



# Coronavirus disease 2019 in immunocompromised patients: a comprehensive review of coronavirus disease 2019 in hematopoietic stem cell recipients

*Antoine Lafarge, Asma Mabrouki, Elise Yvin, Swann Bredin, Yannick Binois, Raphael Clere-Jehl, and Elie Azoulay*

## Purpose of review

Immunocompromised patients are notably vulnerable to severe coronavirus disease 2019. This review summarizes COVID-19 features and outcomes in autologous and allogeneic hematopoietic stem cell transplantation (HSCT) recipients.

## Recent findings

Recent findings suggest that HSCT recipients exhibit a high burden of comorbidities and COVID-19 clinical features almost similar to the general COVID population. Furthermore, HSCT recipients exhibit a protracted SARS-CoV-2 shedding, prolonging duration of symptoms and promoting the generation of highly mutated viruses. Last, most of studies report a higher COVID-19 mortality in HSCT recipients, mainly driven by age, comorbidities, time from transplantation, and immunosuppression because of both treatments and underlying hematological malignancy.

## Summary

Further studies are warranted to determine the proper impact of HSCT-related immune disorders on COVID-19 outcomes, and to evaluate specific treatments and vaccination strategy in this high-risk population. Taken together, those findings emphasize the need for more rigorous surveillance and preemptive measures for all HSCT recipients.

## Keywords

coronavirus disease 2019, hematopoietic stem cell transplantation, immunocompromised

## INTRODUCTION

Immunocompromised patients are notably vulnerable to severe coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1,2<sup>\*\*\*</sup>,3]. Solid-organ transplantation recipients, cancer, and hematological malignancy patients more often present with severe COVID-19 diseases, requiring more frequently ICU management, mechanical ventilation. Furthermore, case fatality is higher when compared with the general population [2<sup>\*\*</sup>,3–5].

By September 2021, almost 5000 HSCT recipients with COVID-19 have been reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) (<https://www.cibmtr.org/Covid19/Pages/default.aspx#repdata>, accessed on 21 September 2021). However, the literature focusing on HSCT recipients and COVID-19 is still limited and gaps in knowledge remain with regards to pathophysiology, clinical features, viral shedding, disease severity, risk factors, and specific therapeutic strategy.

Here we synthesize data from the emerging literature on adult HSCT recipients with COVID-19.

## HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS DISPLAY CLASSICAL CORONAVIRUS DISEASE 2019 CLINICAL FEATURES

In the largest published studies focusing on adult HSCT recipients with COVID-19 (Table 1), median age ranged from 35 to 67 years and most of patients were men [2<sup>\*\*</sup>,4,6<sup>\*\*</sup>,7,8<sup>\*\*</sup>,9<sup>\*</sup>,10–12].

Medical Intensive Care Unit, Saint Louis Hospital, Assistance Publique Hôpitaux de Paris (APHP), University de Paris, Paris, France

Correspondence to Antoine Lafarge, MD, Medical Intensive Care Unit, Saint-Louis Hospital, Medical Intensive Care Unit, Hôpital Saint-Louis, 1 avenue Claude Vellefaux, 75010 Paris, France. Tel: +33 1 42 49 94 21; e-mail: antoinelafarge@outlook.com

**Curr Opin Crit Care** 2022, 28:83–89

DOI:10.1097/MCC.0000000000000907

**KEY POINTS**

- HSCT recipients exhibit a high burden of comorbidities and COVID-19 clinical features almost similar to the general COVID population.
- HSCT recipients exhibit a protracted SARS-CoV-2 shedding, prolonging duration of symptoms and promoting the generation of highly mutated viruses.
- HSCT recipients display poor COVID-19 outcomes, mainly driven by age, comorbidities, time from transplantation, and immunosuppression because of both treatments and underlying hematological malignancy.

Consistently with data reported in the general population, the most frequent comorbidities were hypertension, diabetes mellitus, and cardiovascular diseases. In general, immunocompromised patients had more baseline comorbidities than nonimmunocompromised patients, a finding, however, not reported in the cohort from Belsky *et al.* [2<sup>■</sup>].

