INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

GUIDE TO INFECTION CONTROL IN THE HOSPITAL

COVID-19 RELATED INFECTION PREVENTION PRACTICES FOR THE IMMUNOCOMPROMISED HOST

Author
Jaffar A. Al-Tawfiq, MD, FRCP, FACP, Ziad A. Memish, MD, FRCPC, FACP, Lottie Hachaambwa, MBChB, and Megan K. Morales, MD

Chapter Editor
Michael Stevens, MD

Topic Outline

Chapter last updated: September 15, 2020

ABSTRACT

The COVID-19 pandemic has not spared any nation or group, though has perhaps most severely affected patients with compromised immune systems, including people living with HIV, cancer patients, transplant recipients, or those taking immune suppressing medications for autoimmune conditions. These patients frequently have medical comorbidities which may be additionally immune suppressing, including diabetes or kidney disease, and may have more frequent or prolonged contact with healthcare facilities, warranting increased attention to the prevention of COVID-19 exposure and approach to the treatment of such in this vulnerable population.

KEY ISSUES

COVID-19 infection, caused by the SARS-CoV-2 virus, which initially emerged in Wuhan, China in December 2019 was declared a Public Health Emergency of International Concern (PHEIC) one month later, then reached pandemic status by mid-March 2020.[1] No country has remained untouched and as of 14 September 2020, there have been 29,179,130 cases and 926,923 deaths documented worldwide.[1] Responses to the virus have varied between countries, though have largely relied on basic infection control principles of physical distancing, mask use, and hand hygiene, though to varying degrees. Populations most at risk of infection and serious morbidity include smokers or those with hypertension, diabetes, age greater than 60 years, and immunocompromised status. The latter may be people living with HIV, recipients of an organ or bone marrow transplant, cancer and neutropenic patients, and those on long-term biologic agents,

steroids, or other immune suppressing medications for autoimmune conditions or other diseases. Transplant recipients and cancer patients are at higher risk of severe COVID-19 infection, including hospitalization and death.[3] Though COVID-19 infection may set off a harmful inflammatory response in many people, leading to respiratory compromise or multi-organ failure, it is not yet clear how the preexisting use of immune suppressing medications impacts the infection. The generalized approach for most transplant recipients has been to decrease overall immunosuppression, particularly antimetabolites (azathioprine or mycophenolate mofetil).[4] HIV infected individuals with preserved immune function have a favorable prognosis and may be managed the same as other patients in the general population. Some people with HIV may be significantly immunocompromised due to virologic failure or not being on antiretroviral therapy and they are addressed separately below.[5] Many of these immunocompromised patients also have significant healthcare exposures resulting in potentially increased exposure risk to COVID-19, and also have other comorbidities known to increase the risk of severe COVID-19 infection, such as hypertension, cardiovascular disease, diabetes, or lymphopenia. A number of antiviral, anti-inflammatory, and immune modulating drugs are being used off-label or under the auspices of clinical trials but as there is no cure or vaccine for COVID-19 infection at this time, protecting this especially vulnerable population through preventative measures remains of paramount importance.

KNOWN FACTS

- Traditionally, immunocompromised hosts have displayed prolonged viral shedding with other respiratory viruses.
- Initial reports of COVID-19 from China showed that patients with cancer represented about 1% of the COVID-19 patients.[6]
- 30% of cancer patients had severe disease compared to 16% in other patients.[7]

- The overall mortality in cancer patients was 6-23% vs. 2.3% in the general population.[8]
- In clinical cohort and virologic studies, most respiratory samples did not yield replicating-competent virus beyond 8-15 days from symptom onset, though severe and critical cases and immunosuppressed patients may shed infectious virus for longer periods.[9-13]
- A multicenter cohort study of solid organ transplant recipients found 78% were hospitalized, 31% required mechanical ventilation, and there was a 28-day mortality rate of 20.5%.[14]
- Factors independently associated with mortality in solid organ transplant recipients with COVID-19 infection included age >65, congestive heart failure, chronic lung disease, obesity, lymphopenia on presentation, and abnormal chest imaging on presentation. Interestingly, diabetes mellitus, chronic kidney disease, and hypertension were not associated with mortality, although these have been associated with worse outcomes in the general population. Black and Hispanic patients were disproportionately represented but did not have increased mortality.[14]
- Cirrhotic patients with COVID-19 infection have higher mortality compared to COVID-19 infected patients without cirrhosis.[15]
- Patients with rheumatological disease and COVID-19 infection were more likely to be hospitalized if taking 10mg or more of prednisone daily. There was no difference in hospitalization rates for patients taking NSAIDs, hydroxychloroquine, or methotrexate, biologics, or JAK inhibitors and rates were lower in patients taking TNF inhibitors. Co-morbidities (hypertension, diabetes, kidney disease, older age) were also associated with increased risk of hospitalization.[16]
- In earlier single center cohorts of patients with COVID-19 in New York City, USA, and Madrid, Spain, HIV infection was not identified as a major risk factor for complications.[17,18] In resource limited settings, however, it is possible that there could be a greater proportion of HIV infected patients with severe respiratory disease such as tuberculosis which may increase adverse outcomes of COVID-19.[19] A subsequent

