Hospital. Thanks also to Gilead for access to remdesivir through a compassionate access scheme.

**Author contributions**

All the authors provided clinical care for the patient and were involved in critically revising the manuscript. All the authors have approved the final manuscript.

**Conflicts of interests**

AB has completed paid consultancy work for Gilead relating to the management of COVID-19 in children.

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**Keywords:** COVID-19, SARS-CoV-2, acute lymphoblastic leukaemia (ALL), chemotherapy, remdesivir

First published online 23 August 2020
doi: 10.1111/bjhn.17014

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Thrombocytopenia is independently associated with poor outcome in patients hospitalized for COVID-19

Thrombocytopenia (defined by platelet count \(<150 \times 10^9/\text{l}\)) has been observed in up to 36% of patients with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19).1 In this setting, thrombocytopenia is usually mild, caused by platelet activation and consumption.2,3 In a recent paper published in the British Journal of Haematology, Jiang et al4 conducted a meta-analysis of 31 studies involving 7613 participants and found a significant association between thrombocytopenia and patients hospitalized...
with severe COVID-19, or poor outcome in this setting. However, other clinical, biological and radiological factors strongly impact COVID-19 outcome. Whether or not thrombocytopenia is independently associated with poor outcome in this population is unknown. This study was aimed at addressing this question.

We conducted a study within the Covid-Clinic-Toul cohort, that is the cohort of all patients hospitalized for SARS-CoV-2 at Toulouse University hospital, South of France (a 2,800 bed, unique tertiary hospital covering an area of about 3 million inhabitants); where SARS-CoV-2 infection was proven by reverse transcriptase polymerase chain reaction (RT-PCR). First, patients (from March 11, 2020 to April 1, 2020) were retrospectively included and data from patients hospitalized after April 1, 2020 were prospectively collected. The unique exclusion criterion was opposition to data collection. All patients, or their representatives for those not able to understand the purpose of the study, were informed by a letter given on admission to hospital and/or sent to their place of residency. This cohort was approved by the hospital’s institutional review board (no. RnIPH 2020-31), in accordance with the French data protection authority (MR004, Commission Nationale de l’Informatique et des Libertés, CNIL). In the present study, we selected the patients included in the Covid-Clinic-Toul cohort up to April 20, 2020.

The platelet count within the first 24 h upon admission was considered. Thrombocytopenia was defined by platelet count <150 × 10^9/l. The primary outcome was composite, including admission to ICU, need of mechanical ventilation and death occurring during the 14 days after admission to the hospital. The secondary outcome was death occurring during the 14 days after admission to the hospital. Covariates, assessed upon admission at the time of platelet count measurement, were age (>65 vs. <65 years), sex, presence of comorbidities (>1 vs. 0, including arterial hypertension, cardiovascular disease, cerebrovascular disease, chronic pulmonary disease, chronic liver disease, chronic kidney disease, diabetes, cancer, obesity and immunosuppression), oxygen saturation <92% or need of oxygen therapy, lymphopenia (<1.5 × 10^9/l), C-reactive protein ≥5 mg/dl and severe extension of lesions on chest computed tomography scans ≥50% of lung parenchyma vs. moderate or mild involvement defined by extension <50% of lung parenchyma). Missing values: oxygen saturation, n = 2; lymphocyte count, n = 35; platelet count, n = 10; C-reactive protein, n = 9; extension of lesions on chest computed tomography scans, n = 10.

### Table I. Characteristics of patients admitted to Toulouse University hospital for COVID-19 pneumonia (n = 263).

| Variables                        | Total (n = 263) | Thrombocytopenia* upon admission |
|----------------------------------|----------------|---------------------------------|
| Age ≥65 years, n (%)             | 132 (50.2)     | 40 (63.5)                       |
| Women, n (%)                     | 108 (41.1)     | 17 (27.0)                       |
| Presence of comorbidities, n (%) | 227 (86.3)     | 58 (92.1)                       |
| Oxygen saturation ≤92% or need of oxygen therapy*, n (%) | 117 (44.8) | 37 (58.7) |
| Lymphopenia (<1.5 × 10^9/l)*, n (%) | 189 (82.9) | 54 (93.1) |
| C-reactive protein ≥5 mg/dl*, n (%) | 131 (51.6) | 33 (53.2) |
| Severe extension of lesions on chest CT*, n (%) | 70 (27.7) | 20 (31.7) |
| Death, n (%)                     | 19 (7.2)       | 10 (15.9)                       |
| Admission to ICU, mechanical ventilation or death, n (%) | 122 (48.2) | 43 (68.3) |

CT, computed tomography; ICU, intensive care unit.

