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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Fig S1. (A) Bone marrow aspirate with May–Grünwald Giemsa staining and at 613× magnification. Normal cellularity and an increase in ther amount of megakaryocytes were found.

Fig S1. (B) Bone marrow trephine biopsy (PAS staining, original object lens magnification 20×) with a cluster of three megakaryocytes (Meg). The number is increased; however, they appear morphologically normal. Note the erythropoiesis organised in regularly spaced erythrons (E) and the mestastasis (M) of the neuroendocrine tumour. Although minimal localisation of NET cells was found in the bone marrow, no signs of dysplasia were found. Additionally, with a normal haemoglobin value and leucocyte count we assumed localisation of the NET cells in the bone marrow could not explain the low platelet count, making the diagnosis of ITP more likely.

Fig S2. Petechiae on the left leg of patient 2.

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Clinical outcome of coronavirus disease 2019 in haemato-oncology patients

Since being identified in China in December 2019, coronavirus disease 2019 (COVID-19) has rapidly evolved into a global pandemic with over 4 million cases and more than 270 000 deaths.[1] Following the first reported cases in the United Kingdom (UK) in late January 2020, numbers have continued to rise, with 223 060 cases and 32 065 deaths reported as of May 11, 2020.[2] Initial reports from China have indicated that COVID-19 has an overall mortality rate of 1·4%. However, the prognosis varies widely between groups, with age over 60 years and underlying conditions (including hypertension, diabetes, cardiovascular disease and cancer) identified as risk factors for severe disease and death.[3] The initial reports from China show that patients with cancer are over-represented among individuals who develop severe COVID-19 after contracting the virus.[4] Patients with haematological malignancies are expected to be at increased risk of adverse outcomes from this viral infection, due to being immunosuppressed as a consequence of the underlying cancer, and from the effects of therapy. This has led to a variety of recommendations to reduce the risk from COVID-19, including 'shielding' by self-isolating at home for prolonged periods and alterations to therapy such as delaying or even

Table I. Clinical characteristics of the patients.

Clinical characteristics of the patients	Patients
Enrolment Site – no. (%)	*N* = 35
Barts Health NHS Trust	25 (71%)
Homerton University Hospital NHS Foundation Trust	4 (11%)
The London Clinic	3 (9%)
Southend University Hospital NHS Foundation Trust	1 (3%)
Barking, Havering and Redbridge University Hospitals NHS Trust	1 (3%)
Basildon and Thurrock University Hospitals NHS Foundation Trust	1 (3%)
Median age (range) – years	69 (31–87)
Sex – no. (%)	*N* = 35
Male	23 (66%)
Female	12 (34%)
Haemato-oncological diagnosis – no. (%)	*N* = 35
Multiple myeloma	12 (34%)
Chronic lymphocytic leukaemia/Small lymphocytic lymphoma	5 (14%)
Diffuse large B cell lymphoma	4 (11%)
Acute lymphoblastic leukaemia	4 (11%)
Follicular lymphoma	3 (9%)
Acute myeloid leukaemia	2 (6%)
Mantle cell lymphoma	1 (3%)
Aplastic anaemia	1 (3%)
Myelofibrosis	1 (3%)
Myelodysplastic syndrome	1 (3%)
Monoclonal gammopathy of undetermined significance	1 (3%)
Pre-existing hypogammaglobulinaemia	*N* = 24
Yes	13 (54%)
No	11 (46%)
Number of lines of treatment – no. (%)	*N* = 35
Untreated	3 (9%)
1st line treatment	19 (54%)
2nd line treatment	8 (23%)
≥3rd line treatment	5 (14%)
Patients on active treatment at time of COVID-19 diagnosis	*N* = 35
Yes	24 (69%)
No	11 (31%)
Co-existing disorders – no. (%)	*N* = 35
Hypertension	10 (29%)
Renal failure	5 (14%)
Diabetes	5 (14%)
Previous cancer	4 (11%)
Previous venous thromboembolism	3 (9%)
Atrial fibrillation	3 (9%)
Ischaemic heart disease	2 (6%)
Asthma	2 (6%)
Valvular heart disease	2 (6%)
Chronic lung disease/COPD	2 (6%)
Co-existing non-haematological cancer	1 (3%)
Hyper-obstructive cardiomyopathy	1 (3%)
Liver fibrosis	1 (3%)

Table I. (*Continued*)

Clinical characteristics of the patients	Patients
Symptoms – no. (%)	*N* = 35
Fever	27 (77%)
Cough	21 (60%)
Shortness of breath	19 (54%)
Weakness	5 (14%)
Myalgia	4 (11%)
Diarrhoea	3 (6%)
Coryza	2 (6%)
Chest pain	2 (6%)
Headache	1 (3%)
Vasovagal episode	1 (3%)
Anosmia	1 (3%)

Table II. Correlation of clinical and laboratory findings with outcome.