HSCT indication, underlying disease status, active graft-versus-host disease (GVHD) and proportions of patients receiving immunosuppressants at the time of COVID-19 diagnosis varied considerably across studies. Median time from HSCT to COVID-19 diagnosis ranged from 14.9 to 25.6 months. Thus, being more than a year from transplantation, most of HSCT patients included in these studies were not receiving immunosuppression at the time of COVID-19. No study reported the time from disease onset to admission in critical care, which has been demonstrated to be a critical prognostic factor in severe patients [13].

As described in the general population, in solid organ transplantation and cancer patients, the most frequent COVID-19-related symptoms reported in HSCT patients were fever (range 56–71%), cough (range 41–79%), and shortness of breath (range 24–64%) [2<sup>■</sup>]. Diarrhea, anosmia, and dysgeusia were more rarely reported. Because of these study designs, and the risk of underestimation in case of altered B-cell reconstitution, the rate of asymptomatic disease was rarely reported.

Healthcare-associated COVID-19 has been associated with poor outcomes in cancer patients [14] but data regarding hospital-acquired COVID-19 was mostly missing in HSCT recipients. However, in the study from Shah *et al.* [9<sup>■</sup>], 45% of patients had a known exposure outside of the medical system.

In conclusion, HSCT recipients exhibit a high burden of comorbidities and similar clinical

**Table 1.** Nine studies focusing on adult autologous and allogeneic hematopoietic stem cell transplantation recipients with coronavirus disease-19

Author	N	Demographics	Common symptoms	Follow-up	Time from HSCT to COVID-19	Viral shedding (days)	COVID-19 directed therapies	Outcomes	Risk factors
Belsky <i>et al.</i> , meta-analysis	Auto: 7 Allo: 23	Age range: 10.5–64 years	Fever: 56% Dyspnea: 56% Cough: 56%		77 days to 3 years		Corticosteroids: <1% Convalescent plasma <1% Tocilizumab <1% Remdesivir <1%	Severe COVID-19: 32.2%	IS Pneumonia Thrombopenia
Camargo <i>et al.</i> , USA	Auto: 12 Allo: 15	Age: 67 years (50–67) Male: 57%	Fever: 71% Cough: 54% Dyspnea: 33%	59 days (44-88)	21,5 months (10.6-41.8)	26 (7–64)	IS reduced/discontinued: 45% Corticosteroids: 67% Remdesivir: 60% Convalescent plasma: 27% Tocilizumab: 27% IVIg: 7%	Severe: 36% ICU: 25% MV: 25% Secondary infection: 2.5% Overall mortality: 25%	Age ≥50 Time from HSCT <12 months ≥2 IS
El Fakih <i>et al.</i> , Middle East	Auto: 39 Allo: 52	Age: 35 years Male: 58% GVHD: 13%	Fever: 56% Cough: 41% Dyspnea: 24%		14,9 months (16.3–38.9)	37 (14–116)		Severe COVID-19: 15% ICU: 16% MV: 10% Overall mortality: 4.4%	Time from HSCT <12 months