*Missing values: platelet count, n = 10; oxygen saturation, n = 2; lymphocyte count, n = 35; C-reactive protein, n = 9; extension of lesions on chest computed tomography scans, n = 10.

### Table II. Association of thrombocytopenia upon admission and outcomes at Day 14 after admission to hospital for COVID-19 pneumonia (n = 263).

| Admission to ICU, mechanical ventilation or death | Thrombocytopenia | Crude OR (95% CI) | Adjusted* OR (95% CI) | Death |
|---------------------------------------------------|-----------------|-------------------|-----------------------|--------|
| N (35.8%)                                         | 43 (39-81)      | 3.16 (1.74-5.87)  | 2.48 (1.17-5.23)      | 10 (52.6%) |
| N (48.8%)                                         | 2.39 (1.13-5.23) |                  |                       | 2.70 (0.91-8.01)     |

CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

*Adjusted for the age (>65 vs. <65 years), sex, presence of comorbidities (>1 vs. 0, including hypertension, cardiovascular disease, cerebrovascular disease, chronic pulmonary disease, chronic liver disease, chronic kidney disease, diabetes, cancer, obesity and immunosuppression), oxygen saturation ≤92% or need of oxygen therapy, lymphopenia (<1.5 × 10^9/l), C-reactive protein ≥5 mg/dl and severe extension of lesions on chest computed tomography scans ≥50% of lung parenchyma vs. moderate or mild involvement defined by extension <50% of lung parenchyma). Missing values: oxygen saturation, n = 2; lymphocyte count, n = 35; platelet count, n = 10; C-reactive protein, n = 9; extension of lesions on chest computed tomography scans, n = 10.
models providing odds ratios (ORs) with their 95% CIs). Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

A total of 263 patients were included in this study. The median age was 65 years (IQR: 54–76) and 155 patients (58.9%) were men. The median duration of symptoms at the time of admission to hospital was 7 days (interquartile range: 4–10). Platelet count within admission was assessed in 253 patients. The median platelet count was 186 × 10^9/l (range: 63–795). Thrombocytopenia was observed in 63 (24.9%) patients. Patient’s characteristics are described in Table I. Overall, 122 (46.4%) patients met the primary outcome criteria and 19 (7.2%) died. The prevalence of thrombocytopenia upon admission was 35.8% and 52.6% in these two groups, respectively, while it was 15.0% in patients who did not achieve the composite outcome at day 14 after admission. Results regarding the association of thrombocytopenia upon admission and outcomes are presented in Table II. In adjusted models, thrombocytopenia was associated with primary outcome occurrence with an OR of 2.48 (95% CI: 1.17–5.23). Thrombocytopenia was associated with mortality with an OR of 2.70 (95% CI: 0.91–8.01).

The population of this study was older and more severely affected than the initial cohorts from China.\textsuperscript{1,4,5} However, the prevalence of thrombocytopenia was close to the prevalence previously observed.\textsuperscript{6} We confirmed that, in all cases in our cohort, thrombocytopenia is often mild in the setting of hospitalized patients for COVID-19.\textsuperscript{2,3} The adjusted results of this model highlight that thrombocytopenia upon admission is associated with poor outcome and mortality in patients hospitalized for SARS-CoV-2 pneumonia. This has been described in other settings of hospitalized patients, notably with community-acquired pneumonia.\textsuperscript{7–10} However, this study has some limitations. First, acquisition of data was retrospective for the first patients included in the cohort. Second, some data were missing; however, they were very few (see Tables I and II) and corrected by multiple imputation. Last, the size of the cohort resulted in large 95% CIs for the assessment of the link between thrombocytopenia and death in the multivariate model. However, the value of the OR (2.70) is so high that we can reasonably suppose that there exists a major association. Similarly, the size of the cohort prevented assessment of the association between various levels of thrombocytopenia and outcome occurrence.