multicenter study between the USA and Spain found severe clinical outcomes, including 51.5% mortality among those admitted to an ICU, with risk for poor outcomes increased among those with comorbidities and lower CD4 cell counts, despite viral suppression.[20]

- The effect of COVID-19 on access to HIV medications, HIV pre-exposure prophylaxis, and tuberculosis medicines may affect the progress that has been made in the control of these two major diseases in resource-limited settings.
- People with HIV infection frequent healthcare facilities regularly to collect medicines and access other clinical services. This puts them at risk for COVID-19, especially if clinics are congested. PEPFAR (US President's Emergency Plan for AIDS Relief) has produced technical guidance for providing HIV services to people living with HIV (PLHIV).[21]

SUGGESTED PRACTICE

Medical governance bodies have outlined common infection control practices that pertain to caring for suspected or confirmed COVID-19 patients, and can be reviewed in the ISID COVID-19 chapter (see: https://isid.org/guide/pathogens/covid19/). All routine recommendations including isolation, appropriate personal protective equipment (PPE) selection based on the risk of droplet versus aerosol generation, hand hygiene, and environmental cleaning standards should similarly apply to the care of the immunocompromised host.

While many admissions and surgical cases were canceled due to COVID-19 given concern for healthcare resource shortages, bed availability, and healthcare-associated exposure risk, many immunocompromised hosts continued to receive timely, life-saving care such as chemotherapy, admission for neutropenic fever, or organ transplantation for end-stage organ failure, thus making infection prevention practices in-hospital vital for this cohort. PLHIV must continue to receive antiretroviral drugs and in

some cases, TB preventive therapy (TPT), in both the inpatient and outpatient settings. Special infection prevention measures should be considered for all immunocompromised hosts in the setting of the COVID-19 pandemic to prevent this high-risk group with frequent healthcare exposures from healthcare-associated acquisition of COVID-19 infection.

- **Universal contact precautions -- PPE, mask and hand hygiene recommendations.**

As mentioned above, healthcare workers should observe the recommended PPE and hand hygiene measures. Immunocompromised patients are at increased risk for multidrug-resistant infections and other healthcare-associated infections, though hand hygiene among units caring for these patients may be inconsistent.[22] Most immunocompromised patients were aware of and practicing some degree of increased crowd avoidance and hand hygiene before the pandemic, and with the incremental reopening of societies and communities, they should be routinely reminded by their healthcare providers to continue the use of masks and eye protection, hand hygiene, and physical distancing to protect themselves. Their household members and caregivers should do the same, and also need frequent re-education from care teams.[23] Many transplant or hematology-oncology units have communal areas for visiting, shared recreational book or movie supplies, or kitchens due to often prolonged hospital stays. Shared areas should be restricted with frequent cleaning, or closed while community spread of virus is ongoing. Even with preexisting education about the need for infection prevention, transplant patients still show extremely low compliance with hand hygiene measures while hospitalized.[24]

- **Create a "COVID-19 free" pathway of travel through the hospital or healthcare facility.**

Consider patient flow through hospital or outpatient office settings, and wherever possible, separate entrances or in-hospital transportation routes between COVID-19-infected and non-COVID-19 patients. Suspected or

confirmed cases presenting for admission should be promptly isolated. Use of procedure suites or radiology rooms for COVID-19 infected patients should be separate from non-COVID-19 patients or allow time for terminal cleaning between procedures.

- **Utilize telemedicine or alter clinic patient flow.**

Patients can be screened for symptoms of COVID-19 infection by phone the day before appointments to aid in appropriate triage. This should be repeated upon entry into a healthcare facility. Consider telemedicine visits in place of in-person visits where appropriate. Limit lab and radiology orders to those truly necessary for patient care. Routine labs to update the Model for End-stage Liver Disease (MELD) scores of patients awaiting liver transplantation, for instance, are no longer necessary per updated listing guidelines in the USA. For patients in clinic, use visual cues to maintain physical distancing in waiting areas.

