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Impact of Covid-19 epidemic on the activities of a blood centre, transfusion support for infected patients and clinical outcomes

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Abstract

Objectives: We evaluated how the Severe Acute Respiratory disease from Coronavirus 2 (SARS-CoV-2) epidemic impacted transfusion services, transfusion support required by Covid-19 patients and their clinical outcome.

Background: In Italy, the first confirmed case of SARS-CoV-2 infection was registered on 21 February 2020. As of 20 April, about 250 000 cases were registered, 1143 of which were in the province of Pescara.

Methods: We compared transfusion services provided by the blood centre of Pescara between 1 March and 20 April 2019 and between 1 March and 20 April 2020. We assessed the number and type of blood components donated, those transfused in the various hospital departments and those transfused to Covid-19 patients.

Results: Compared to 2019, we documented a decrease of 32% in the number of donations. The number of transfusions increased by 139% in the infectious diseases department (IDD), dedicated to Covid-19 patients, and by 76% in the intensive care unit (ICU), whereas it markedly decreased in the other departments. Of 299 patients with Covid-19, 60 were transfused (20.1%). Transfused patients in the ICU were significantly younger than those in IDD and had a lower number of lymphocytes, lower post-transfusion increment of haemoglobin levels and higher D-dimer and C reactive protein values. Mortality rate was 60.7% among transfused patients in the ICU and 39.0% among those in the IDD (p = 0.02).

Conclusion: The Covid-19 epidemic had a profound impact on transfusion activities. The important blood demand for Covid-19 patients was satisfied because of the reduction in activities in other hospital wards. Covid-19-positive transfused patients showed a very poor prognosis.

KEYWORDS

Covid-19, mortality, transfusion efficacy, transfusion support

1 | INTRODUCTION

In Italy, the first confirmed case of Severe Acute Respiratory disease from Coronavirus 2 (SARS-CoV-2) infection was registered on 21 February 2020 in a young patient residing in the Lombardy region. As of 20 April, about 250 000 positive cases were registered, about 3000 of which were in the Abruzzo region and 1143 of which in the province of Pescara. As the number of cases increased, the national

blood centre, regional blood centres, hospitals and transfusion services responded with measures aimed at providing appropriate health care services.[1,2] This report describes how the Coronavirus Disease 2019 (Covid-19) pandemic impacted transfusion services. More specifically, we evaluated how the epidemic changed donor access and the number of transfusions performed compared to the same period of the previous year, the transfusion support required by Covid-19 patients and clinical outcomes.

2 | MATERIALS AND METHODS

The Civil Hospital of Pescara is a general hospital with 653 beds and includes, among others, departments of surgery, internal medicine, haematology-oncology, maternal and child health and emergency. The haematology ward is the largest in Italy, with 62 beds, and also includes a haematopoietic stem cell transplant unit. The haematology department represents the reference centre for the Abruzzo region, which has 1.3 million inhabitants, and provides inpatient and outpatient care for a large array of different haematological conditions, including acute and chronic leukaemia, lymphoma, multiple myeloma, myelodysplastic syndromes, congenital and acquired anaemia, haemophilia and other coagulation disorders. A multidisciplinary outpatient "anaemia clinic" for patient blood management is operated in the blood centre of the hospital, under the coordination of a transfusion medicine specialist.

The department of haematology also includes a blood centre for the collection, processing, qualification and distribution of blood components and is self-sufficient to meet the needs of the hospital. On average, about 20 000 transfusions per year are performed.

During the Covid-19 pandemic, our hospital faced an exponential increase in the demand for intensive care unit (ICU) beds even outside the conventional setting. Pescara Hospital was equipped with 10 ICU beds, of which 2 had negative pressure. The speed of the local epidemic required immediate operational planning to contain mortality and morbidity. The Crisis Unit defined a plan for a 180-bed Covid-19 hospitalisation area. The Covid-19 area was organised by intensity of care, and patients with worsening clinical conditions were placed in a sub-intensive area or in a critical care area. Within the Covid-19 area, a 22 pressure-negative beds section of the ICU was organised, with complete equipment except extracorporeal membrane oxygenation (ECMO). This section was placed next to the sub-intensive care area, managed by a multi-specialist internal medicine team, coordinated by the infection disease department (IDD) and equipped with monitoring and non-invasive ventilation. Stable patients were placed in the non-negative pressure rooms. Patient location was reassessed daily. Due to the growing demand for ICU beds, an additional intensive hospitalisation area was placed under negative pressure, including 10 beds. The system was progressively implemented and gradually downgraded in the period 07 March 2020–31 May 2020, when the areas were returned to the pre-COVID-19 destination.