**Table 1 (Continued)**

Author	N	Demographics	Common symptoms	Follow-up	Time from HSCT to COVID-19	Viral shedding (days)	COVID-19 directed therapies	Outcomes	Risk factors
Mushtaq <i>et al.</i> , USA	Auto: 23 Allo: 32	Age: 58 years (24–77) Male: 64% GVHD: 22%		6.1 months (0.5–13.6)	17.7 months (0.2–201.9)	54 (14–131)	Remdesivir: 41% Convalescent plasma: 35% Corticosteroids: 22% Monoclonal antibodies: 19% Tocilizumab: 3%	Overall mortality: 16.3% Severe COVID-19: 28% ICU: 19% MV: 10% Secondary infection: 19%	Allogeneic HSCT IS Prior GVHD
Passamonti <i>et al.</i> , Italy	Auto: 51 Allo: 31	Age: 56.4 years (± 11.2)		20 days (10–34)				Overall mortality: 34.1%	Progressive disease status
Sharma <i>et al.</i> , USA	Auto: 134	Age: 60 years (49–65) Male: 60%		25 days (12–35)	23 months (8–51)		Corticosteroids 1% Remdesivir 11.5% Convalescent plasma 6%	Overall mortality: 19% Empiric antibiotics: 14%	Underlying lymphoma
	Allo: 184	Age: 47 years (30–60) Male: 58% GVHD: 33%	Fever: 57%	21 days (8–41)	17 months (8–46)		Corticosteroids 1% Remdesivir 15% Convalescent plasma 7%	Overall mortality: 22% Empiric antibiotics 5%	Age ≥50 Male sex Time from HSCT <12 months
Shah <i>et al.</i> , USA	Auto: 37 Allo: 35	Age: 62 years (25–78) Male: 64% GVHD: 17%	Cough: 65% Fever: 58% Fatigue: 39%	23 days (14–35)	25.6 months (11.6–52.8)	28 (22–35)	Corticosteroids: 18% Convalescent plasma: 16% Tocilizumab 10% Remdesivir 4%	Overall mortality: 22% Secondary infection: 14% MV: 15%	Number of comorbidities Chest infiltrates Neutropenia
Varma <i>et al.</i> , USA	Auto: 14 Allo: 20	Age: 57 (24–76) Male: 65% GVHD: 26%	Fever 71% Cough 79% Dyspnea: 64%		17.4 months (1–248.7)		IS reduced/discontinued: <1% Hydroxychloroquine: 44% Tocilizumab: 18% Remdesivir: 15% Convalescent plasma: 6%	Severe COVID-19: 41% Hospitalization: 74% ICU: 32% Mechanical ventilation: 24% Overall mortality: 21%	Age >40 BMI ≤20 Steroids at diagnosis of COVID-19 Time from HSCT <12 months Anemia Thrombopenia Lymphopenia
Xhaard <i>et al.</i> , Europe	Auto: 54 Allo: 54	Age: 55 years Male: 57.4	Fever: 72% Cough: 44.4%		15.6 months (0–108)		Corticosteroids: 25.9%	Overall mortality: 25.9% ICU: 24.1%	

Allo, allogeneic HSCT; auto, autologous HSCT; GVHD, graft-versus-host disease; HSCT, hematopoietic stem-cell transplantation; IS, immunosuppressants; MV, mechanical ventilation.

features to those reported in the general population and in other immunocompromised patients, suggesting a common host response to SARS CoV-2 infection [2<sup>••</sup>,4].

### **LABORATORY EVALUATIONS AND PROTRACTED SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 SHEDDING IN HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS**

As reported for other immunocompromised patients (solid organ transplantation (SOT), solid tumors) [2<sup>••</sup>], most HSCT recipients displayed lymphopenia at the time of infection, while median leukocyte and neutrophil counts were within the normal range [2<sup>••</sup>,6<sup>••</sup>,7,9<sup>•</sup>,10–12,15]. In the series from Shah *et al.* [9<sup>•</sup>], COVID-19 was associated with a reduction in all lymphocytes subsets, not only including CD4 and CD8 T cells but also B lymphocytes and natural killers. Whenever reported, inflammatory markers, such as ferritin, C-reactive protein, and IL-6 were elevated [6<sup>••</sup>,7,9<sup>•</sup>,12,15], whereas renal and hepatic functions were rarely provided.

Data regarding chest radiography and computed tomography (CT) was scarce but most of HSCT patients exhibited bilateral infiltrates [6<sup>••</sup>,10,11,15]. In the study from Xhard *et al.*, the central review of CT scans showed that atypical lesions were not rare, suggesting that COVID-19 should not be ruled out on the sole basis of radiological findings in HSCT recipients [11].

Nasal swab was the predominant method of COVID-19 diagnosis. Four studies provided data suggesting a consistent protracted viral shedding in HSCT patients [6<sup>••</sup>,7,9<sup>•</sup>,12]. The median shedding time among HSCT patients with at least two consecutive positive tests ranged from 26 to 54 days. It has been reported that some HSCT patients may shed viable SARS-CoV-2 for at least 2 months, arguing for longer periods of isolation in such immunocompromised patients [16]. Protracted COVID-19 disease in immunocompromised patients relying on altered B-cell and T-cell immune responses could favor the generation of highly mutated viruses [17]. Further studies are needed to identify the HSCT-related immune determinants of COVID-19-shedding duration.