- **Limit visitors.**

Implement hospital policies that limit visitors and mandate screening of visitors for symptoms compatible with COVID-19 infection and fever. Visitors may be limited to immediate family and/or caregivers and should observe institutional hand hygiene and mask regulations.

- **Cohort care teams when possible.**

Grouping healthcare workers onto shared standard shift schedules may limit the number impacted by unintentional exposure (and thus limit the number of staff who may require testing and quarantine). This may be particularly relevant in some settings such as dialysis centers, where many patients may be immunocompromised and spending hours in an indoor communal setting. Keeping consistent staffing with thrice weekly dialysis shifts may help to limit exposures.

- **Negative pressure rooms.**

Many units caring for hematology-oncology or transplant patients routinely utilize positive pressure rooms, however, the use of negative pressure is recommended for COVID-19 infected individuals. There is increasing concern about post-COVID-19 aspergillosis, and many of these patients

may additionally be at risk due to immunosuppressant use or neutropenia. Airlocks and positive pressure environments, where appropriate, may help to limit environmental exposures.

- **Presenteeism.**

Healthcare workers often feel pressured to be present and caring for patients even when ill themselves for a variety of reasons. Those caring for transplant patients are no exception and have high rates of presenteeism, or working when ill.[25]

Symptoms of COVID-19 may be subtle for some individuals, and healthcare workers may be asymptomatic but inadvertently have exposures outside of the hospital, such as through their child's daycare or a spouse with an ill coworker that should prompt their quarantine and testing. Hospital policies to support quarantine and easy access to testing with timely results without unnecessarily penalizing workers will promote these practices and decrease presenteeism, which puts immunocompromised patients and other healthcare workers at risk.

- **Screening of asymptomatic patients pre-procedure or upon hospital admission.**

Like immunocompetent individuals, some immunocompromised patients may be asymptomatic with COVID-19 infection. To avoid infection of other immunocompromised patients and healthcare teams, patients should undergo PCR-based COVID-19 screening before admission or procedures. Organ procurement organizations are screening deceased donors with PCR-based testing. As of 14 September 2020, no confirmed cases of donor-derived COVID-19 infection have occurred, though this remains a theoretical risk. Transplant teams should follow government, transplant society, or institutional guidelines for screening of donors and recipients before transplantation. Patients imminently awaiting organ donation offers should be especially cautious of community COVID-19 acquisition as this would delay transplantation.

- **Prolonged viral shedding may necessitate repeat follow up testing.**

For severely immunocompromised patients with COVID-19 infection, repeat PCR testing may be considered prior to discontinuation of isolation precautions (test-based strategy).[26] Time-based strategies can also be used for most immunocompromised patients with non-severe disease. For time-based strategy, the time should be extended to 20 days at least for those who are severely immunocompromised.[13]

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS

- The World Health Organization (WHO) has recommended continuous medical masks for health workers throughout their shift in clinical areas in localities where there is community transmission. In addition, WHO recommends medical masks for people over 60, those with underlying health conditions, and anyone with symptoms suggestive of COVID-19.[27]
- WHO has also published guidelines on the rational use of PPE for COVID-19.[28]
- Isolate the patient and ensure that at least minimum requirements for infection prevention and control are in place as soon as possible.
- Apply standard precautions for all patients at all times.
- Wear gloves, a gown, and regular surgical masks (or N-95, especially when performing aerosol generating procedures).
- Just before leaving the room, remove the gown, mask, and gloves.
- Discard in an infectious waste container.
- Perform hand hygiene after removing gloves, and as indicated, apply the WHO's the 'My Five Moments for Hand Hygiene'.
- Limit the number of healthcare workers caring for the patient.
- Restrict the number of visitors to health facilities.
- Enforce a minimum distance of 1 m (3 ft) between staff.
- Require staff, visitors, and employees to avoid unnecessary touching or sharing of equipment.

- Maintain a clean environment. Use a sodium hypochlorite concentration of 0.1% (1,000 ppm) in the context of COVID-19 or 70% alcohol on bedside counters and on medical equipment that can tolerate the disinfectant, such as IV poles, at least daily. Note that chlorine is corrosive and also an irritant for the respiratory tract, thus making clinical symptoms worse.
- Limit clinic visits for PLHIV by ensuring they have a 3-6 month supply of antiretroviral drugs on hand.[21]

SUMMARY

Immunocompromised patients frequently have a higher than average exposure to healthcare systems, potentially putting them at risk of healthcare-acquired infection which may include COVID-19 infection. Modifications to the delivery of routine and preventive care can mitigate the risk of exposure while ensuring these patients continue to receive necessary care. For immunocompromised hosts who have suspected or confirmed COVID-19 infection, key infection control practices include hand hygiene, universal PPE use, targeted use of negative pressure rooms, increased awareness of secondary bacterial and fungal infections, and tailored isolation precautions de-escalation that incorporates expert guidance and potentially COVID-19 PCR testing where available.