The other activities of the hospital were also reorganised. During the first 10 days of March, indications were given by the Ministry of Health on the identification of Covid-19 hospitals, the definition of access routes to health facilities with access restrictions and closure of non-urgent outpatient activities. Blood donation was considered an urgent procedure. Elective surgeries have been cancelled starting from 13 March, with the exception of surgeries for cancer patients or high-specialty surgical interventions.

Haematological patients hospitalised in the ward and in the transplant unit were fully supported during the pandemic.

The aim of this study was to compare transfusion services provided by the Blood Centre of Pescara General Hospital between 1 March and 20 April 2019 and those provided between 1 March and 20 April 2020. We assessed the number and type of blood components donated and number and type of blood components transfused in the various hospital departments (onco-haematology, surgery, internal medicine, paediatrics, infectious diseases and intensive care). The number of transfused patients and transfusions/patient were compared between the two periods of observation. Patient Blood Management (PBM) consultancy activities for hospitalised and outpatient patients were also assessed.

Characteristics of patients with confirmed Covid-19 and admitted to the infectious diseases and intensive care wards were also analysed. We evaluated the number and type of transfused blood components in Covid-19 patients, along with transfusion threshold, transfusion efficacy, laboratory tests indicative of clinical status and outcome of transfused patients.

2.1 | Statistical methods

Continuous variables were summarised as median and interquartile range (IQR), whereas categorical variables were summarised as percentages. Between-group comparisons were based on the Mann-Whitney *U* test for continuous variables and the chi-squared test for categorical variables. All *p* values are two-sided, and values <0.05 were considered statistically significant.

3 | RESULTS

3.1 | Donations and blood components collected

Overall, 2136 donations were made between 1 March and 20 April 2020 for a total of 2293 blood components collected, of which 1448 were red blood cells (RBC), 431 platelet concentrates (PLT) and 685 fresh-frozen plasma (FFP). In the same period of 2019, 3143 donations were made, for a total of 3310 blood components collected, of which 2226 were RBC, 638 PLT and 850 FFP. Therefore, compared to 2019, we documented a decrease of 32% in the total number of donations. The number of donations and the number of blood components per week are given in Figure 1. Following an awareness campaign in early March, the number of donations in the third week of March was similar to that of 2019; however, in the following weeks, a substantial decrease was observed. The drop in