### **HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS EXHIBIT POOR CORONAVIRUS DISEASE 2019 OUTCOMES**

In HSCT patients, estimated pooled prevalence of severe COVID-19, overall mortality, and ICU

admission ranged from 15 to 41%, from 4.4 to 34%, and from 16 to 32%, respectively. However, there is no specific data focusing on outcomes among HSCT patients with COVID-19 requiring critical care. Mechanical ventilation was provided in 10–25% of the patients. These outcomes should be interpreted in light of the pandemic context, knowing that most of HSCT patients were not considered eligible for critical care.

In the largest series reported by Sharma *et al.*, severe COVID-19 requiring mechanical ventilation occurred in 15% of 184 allogeneic HSCT recipients and 13% of 134 autologous HSCT recipients. The mortality of mechanically ventilated patients was not provided. The day-30 all-cause mortality was 22% for allogeneic HSCT recipients and 19% for autologous HSCT recipients. Importantly there was no association between survival and the type of transplantation [8<sup>••</sup>].

Despite an important heterogeneity between studies, these findings suggest a higher mortality among HSCT recipients with COVID-19 compared with the general population. In contrast, favorable outcomes reported by few studies seems attributable to highly selected population of HSCT recipients [12,18].

Ventilator-associated pneumonia and invasive fungal infections have emerged as important causes of morbidity and mortality in HSCT recipients [19,20]. In studies focusing on HSCT recipients with COVID-19, documented secondary infections were uncommon, including in patients under corticosteroids or tocilizumab [6<sup>••</sup>,7,8<sup>••</sup>,9<sup>•</sup>,15]. Whenever reported, concurrent infections included ventilator-associated pneumonia, bacteremia, cytomegalovirus and herpes viremia, and aspergillus pneumonia [6<sup>••</sup>,7,9<sup>•</sup>].

However, proportions of HSCT recipients receiving empiric antibiotics could reach 80% among hospitalized patients, suggesting a high level of inappropriate antibiotherapy [15]. In our institution, antibiotics are prescribed only in HSCT recipients with clinically or radiologically suspected superimposed bacterial infection or in those with febrile neutropenia.

### **UNCERTAIN HEMATOLOGICAL OUTCOMES IN HEMATOPOIETIC STEM CELL TRANSPLANTATION POSTCORONAVIRUS DISEASE 2019**

In SOT recipients, both patient and graft survival need to be taken account. Similarly, given the high prevalence of lymphopenia at the time of diagnosis, the potential need for immunosuppression tapering or discontinuation, the role of viral infections in altering the immune reconstitution and promoting GVHD,



studies focusing on HSCT recipients with COVID-19 should monitor hematological outcomes.

In this regard, Shah *et al.* provided reassuring data, demonstrating that even within the first year after transplantation, HSCT patients displayed an efficient lymphocyte reconstitution after COVID-19 [16]. Despite marked lymphopenia, including a lack of circulating B cells, several patients were able to develop SARS-CoV-2 antibodies, suggesting antibody production from noncirculating lymph node or tissue-resident cells. Obviously, the level and sustainability of this response remain uncertain [16].

The study recently published by Mushtaq *et al.* is the only one providing data regarding GVHD. After a median follow-up of 6.1 months, five allogeneic HCT recipients (16%) developed subsequent pulmonary chronic GVHD requiring systemic steroids and additional immunosuppressive drugs [6<sup>\*\*</sup>]. In other studies, no GVHD is reported after COVID-19 infection but no conclusion can be drawn in such limited follow-up time-windows.

Comparing longitudinal lymphocyte subsets before and after COVID-19 infection, Shah *et al.* [9<sup>\*</sup>] demonstrated that most of HSCT patients can develop IgG antibody responses to SARS-COV-2 despite lymphopenia, including a lack of circulating B cells. Further studies with longer follow-up are warranted to investigate the sustainability of this immune response and its clinical impact on COVID-19 incidence.