Clinical/laboratory parameter	Patients	*P* value
Median age (range) – years		
Deceased patients (*N* = 14)	78 (33–87)	<0·0001
Recovered patients (*N* = 21)	59 (31–81)	
Patients on treatment at COVID-19 diagnosis – no. (%)		
Deceased patients (*N* = 14)	9 (64%)	0·72
Recovered patients (*N* = 21)	15 (71%)	
Patients on ≥3rd line treatment – no. (%)		
Deceased patients (*N* = 14)	3 (21%)	0·37
Recovered patients (*N* = 21)	2 (10%)	
Median number of major comorbidities		
Deceased patients (*N* = 14)	2·5 (1–4)	<0·0001
Recovered patients (*N* = 21)	1 (0–2)	
Median admission oxygen saturations (%)		
Deceased patients (*N* = 13)	88 (60–100)	0·0038
Recovered patients (*N* = 17)	96 (88–100)	
Median admission haemoglobin (g/l)		
Deceased patients (*N* = 12)	108 (53–123)	0·46
Recovered patients (*N* = 17)	103 (78–146)	
Median admission neutrophil count ($\times 10^9$/l)		
Deceased patients (*N* = 12)	5·0 (1·6–14·2)	0·0020
Recovered patients (*N* = 17)	2·1 (0·1–10·1)	
Median admission lymphocyte count ($\times 10^9$/l)		
Deceased patients (*N* = 12)	1·2 (0·3–306)	0·048*
Recovered patients (*N* = 17)	0·5 (0·1–1·5)	
Median admission platelet count ($\times 10^9$/l)		
Deceased patients (*N* = 12)	130 (21–244)	0·80
Recovered patients (*N* = 17)	144 (36–280)	
Median admission neutrophil:lymphocyte ratio		
Deceased patients (*N* = 12)	6·1 (0·0–20·7)	0·49*
Recovered patients (*N* = 17)	3·7 (0·3–14·4)	
Median maximum c-reactive protein (mg/l)		
Deceased patients (*N* = 13)	279 (88–367)	0·0006
Recovered patients (*N* = 17)	102 (3–400)	

*A patient with a lymphocytosis due to CLL was excluded for these calculations.

omitting chemotherapy, radiotherapy or transplantation.[5-8] However, at the time of writing there are virtually no published data on the impact of COVID-19 in patients with haematological malignancies.

We identified 35 adult patients with a known diagnosis of a haematological malignancy under the care of Barts Cancer Centre who developed a laboratory-confirmed COVID-19 infection between March 11 and May 11, 2020. A confirmed case of COVID-19 was defined by a positive result on a reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of a specimen collected on a nasopharyngeal swab. Only laboratory-confirmed cases were included, and each patient had at least 14 days of follow-up. The demographic and clinical characteristics of the patients are shown in Table I. The median age of the patients was 69 years; 66% were men. Of 12 patients who had multiple myeloma, five patients had chronic lymphocytic leukaemia, four patients had each of diffuse large B cell lymphoma and acute lymphoblastic leukaemia, three patients had follicular lymphoma, two patients had acute myeloid leukaemia, along with one patient with each of aplastic leukaemia, myelofibrosis, monoclonal gammopathy of undetermined significance, mantle cell lymphoma and myelodysplastic syndrome. 54% of patients were known to have pre-existing hypogammaglobulinaemia at baseline. 24 patients (69%) were on active treatment at the time of COVID-19 diagnosis; the treatment history for each case is given in Data S1. Many patients had co-existing chronic medical conditions: most frequently, hypertension (29%), chronic kidney disease (14%) and diabetes mellitus (15%). The most common symptoms were fever (77%), cough (60%) and shortness of breath (54%).