REFERENCES

1. Listings of WHO's response to COVID-19. Available at: https://www.who.int/news-room/detail/29-06-2020-covidtimeline. Accessed 14 September 2020.
2. COVID-19 Map; available at https://coronavirus.jhu.edu/map.html. Accessed 5 May 2020.

3. Fung, Babik JM. COVID-19 in Fung M, Babik JM. COVID-19 in Immunocompromised Hosts: What We Know So Far [published online ahead of print, 2020 Jun 27]. Clin Infect Dis. 2020;ciaa863. doi:10.1093/cid/ciaa863; available at https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa863/5864040. Accessed 19 July 2020.
4. Parente A, Manzia TM, Angelico R, et al. COVID-19, liver transplant, and immunosuppression: Allies or foes? [published online ahead of print, 2020 Jul 15]. Transpl Infect Dis. 2020;e13417. doi:10.1111/tid.13417; available at https://onlinelibrary.wiley.com/doi/full/10.1111/tid.13417.
5. Interim Guidance for COVID-19 and Persons with HIV COVID-19 and Persons with HIV (Interim Guidance); available at https://aidsinfo.nih.gov/guidelines/html/8/covid-19-and-persons-with-hiv--interim-guidance-/554/interim-guidance-for-covid-19-and-persons-with-hiv. Accessed 24 August 2020.
6. Liang W, Guan W, Chen R, et al. Cancer Patients in SARS-CoV-2 Infection: A Nationwide Analysis in China. Lancet Oncol. 2020;21(3):335–337. doi:10.1016/S1470-2045(20)30096-6; available at https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30096-6/fulltext.
7. Lee LY, Cazier JB, Angelis V, et al. COVID-19 Mortality in Patients with Cancer on Chemotherapy or Other Anticancer Treatments: A Prospective Cohort Study [published correction appears in Lancet. 2020 Aug 22;396(10250):534]. Lancet. 2020;395(10241):1919–1926. doi:10.1016/S0140-6736(20)31173-9; available at https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31173-9/fulltext.
8. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical Impact of COVID-19 on Patients with Cancer (CCC19): A Cohort Study. Lancet. 2020;395(10241):1907-1918. doi:10.1016/S0140-6736(20)31187–9; available at

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31187-9/fulltext.
9. Wölfel R, Corman VM, Guggemos W, et al. Virological Assessment of Hospitalized Patients with COVID-2019. Nature. 2020;581(7809):465–469. doi:10.1038/s41586-020-2196-x; available at https://www.nature.com/articles/s41586-020-2196-x.
10. 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(22):2081–2090. doi:10.1056/NEJMoa2008457; available at https://www.nejm.org/doi/full/10.1056/NEJMoa2008457. Accessed 30 August 2020.
11. Bullard J, Dust K, Funk D, et al. Predicting Infectious SARS-CoV-2 from Diagnostic Samples [published online ahead of print, 2020 May 22]. Clin Infect Dis. 2020;ciaa638. doi:10.1093/cid/ciaa638; available at https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa638/5842165.
12. Lu J, Peng J, Xiong Q, et al. Clinical, Immunological and Virological Characterization of COVID-19 Patients That Test Re-Positive for SARS-CoV-2 by RT-PCR [published online ahead of print, 2020 Aug 24]. EBioMedicine. 2020;59:102960. doi:10.1016/j.ebiom.2020.102960; available at https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(20)30336-4/fulltext.
13. Kampen JJA van, Vijver DAMC van de, Fraaij PLA, et al. Shedding of Infectious Virus in Hospitalized Patients with Coronavirus Disease-2019 (COVID-19): Duration and Key Determinants. medRxiv 2020.06.08.20125310; doi: 10.1101/2020.06.08.20125310; available at https://www.medrxiv.org/content/10.1101/2020.06.08.20125310v1.
14. Kates OS, Haydel BM, Florman SS, et al. COVID-19 in Solid Organ Transplant: A Multi-Center Cohort Study [published online ahead of print, 2020 Aug 7]. Clin Infect Dis. 2020;ciaa1097. doi:10.1093/cid/ciaa1097; available at

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1097/5885162. Accessed 21 August 2020.