### **DETERMINANTS OF DISEASE SEVERITY IN HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS WITH CORONAVIRUS DISEASE 2019**

The baseline risk factors associated with HSCT recipients COVID-19 mortality were: older age [7,8<sup>\*\*</sup>,10], male sex [8<sup>\*\*</sup>], number of comorbidities [9<sup>\*</sup>], time from HSCT to COVID-19 infection less than 12 months [7,8<sup>\*\*</sup>,10,12], the use of steroids or at least two immunosuppressants [2<sup>\*\*</sup>,6<sup>\*\*</sup>,7,10], prior GVHD [6<sup>\*\*</sup>], progressive disease status [4], and cytopenia [2<sup>\*\*</sup>,9<sup>\*</sup>,10].

The association between COVID-19 mortality and older age, male sex, progressive malignancy, and baseline lymphopenia has already been demonstrated in the general population [1,4]. It is, thus particularly challenging to distinguish the relative contribution of HSCT immune dysregulation and its related complications on COVID-19 prognosis.

Risk factors, such as time from HSCT, use of immunosuppressive drugs, and active GVHD emphasize the burden of both procedure and drug-induced immunosuppression during the first

months after HSCT. The impact of recent chemotherapy on COVID-19 prognosis in cancer patients remains controversial [21,22]. Interestingly, in the meta-analysis performed by Liu *et al.* [22], mortality was associated with recent chemotherapy in patients with hematological (RR 2.68, 1.90–3.78) but not with solid cancer.

Last, in most published studies focusing on HSCT and COVID-19, autologous and allogeneic HSCT recipients displayed similar short-term mortality rates. In contrast, in the single-center prospective study published by Mushtaq *et al.* after a median follow-up of 6.1 months, the mortality rate was higher in allogeneic HSCT recipients in comparison with autologous HSCT patients (28 and 16%, respectively). In this cohort, allogeneic HSCT was an independent predictor of COVID-19 severity [odds ratio 3.6; 95% confidence interval (CI) 1.2–10.8] [6<sup>\*\*</sup>].

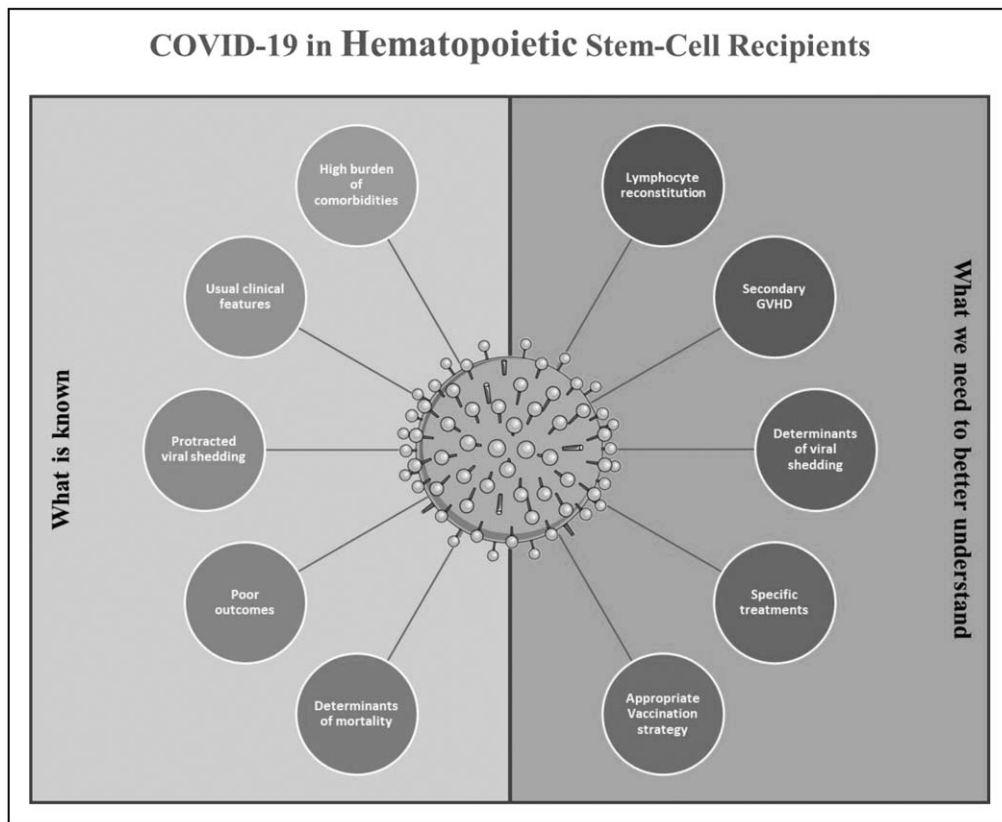
### **CORONAVIRUS DISEASE 2019-DIRECTED THERAPIES AND VACCINATION NEED TO BE EVALUATED IN HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS**

