kumar D, Green M, Pruett TL, Wolfe CR. Coronavirus disease 2019: Implications of emerging infections for transplantation. American Journal of Transplantation. 2020 Feb 24. <https://doi.org/10.1111/ajt.15832>
3. Ju CR, Lian QY, Zhang JH, Qiu T, Cai ZT, Jiang WY, Zhang J, Cheng Q, Chen G, Li N, Wang CY. Recommended prophylactic and management strategies for severe acute respiratory syndrome coronavirus 2 infection in transplant recipients. Chronic Diseases and Translational Medicine. 2020 Mar 27. <https://doi.org/10.1016/j.cdtm.2020.02.003>
PMid:32363045 PMCID:PMC7194659