15. Bajaj JS, Garcia-Tsao G, Biggins SW, et al. Comparison of Mortality Risk in Patients With Cirrhosis and COVID-19 Compared with Patients with Cirrhosis Alone and COVID-19 Alone: Multicentre Matched Cohort [published online ahead of print, 2020 Jul 13]. Gut. 2020;gutjnl-2020-322118. doi:10.1136/gutjnl-2020-322118; available at https://gut.bmj.com/content/early/2020/07/29/gutjnl-2020-322118.long. Accessed 10 September 2020.
16. Plain Language Summary of COVID-19 Global Rheumatology Alliance's First Provider-Reported Data Analysis | The COVID-19 Global Rheumatology Alliance; available at https://rheum-covid.org/summary-paper-1/. Accessed 21 August 2020.
17. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area [published correction appears in doi: 10.1001/jama.2020.7681]. JAMA. 2020;323(20):2052–2059. doi:10.1001/jama.2020.6775; available at https://jamanetwork.com/journals/jama/fullarticle/2765184.
18. Borobia AM, Carcas AJ, Arnalich F, et al. A Cohort of Patients with COVID-19 in a Major Teaching Hospital in Europe. J Clin Med. 2020;9(6):1733. Published 2020 Jun 4. doi:10.3390/jcm9061733; available at https://www.mdpi.com/2077-0383/9/6/1733.
19. Tadolini M, Codecasa LR, García-García JM, et al. Active Tuberculosis, Sequelae and COVID-19 Co-Infection: First Cohort of 49 Cases. Eur Respir J. 2020;56(1):2001398. Published 2020 Jul 9. doi:10.1183/13993003.01398-2020; available at https://erj.ersjournals.com/content/56/1/2001398.long. Accessed 24 August 2020.
20. Dandachi D, Geiger G, Montgomery MW, et al. Characteristics, Comorbidities, and Outcomes in a Multicenter Registry of Patients with HIV and Coronavirus Disease-19 [published online ahead of

print, 2020 Sep 9]. Clin Infect Dis. 2020;ciaa1339. doi:10.1093/cid/ciaa1339; available at https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1339/5903368.

21. PEPFAR's HIV Response in the Context of Coronavirus Disease 2019 (COVID-19). U.S. Dep. State; available at https://www.state.gov/pepfar/coronavirus/. Accessed 24 August 2020.
22. Graf K, Ott E, Wolny M, et al. Hand Hygiene Compliance in Transplant and Other Special Patient Groups: An Observational Study. Am J Infect Control. 2013;41(6):503–508. doi:10.1016/j.ajic.2012.09.009; available at https://www.ajicjournal.org/article/S0196-6553(12)01250-3/fulltext.
23. Fernandes DR, Braga FTMM, Silveira RCCP, Garbin LM. Hand Hygiene: Knowledge and Skill of Caregivers in the Hematopoietic Stem Cell Transplantation. Rev Bras Enferm. 2019;72(6):1653–1662. Published 2019 Oct 21. doi:10.1590/0034-7167-2018-0788; available at https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-71672019000601653&tlng=en.
24. Srigley JA, Furness CD, Gardam M. Measurement of Patient Hand Hygiene in Multiorgan Transplant Units Using a Novel Technology: An Observational Study. Infect Control Hosp Epidemiol. 2014;35(11):1336–1341. doi:10.1086/678419; available at https://pubmed.ncbi.nlm.nih.gov/25333427/.
25. Mossad SB, Deshpande A, Schramm S, Liu X, Rothberg MB. Working Despite Having Influenza-Like Illness: Results of An Anonymous Survey of Healthcare Providers Who Care for Transplant Recipients. Infect Control Hosp Epidemiol. 2017;38(8):966-969. doi:10.1017/ice.2017.91; available at https://pubmed.ncbi.nlm.nih.gov/28514976/.
26. CDC. Coronavirus Disease 2019 (COVID-19). Duration of Isolation and Precautions for Adults with COVID-192020; available at

https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html. Accessed 10 September 2020.

27. WHO. Advice on the Use of Masks in the Community, During Home Care and in Healthcare Settings in the Context of the Novel Coronavirus (COVID-19) Outbreak; available at https://www.who.int/publications-detail-redirect/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak. Accessed 24 August 2020.
28. WHO. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed; available at https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-IPC-2020.4. Accessed 24 August 2020.