COVID-19 clinical management algorithms and healthcare resources varied considerably depending on countries and pandemic waves. Thus, a careful critical review of therapeutic management in HSCT recipients with COVID-19 is hampered by the number of patients and the heterogeneity between studies and centers.

In most of patients, no specific treatment was described. In the series reported by Sharma *et al.* HSCT recipients with moderate or severe COVID-19 were more likely to receive COVID-19-directed therapies, such as corticosteroids, remdesivir, convalescent plasma, tocilizumab. The need for mechanical ventilation ranged from 10 to 25% but data regarding organ support were not routinely reported [8<sup>\*\*</sup>]. In a variable proportion of HSCT patients across studies, therapeutic immunosuppression was reduced or discontinued.

Dexamethasone is now standard of care for patients with hypoxemia in COVID-19 pneumonia [23]. The efficacy of other directed therapies remains debated. Convalescent plasma might have a beneficial role for HSCT recipients without antibody response because of B-cell aplasia. In our institution, immunosuppressants are not systematically discontinued in HSCT patients with COVID-19.

The efficacy of SARS-CoV-2 mRNA vaccines has been successfully demonstrated in healthy populations [24]. A recent single-center cohort study reported a high response rate of 83% in allogeneic HSCT recipients after two doses of Pfizer-BioNTech COVID-19 vaccine [25<sup>\*</sup>]. However, the efficacy to



**FIGURE 1.** Coronavirus disease 2019 features and outcomes in autologous and allogeneic hematopoietic stem cell transplantation recipients. Left panel: recent findings suggest that HSCT recipients exhibit a high burden of comorbidities and COVID-19 clinical features almost similar to the general COVID population. HSCT recipients exhibit a protracted SARS-CoV-2 shedding, prolonging duration of symptoms and promoting the generation of highly mutated viruses. Most of the studies report a higher COVID-19 mortality in HSCT recipients, mainly driven by age, comorbidities, time from transplantation, and immunosuppression because of both treatments and underlying hematological malignancy. Right panel: further studies are warranted to evaluate COVID-19-related hematological outcomes, to determine the proper impact of HSCT-related immune disorders on COVID-19 outcomes, and to evaluate directed therapeutic strategies in this high-risk population. COVID-19, coronavirus disease 2019; HSCT, hematopoietic stem-cell recipients; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

prevent severe COVID-19 in HSCT recipients needs to be confirmed. In this regard, a Blood and Marrow Transplant Clinical Trials Network study is currently investigating SARS-CoV-2 vaccine immunogenicity in HCT recipients [26].

## DISCUSSION

This review summarizes COVID-19 features and outcomes in autologous and allogeneic HSCT recipients (Fig. 1). The interpretation of the emerging literature is limited by the heterogeneity between studies (pandemic time-period, geography, hematological malignancies, time from HSCT, age, ICU resources, proportion of outpatients), the short-term outcomes, the limited samples, the lack of transplant-related outcomes, and the retrospective design of

these studies. Last, it should be noted that, in the context of overwhelmed health system because of the pandemic, most of HSCT patients were not considered eligible for critical care (including mechanical ventilation, extracorporeal membrane oxygenation support, ICU admission).

Further studies are warranted to analyze outcomes of HSCT patients admitted in ICU, determine the proper impact of HSCT-related immune disorders on COVID-19 outcomes, and evaluate directed therapeutic strategies, such as convalescent plasma in this high-risk population.