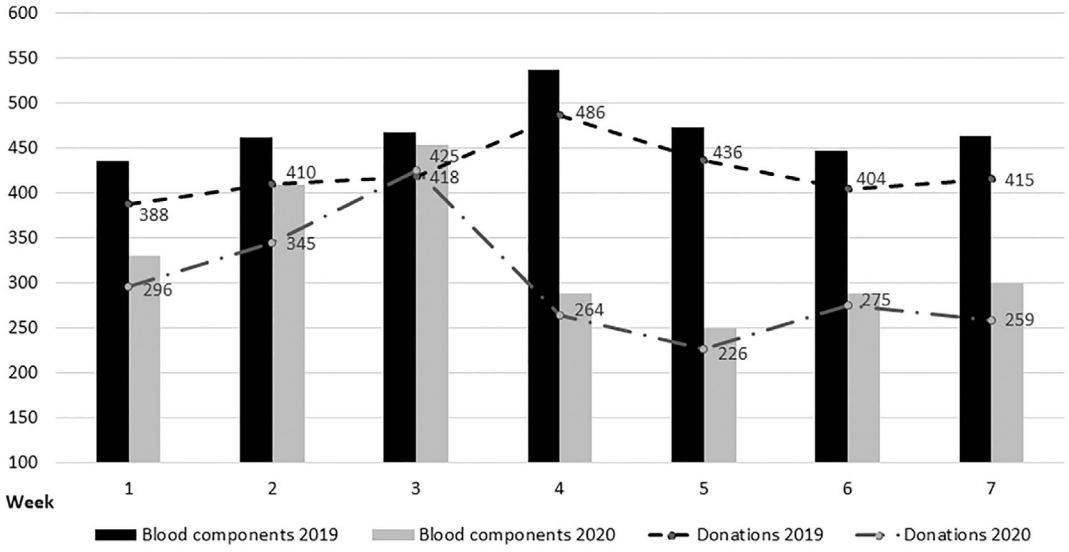

FIGURE 1 Number of weekly blood donations (dotted lines) and blood components (bars) between 1 March and 20 April: comparison between the years 2019 and 2020

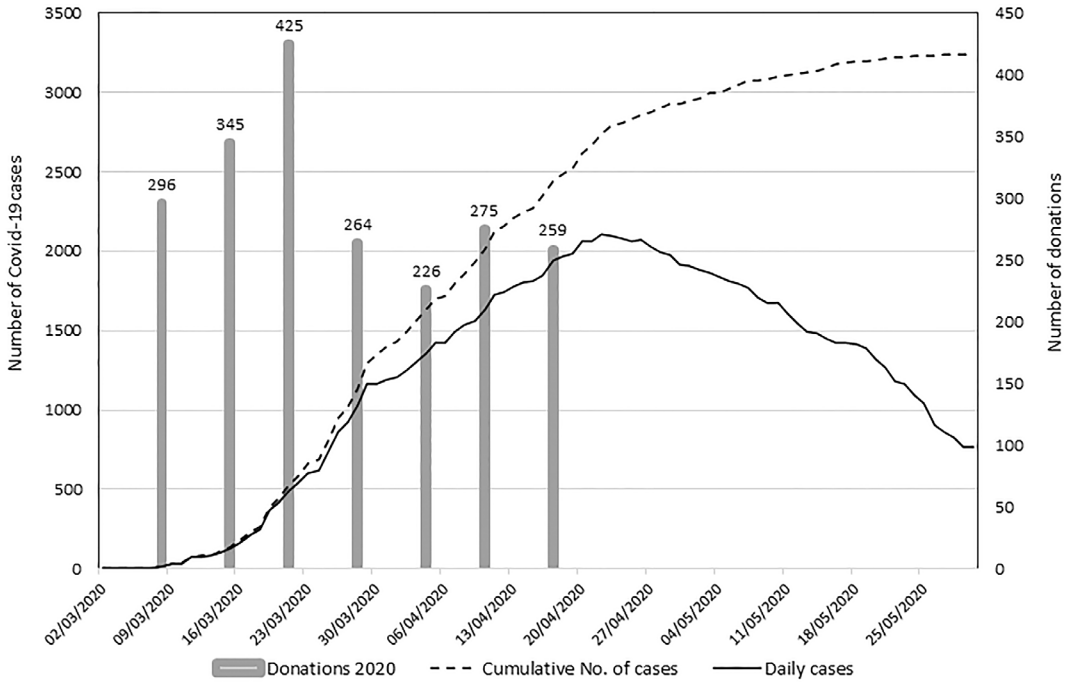

FIGURE 2 Number of weekly blood donations in relation to the number of daily new cases and cumulative number of cases of Covid-19 in Abruzzo region

number of donors occurred in parallel with the worsening of the pandemic (Figure 2).

3.2 | Patients and transfusions

Overall, 824 patients were transfused between 1 March and 30 April 2019, for a total of 3191 blood components infused. In the same period of 2020, 612 patients were transfused (−25.7%), for a total of 2341 components infused (−26.6%); 166 blood components were infused to 60 patients affected by Covid-19.

The number of blood components transfused in the different hospital departments in 2019 and 2020 is reported in Table 1. A marked reduction was documented in the number of transfusions performed in the surgery (−56.0%) and internal medicine departments (−48.7%). On the other hand, the number of transfusions increased by 139.1% in the infectious diseases department (IDD—entirely dedicated to Covid-19 patients) and by 76.4% in the ICU.

