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LETTER TO THE EDITOR

WILEY

Controversies regarding shielding and susceptibility to COVID-19 disease in liver transplant recipients in the United Kingdom

December 2019 saw the emergence of a novel coronavirus, SARS-CoV-2, which rapidly escalated to a global pandemic,[1] with an unprecedented impact on healthcare systems worldwide. The objective of this case series was to report on SARS-CoV-2 infection in liver transplant recipients and discuss the role of immunosuppression, comorbidities, and shielding. In the UK, transplant recipients were classified as individuals vulnerable to SARS-CoV-2 infection due to immunosuppression. They were advised in late March 2020 (Figure 1) by Public Health England to take additional social distancing precautions, a process referred to as "*shielding*".[2] This is a more rigorous form of isolation that requires the individual to not leave their place of residence or come into contact with others. In essence, completely isolate to minimize the risk of being exposed to SARS-CoV-2.

Age, male gender, obesity, hypertension, diabetes, heart disease, and lung or kidney disease have been established as risk factors for severe SARS-CoV-2 infection;[3-5] however, immunosuppression is debated as a risk factor. A report from a high incidence area of northern Italy did not see fatalities in SARS-CoV-2-infected liver transplant patients, unless they were elderly and comorbid.[6] Therefore, these authors suggest that immunosuppression alone is not a risk factor for development of severe SARS-CoV-2 disease. Previous literature from a previous coronavirus outbreak in 2013, MERS-CoV, reports an immunocompromised state as a risk factor for increased severity and death.[7]

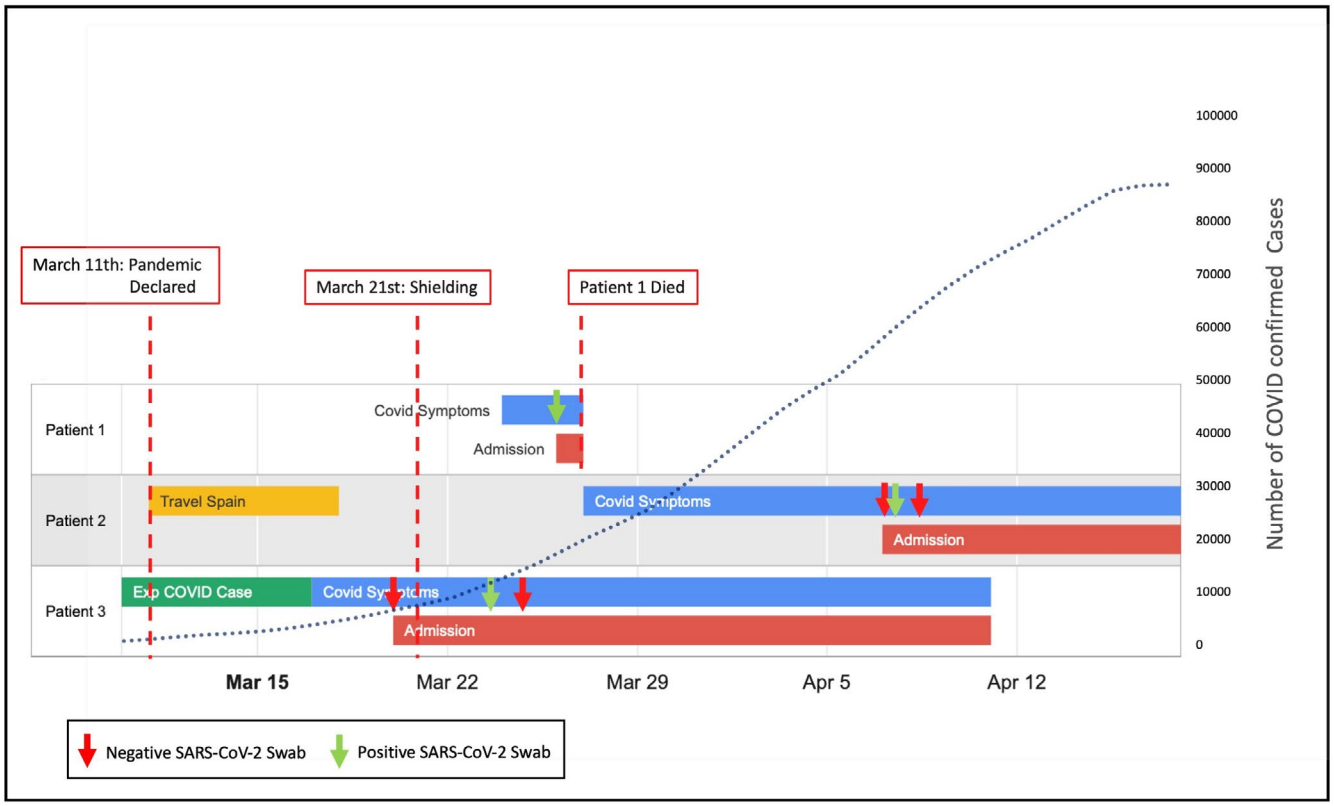

FIGURE 1 Timeline of COVID-related events in Birmingham case cohort; the dashed blue curve demonstrates the confirmed cases in the UK,* and vertical dash lines (in red) represent the important timelines and the possible exposure and diagnosis of cases described in the case series *Source: https://coronavirus.data.gov.uk