## CONCLUSION

Available data suggest that HSCT recipients exhibit a high burden of comorbidities and COVID-19

clinical features similar to the general population. Furthermore, HSCT recipients exhibit a protracted SARS-CoV-2 shedding with prolonged symptoms and high risk of highly mutated viruses. Last, most studies report a higher COVID-19 mortality in HSCT recipients, mainly driven by age, comorbidities, time from transplantation, and immunosuppression because of both treatments and underlying hematological malignancy.

Taken together, those findings emphasize the need for more rigorous surveillance and preemptive measures for all HSCT recipients.

## Acknowledgements

None.

## Financial support and sponsorship

None.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Feng Y, Ling Y, Bai T, *et al.* COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med* 2020; 201:1380–1388.
  2. Belsky JA, Tullius BP, Lamb MG, *et al.* COVID-19 in immunocompromised patients: a systematic review of cancer, hematopoietic cell and solid organ transplant patients. *J Infect* 2021; 82:329–338.
- In this is first systematic review evaluating COVID-19 phenotype and outcomes in immunocompromised patients and comparing them to the general population, Belsky *et al.* identify poor COVID-19 outcomes, mainly driven by a higher comorbidity burden.
3. Mirouse A, Darmon M, Zafrani L, *et al.* Impact of immunosuppression on mortality in critically ill COVID-19 patients. *Br J Haematol* 2020; 191:394–395.
  4. Passamonti F, Cattaneo C, Arcaini L, *et al.*, ITA-HEMA-COV Investigators. Clinical characteristics and risk factors associated with COVID-19 severity in patients with hematological malignancies in Italy: a retrospective, multicentre, cohort study. *Lancet Haematol* 2020; 7:e737–e745.
  5. ElGohary GM, Hashmi S, Styczynski J, *et al.* The risk and prognosis of COVID-19 infection in cancer patients: a systematic review and meta-analysis. *Hematol Oncol Stem Cell Ther* 2020. S1658-3876(20)30122-9. [Epub ahead of print]
  6. Mushtaq MU, Shahzad M, Chaudhary SG, *et al.* Impact of SARS-CoV-2 in hematopoietic stem cell transplantation and chimeric antigen receptor T cell therapy recipients. *Transplant Cell Ther* 2021; 27:796e1–796e7.
- In this single-center prospective study with a median follow-up of 6.1 months, the mortality rate was 16% in all patients and 28% in allogeneic HSCT recipients. Among allogeneic HSCT recipients, 5 (16%) developed subsequent pulmonary chronic GVHD necessitating systemic steroids and additional IST. Significant predictors of COVID-19 severity included allogeneic HSCT, history of grade II-IV acute GVHD, and concurrent immunosuppressive drugs.
7. Camargo JF, Mendoza MA, Lin R, *et al.* Clinical presentation and outcomes of COVID-19 following hematopoietic cell transplantation and cellular therapy. *Transpl Infect Dis Off J Transplant Soc* 2021; 23:e13625.

8. Sharma A, Bhatt NS, St Martin A, *et al.* Clinical characteristics and outcomes of COVID-19 in haematopoietic stem-cell transplantation recipients: an observational cohort study. *Lancet Haematol* 2021; 8:e185–e193.

Three hundred and eighteen HSCT recipients diagnosed with COVID-19 were included in this retrospective study. At 30 days after the diagnosis of COVID-19, overall survival was 68% for recipients of allogeneic HSCT and 67% for recipients of autologous HSCT. Age 50 years or older, male sex, and development of COVID-19 within 12 months of transplantation were associated with a higher risk of mortality among allogeneic HSCT recipients.

9. Shah GL, DeWolf S, Lee YJ, *et al.* Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation. *J Clin Invest* 2020; 130:6656–6667.

This retrospective study provides preliminary insights into the lymphocyte populations that are key for the antiviral response and immune reconstitution. Immune profiling reveals reductions and rapid recovery in lymphocyte populations across lymphocyte subsets. Antibody responses were seen in a subset of patients.