Table II shows the correlation of clinical and laboratory findings with outcome. As of May 11, 14 patients (40%) had died and 21 (60%) had recovered. Age was most significantly associated with outcome in our series, with all but one of the patients who died being 70 years or older at the time of COVID-19 diagnosis. The number of co-existing comorbidities (such as hypertension, chronic kidney disease or diabetes) was also predictive of outcome, with patients who died having significantly more concurrent diagnoses than patients who recovered. This reflects the observations seen in initial studies where the elderly and those with underlying conditions were at a significantly higher risk for severe disease and death.[3] Importantly, we did not see a correlation between active treatment and outcome in our series. Furthermore, we document 15 patients who have recovered from COVID-19 despite being on treatment at the time of diagnosis of their infection, including patients on highly immunosuppressive regimens such as R-CHOP for lymphoma, induction regimens for acute leukaemia and triplet combinations for myeloma. In terms of laboratory parameters, hypoxia on admission and a highly elevated C-reactive protein level were predictive of a poor outcome. In contrast, there was no association between admission haemoglobin concentration, platelet count or neutrophil/lymphocyte ratio and outcome. Perhaps unexpectedly, patients who recovered had a lower neutrophil and lymphocyte count on admission than the patients who died. This probably reflects inclusion of younger, fitter patients receiving more myelosuppressive and lymphodepleting therapy who nevertheless went on to recover from their infection. However, this highlights that the impact of COVID-19 on haematological parameters such as a lymphopenia or the prognostic utility of neutrophil/lymphocyte ratio may be confounded by other factors in haemato-oncology patients.[9,10]

Given the focus on hospital-based testing for suspected COVID-19 in the UK, a crude case fatality rate in a comparable group of hospital-assessed patients of 14·4% can be calculated from current UK government statistics.[2] In contrast, we observed a case fatality rate of 40% in haemato-oncology patients, which is comparable to the proportion of patients with cancer who reached a composite endpoint of requiring admission to intensive care, invasive ventilation or death in a previous report.[4] Therefore, our patients who developed COVID-19 had an approximately three-fold increased risk of death compared to the general population. Due to the current lack of widespread community testing for COVID-19 in the UK, the case fatality rate reported here is likely to be an overestimate within this patient group. While only patients with laboratory-confirmed COVID-19 were included in our series, we were aware of other haemato-oncology patients who had mild symptoms and were advised to self-isolate at home rather than visit hospital for assessment and were therefore not tested for SARS-CoV-2. Furthermore, it is likely that other patients with no or mild symptoms have not presented to our network.

Our study does have several limitations, including the relatively small sample size and lack of data on patients who developed COVID-19 in the community and were not tested. Ultimately, some of these questions will be addressed by larger multi-national and registry studies. However, given the rapidly-evolving nature of the global COVID-19 pandemic, there is a place for case series in guiding haematological practice during these challenging times. Our data demonstrate that while patients with haematological cancers have worse outcomes after COVID-19 than the background population, the majority still survive.

Conflict of interest

The authors declare no potential conflicts of interest.

Author contributions

J.A. and J.C.R. devised and directed the research project, analysed the data and wrote the paper. J.K.D., J.G.G., J.D.C. and R.L.A. provided the clinical data, contributed to the interpretation of results and wrote the paper. S.L.H., S.M., S.A., H.O., B.S., M.S., J.O., B.W., V.F., S.A., R.L.D., K.Z., E.T. and T.E. worked on patient enrolment and provided

clinical data. All authors provided critical feedback and approved the final version of the manuscript.

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Supporting Information

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Data S1. Supplemental data.

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COVID-19 in bone marrow transplant recipients: reflecting on a single centre experience

Coronavirus disease 2019 (COVID-19) is caused by the novel SARS-CoV-2 virus and has been declared a pandemic on the 9th of March by the WHO. A hallmark of COVID-19 management is supportive care and there is still no convincing evidence for a treatment which will reduce mortality. Severe COVID-19-associated sepsis characterized by acute respiratory distress syndrome (ARDS), secondary bacterial pneumonias, thrombotic complications, myocarditis, and gastrointestinal involvement are more prevalent in those with comorbidities such as hypertension, diabetes, cardiac disease, cancer and age >70 years.[1,2] There is a paucity of data on COVID-19's impact on bone marrow transplant patients. Herein we reflect on the course of seven bone marrow transplant recipients in Birmingham Heartlands Hospital who have been found positive for SARS-CoV-2 RNA on real time polymerase chain reaction (RT-PCR) from nasopharyngeal swabs done in the context of symptoms (fever, cough, dyspnoea, and fatigue) or inpatient contact. The median age was 61 years (range 40–74). Out of these, five (71%) were female and two (29%) were male. The median time from stem cell infusion to the diagnosis of SARS-CoV-2 virus was 61 days (range 7–343). Patients were screened for SARS-CoV-2 via an RT-PCR-based technique.