TABLE 1 Transfusions performed, overall and by hospital department: Comparison between 2019 and 2020

	1 March–20 April 2019	1 March–20 April 2020	2020–2019% change
No. of transfused patients	824	612	−25.7%
Total No. of transfusions	3191	2341	−26.6%
Onco-haematology	1667	1393	−16.4%
Surgery	812	357	−56.0%
Internal medicine	417	214	−48.7%
Emergency	144	98	−31.9%
Infectious diseases	46	110	+139.1%
Intensive care unit	89	157	+76.4%
Paediatrics	16	12	−25.0%

During the period evaluated, there was a 68.4% decrease in PBM consultancies (133 in 2019 vs. 42 in 2020), mainly due to the closure of the anaemia outpatient centre and the drastic reduction of the scheduled surgical interventions.

Overall, 299 patients were admitted to our hospital with confirmed Covid-19, 73 of whom were admitted to ICU and 226 admitted to IDD. The median age was 64 years (55–68) for patients in the ICU and 73.0 years (54.0–84.0) for those in IDD.

Of a total of 612 patients transfused during the period of observation, 60 were Covid-19-positive (9.8%), 36 of whom were men (60.0%) and 24 were women (40.0%), with a median age of 72.0 (64.3–82.7) years. Covid-19 patients were transfused with 154 RBC (79 in ICU and 75 in IDD), 10 PLT (5 in ICU and 5 in IDD) and 2 FFP (both in ICU). The proportion of patients transfused was 37.0% among those admitted to ICU (27 out 73) and 14.6% among those admitted to IDD (33 of 226).

The trigger for transfusion in Covid-19 patients was generally set at 8 g/L of haemoglobin for both patients admitted to the ICU and those in the IDD. However, the transfusion trigger was decided on the basis of multiple parameters, including PaO_2/FiO_2 ratio (severity of respiratory failure), presence of haemodynamic instability, sepsis/septic shock and increased lactate levels. The average number of units transfused was 2 (range 1–12) for patients admitted to ICU and 2 (range 1–12) for patients admitted to the IDD.

Table 2 demonstrates the number of patients transfused in the ICU and IDD in 2019 and those admitted for Covid-19 in 2020. Gender distribution (61.1% and 60.0% males in 2019 and 2020, respectively; $p = 0.91$), median age (71 [56–80] years in 2019 and 72 [64–83] in 2020; $p = 0.35$) and average number of transfusions per patient (2.0 [2.0–4.0] in 2019 and 2.0 [1.0–3.0] in 2020; $p = 0.07$) were similar in the two periods, but an increase in the number of transfusions (+22.9%), patients transfused (+66.7%) and number of RBC transfusions (+65.6%) was documented for patients with Covid-19.

TABLE 2 Blood components in transfused Covid-19 patients admitted to intensive care unit or infectious diseases department between 1 March and 20 April 2020 compared with transfused patients in the same departments between 1 March and 20 April 2019

Characteristics	1 March–20 April 2019	1 March–20 April 2020	2020–2019% change
No. of transfused patients	36	60	+66.7%
No. of transfusions	135	166	+22.9%
No. of RBC transfusions	93	154	+65.6%
No. of PLT transfusions	34	10	−70.6%
No. of FPC transfusions	8	2	−75.0%

3.3 | Transfusion threshold and efficacy

Patients with Covid-19 requiring RBC transfusions had an average haemoglobin level of 7.8 (7.5–8.2) g/dl, an average platelet count of 178 (78–239) $\times 10^9$/L and an average number of lymphocytes of 0.8 (0.5–1.2) $\times 10^3$/μl.

Average post-transfusion haemoglobin levels were 8.8 (8.1–9.4) g/dl, corresponding to a post-transfusion increment of 0.84 (0.39–1.40) g/dl. Four patients were transfused with a total of 10 units of PLT from buffy coat pool, with a median pre-transfusion count of 14 $\times 10^9$/L (9–23), a median post-transfusion count at 18–24 hours of 43 $\times 10^9$/L (28–48) and a median increment of 25 $\times 10^9$/L (range 7–34).