10. Varma A, Kosuri S, Ustun C, *et al.* COVID-19 infection in hematopoietic cell transplantation: age, time from transplant and steroids matter. *Leukemia* 2020; 34:2809–2812.
  11. Xhaard A, Xhaard C, D'Aveni M, *et al.* Risk factors for a severe form of COVID-19 after allogeneic haematopoietic stem cell transplantation: a Société Francophone de Greffe de Moelle et de Thérapie cellulaire (SFGM-TC) multicentre cohort study. *Br J Haematol* 2021; 192:e121–e124.
  12. El Fakih R, Haroon A, Alfraih F, *et al.* Clinical course and outcomes of COVID-19 in hematopoietic cell transplant patients, a regional report from the Middle East. *Bone Marrow Transplant* 2021; 56:2144–2151.
  13. COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. *Intensive Care Med* 2021; 47:60–73.
  14. Elkrief A, Desilets A, Papneja N, *et al.* High mortality among hospital-acquired COVID-19 infection in patients with cancer: a multicentre observational cohort study. *Eur J Cancer Oxf Engl* 1990 2020; 139:181–187.
  15. Kanellopoulos A, Ahmed MZ, Kishore B, *et al.* COVID-19 in bone marrow transplant recipients: reflecting on a single centre experience. *Br J Haematol* 2020; 190:e67–e70.
  16. Aydillo T, Gonzalez-Reiche AS, Aslam S, *et al.* Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer. *N Engl J Med* 2020; 383:2586–2588.
  17. Choi B, Choudhary MC, Regan J, *et al.* Persistence and evolution of SARS-CoV-2 in an immunocompromised host. *N Engl J Med* 2020; 383:2291–2293.
  18. Lupo-Stanghellini MT, Xue E, Mastaglio S, *et al.* COVID-19 in recipients of allogeneic stem cell transplantation: favorable outcome. *Bone Marrow Transplant* 2021; 56:2312–2315.
  19. Aguilar-Guisado M, Jiménez-Jambrina M, Espigado I, *et al.*, Spanish Network for Research in Infectious Diseases. Pneumonia in allogeneic stem cell transplantation recipients: a multicenter prospective study. *Clin Transplant* 2011; 25:E629–E638.
  20. Wang J, Zhou M, Xu J-Y, *et al.* Comparison of antifungal prophylaxis drugs in patients with hematological disease or undergoing hematopoietic stem cell transplantation: a systematic review and network meta-analysis. *JAMA Netw Open* 2020; 3:e2017652.
  21. Song K, Gong H, Xu B, *et al.* Association between recent oncologic treatment and mortality among patients with carcinoma who are hospitalized with COVID-19: a multicenter study. *Cancer* 2021; 127:437–448.
  22. Liu H, Yang D, Chen X, *et al.* The effect of anticancer treatment on cancer patients with COVID-19: A systematic review and meta-analysis. *Cancer Med* 2021; 10:1043–1056.
  23. RECOVERED Collaborative Group. Horby P, Lim WS, *et al.* Dexamethasone in hospitalized patients with Covid-19 — preliminary report. *N Engl J Med* 2020; 384:693–704.
  24. Polack FP, Thomas SJ, Kitchin N, *et al.*, C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. *N Engl J Med* 2020; 383:2603–2615.
  25. Le Bourgeois A, Coste-Burel M, Guillaume T, *et al.* Safety and antibody response after 1 and 2 doses of BNT162b2 mRNA vaccine in recipients of allogeneic hematopoietic stem cell transplant. *JAMA Netw Open* 2021; 4:e2126344.
- This small observational cohort study examines safety and antibody responses after BNT162b2 mRNA vaccine in allogeneic HSCT recipient. Le Bourgeois *et al.* found a high response rate of 83% in allogeneic HSCT recipients after two doses of BNT162b2 vaccine. This is much more than the 54% rate of seroconversion that has been reported after two doses in solid-organ transplant recipients.
26. BMTCTN website [Internet]. [cited 28 September 2021]. Available at: [https://web.emmes.com/study/bmt2/protocol/2101\\_protocol/2101\\_protocol.html](https://web.emmes.com/study/bmt2/protocol/2101_protocol/2101_protocol.html).