TABLE 1 Demographic, medical, and immunosuppression information for the three cases

Pt	Age/ Gender	Time from transplant	Indication for Transplant	Comorbidities	IS regimen	Admission TAC level	COVID symptoms	SARS-CoV-2 Contacts	Risk situation	outcome
1	47 y Male	7 mo (1st) (09/2019) 4 mo (2nd) (12/2019)	Autoimmune Hepatitis Graft Failure (Vasculitis—fibrotic changes)	IDDM Perioperative C. Diff Perioperative AKI BMI 27 HTN	PRED. 7.5 mg TAC 8 mg AZA 50 mg	12.6 ng/ml	Fever SOB	Not aware	GP Visit 10th March 24th March	Died 27th March
2	69 y Male	9 y (2011)	PSC	Ulcerative Colitis Ischemic Cholangiopathy Stage 3 CKD 2ry Adrenal suppression Recent NIDDM BMI 33	HCT 20 mg TAC 5 mg AZA 125mg	11.8 ng/ml	Cough SOB Fever	Not Aware	Travel to Spain (11-18th March)	Discharged on day 16.
3	66 y Female	15 y (2005)	HCV-related Liver disease HCC	IDDM HTN Stage 3 CKD BMI 26	PRED 5mg TAC 1mg AZA 50mg	2.9 ng/ml	Fever SOB Vomiting Diarrhea Myalgia	Husband had clinically suspected SARS-CoV-2	Daughter worked in NHS Accident and Emergency department	Discharged on day 22.

Abbreviations: AKI, acute kidney injury; AZA, azathioprine; CKD, chronic kidney disease; GP, General Practitioner; HTN, hypertension; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; PRED, prednisolone; TAC, tacrolimus.

We highlight three contrasting cases of SARS-CoV-2 infection in liver transplant recipients from the early stages of the pandemic in the UK (Table 1). All patients had similar comorbidities, previously highlighted as risk factors, and were shielded as soon as the government response advised. However, they exhibited a spectrum of COVID-19, with a clinical course ranging from mild-to-severe disease resulting in death in one case. Our patient with a high-level of immunosuppression (Case 1) experienced a severe course of illness, rapidly deteriorated, and died. The other cases described, despite a similar comorbidity profile, had a less severe clinical course. With the clarity of hindsight, it is our opinion that the advice for vulnerable individuals to strictly "shield" came too late for many.

The rapid progression of respiratory failure, leading to the death of one of our patients on immunosuppression, served as a wake-up call after the previous reports that there were no additional risks. We suggest that liver transplant recipients are at high risk for severe SARS-CoV-2 infection and should continue to undergo strict isolation until the pandemic has passed, or robust evidence proves a lack of risk. Shielding, however, is not without a potentially negative impact, with a considerable risk of social isolation and psychological deterioration. It is therefore a priority to develop a robust evidence base to support or refute the risk of immunosuppression and severe COVID-19 and assess the risk/benefit profile of shielding for the wider transplant community.

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CONFLICTS OF INTEREST

All authors declare no financial or other conflicts to declare.

CLINICAL RESEARCH GOVERNANCE

This study was approved by the Information Governance Department at Queen Elizabeth Hospital Birmingham (Clinical Research and Audit Management System approval number 16022) to assess the impact of SARS-CoV-2 on our transplant population via telephone interview and data access.

REFERENCES

1. Zhu N, Zhang D, Wang W et al. A novel coronavirus from patients with pneumonia in China, 2019. *New Engl J Med*. 2020;382:727-733.
2. Public Health England. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19. March 2020. https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19.
3. Guan W-J, Ni Z-Y, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *New Engl J Medicine*. 2020;382(18):1708-1720. https://doi.org/10.1056/nejmoa2002032
4. COVID-19 Surveillance Group, Instituto Superiore di Sanita. Characteristics of COVID -19 patients dying in Italy Report based on available data on March 20th, (2020).

5. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020. *Morbidity Mortal Wkly Rep*. 2020;69(13):382-386.
6. Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol*. 2020;5(6):532-533. https://doi.org/10.1016/s2468-1253(20)30116-3
7. Hui DS, Azhar EI, Kim YJ, Memish ZA, Oh MD, Zumla A. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. *Lancet Infect Dis*. 2018;18:e217-e227.

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