The aim of this study was to assess the impact of thrombocytopenia upon admission on poor outcomes, whatever the mechanism. It should be noted that some mechanisms of thrombocytopenia may be particularly associated with worsening, such as disseminated intravascular coagulation in patients admitted to ICU, and need to be evaluated in specific studies.\textsuperscript{11}

This study confirms that thrombocytopenia upon admission is a strongly associated with poor outcome and mortality in patients hospitalized for SARS-CoV-2 pneumonia, independently from other markers of severity.

Acknowledgements

The authors are deeply grateful to Christophe Morin, Gaëlle Barencoeur, Caroline Hurault-Delarue, Charlotte Vert and Julien Jacquot for their help in data acquisition and Isabelle Olivier for regulatory aspects.

The Covid-clinic-Toul cohort is funded by Toulouse University hospital.

Conflicts of interest

The authors declare no conflicts of interest.

Authors contributions

JM, ML, AS and GM designed the study. JM and ML carried out the data management and wrote the manuscript. JM and GM conducted the statistical analyses. The collaborators in the ‘Covid-clinic-Toul investigators group’ included the patients and participated to data collection. JM, ML, AS and GM participated in the interpretation of the results, critically reviewed the manuscript and gave final approval for submission.

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Covid-Clinic-Toul collaborators are listed in Appendix I.

Keywords: COVID-2019, SARS-CoV-2, thrombocytopenia, mortality, intensive care unit

First published online 31 August 2020

doi: 10.1111/bjh.16950

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British Journal of Haematology, 2020, 190, e268–e288
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Poor outcome and prolonged persistence of SARS-CoV-2 RNA in COVID-19 patients with haematological malignancies; King’s College Hospital experience

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), emerged at the end of 2019 and caused an infection named coronavirus disease 19 (COVID-19).1 Patients with compromised immune systems are at increased risk of complications of COVID-19 but this risk is not precisely defined.2 Although age, gender, comorbidities and ethnicity are risk factors for adverse outcomes,3 various pre-existing conditions, including haematological cancers, have also been reported to correlate with poor outcomes.4–8

Our aim was to compare the first 80 patients with a haematological malignancy with all other patients admitted to our hospital with COVID-19 in the same time frame, to precisely define their relative risk and identify factors that increase mortality within this subgroup.

The mean age of our cohort was 69.4 years (range 30–95 years); 52 (65%) males; 76% had at least one comorbidity. Overall, 62 (77%) patients had lymphoid malignancies/plasma cell dyscrasias and 18 (23%) had myeloid neoplasms. Nine patients had previously undergone allogeneic (n = 6) and autologous (n = 3) haematopoietic stem cell transplantation. One patient had received chimeric antigen receptor T-cell (CAR-T) therapy. Treatment type included intensive therapy (n = 16; 20%), non-intensive therapy (n = 35; 44%) and 'watch and wait' (n = 29, 36%), with 31 (40%) on active treatment (Tables SI and SII).

The most common symptoms on admission were fever (60%), cough (58%), dyspnoea (54%) and gastrointestinal symptoms (13%) (Table SI). Both the baseline pre-COVID-19 lymphocyte count (15 × 109/l) and the nadir (median 0 × 109/l) lymphocyte count were lower than the normal range (1–3). The haemato-oncology patients who died or were transferred to the intensive care unit were older (73 vs. 66 years; P = 0.065); but male gender (61% vs. 67%, P = 0.76) was not associated with poorer outcome. Differences in ethnicity were noted, with a higher black population among those who died (45% vs. 17%, P = 0.02). Higher total white cell count (15–8 vs. 4.9 × 109/l, P = 0.015), neutrophil count (5.7 vs. 3.8 × 109/l, P = 0.04) and C-reactive protein (CRP) (200 vs. 82, P < 0.001) were associated with poorer outcome (Table SI). A lower baseline pre-COVID-19 lymphocyte count was associated with poorer outcome (Table SI)