Two units of FFP were transfused to two patients with an international normalised ratio (INR) > 1.5.

Transfused patients admitted to the ICU were significantly younger than those admitted to the IDD, were more frequently of male gender, showed slightly higher pre-transfusion haemoglobin levels and a lower number of lymphocytes and had a significantly lower post-transfusion increment of haemoglobin levels (Table 3).

3.4 | Laboratory tests indicative of clinical status

At the time of transfusion, Covid-19 patients had a prothrombin time (PT) of 13.9 (12.7–16.7) s, activated partial thromboplastin time (APTT) of 30.2 (27.0–38.5) s, international normalised ratio (INR) of 1.17 (1.11–1.32), antithrombin 3 activity (AT3) of 68 (52–80) %, fibrinogen levels of 352 (218–550) mg/L and D-dimer levels of 3.6 (1.6–6.0) mg/L. Among the indices of inflammation and sepsis, levels of C-reactive protein (CRP) and procalcitonin (PCT) were 76.7 (35.2–183) mg/L and 0.55 (0.15–1.67) mg/L, respectively. The same parameters were compared between Covid-19 patients admitted to the ICU and those admitted to the IDD. Transfused patients in the ICU had significantly higher D-dimer and CRP levels, whereas no statistically significant differences were documented for the other parameters examined (Table 3).

TABLE 3 Laboratory characteristics of Covid-19 patients admitted to ICU or infectious diseases department

Characteristics	ICU	Infectious diseases dept.	*p* Value
Age	66.3 (59.0–71.2)	81.2 (71.5–88.2)	<0.0001
Gender: Male	70.0%	51.5%	0.18
ABO group			0.20
O	37.0%	51.5%	
A	55.6%	33.3%	
B/AB	7.4%	15.2%	
Pre-transfusion haemoglobin (g/L)	8.0 (7.7–8.4)	7.7 (7.2–8.0)	0.07
Platelets ($\times 10^9$/L)	155 (87–237)	184 (70–250)	0.44
Lymphocytes ($\times 10^3$/μl)	0.60 (0.50–1.10)	0.90 (0.60–1.20)	0.029
Post-transfusion increment of haemoglobin (g/L)	0.69 (0.29–1.19)	1.1 (0.50–1.60)	0.028
PT (s)	14.0 (12.7–19.5)	13.8 (12.8–16.1)	0.96
APTT (s)	33.2 (27.1–41.1)	29.4 (26.1–34.2)	0.10
INR	1.17 (1.11–1.32)	1.19 (1.07–1.33)	0.21
AT3 (%)	66.0 (50.3–78.8)	68.0 (54.0–88.0)	0.19
Fibrinogen (mg/L)	353 (223–554)	342 (213–522)	0.63
D-dimer (mg/L)	4.1 (2.1–6.3)	1.9 (1.2–4.9)	0.027
CRP (mg/L)	89.2 (41.7–195.5)	62.2 (12.3–133.0)	0.039
Procalcitonin (mg/L)	0.70 (0.23–1.85)	0.46 (0.10–0.97)	0.30

Abbreviation: ICU, intensive care unit.

3.5 | Outcome of transfused patients

Information on vital status was available for all Covid-19-positive, transfused patients. Overall, 27 patients died (45.0%); the mortality rate was significantly higher among patients admitted to the ICU (17 of 27 patients; 60.7%) compared to those admitted to the IDD (11 of 33 patients; 39.3%) (p = 0.02). Patients who died differed from those who survived in terms of number of lymphocytes (0.60×10^3/μl [0.37–1.10] vs. 0.95×10^3/μl [0.60–1.20]; p = 0.028) and PCT levels (1.03 [0.52–4.52] mg/L vs. 0.14 [0.07–0.46] mg/L; p < 0.001). No statistically significant differences emerged in terms of age, gender, ABO group, pre-transfusion haemoglobin, platelet count, post-transfusion haemoglobin increment, PT, PTT, INR, AT3, D-dimer and CRP levels.

4 | DISCUSSION

4.1 | Main findings

The Covid-19 pandemic has had a profound impact on many aspects of transfusion medicine, from donation to the availability of blood components to the need of managing transfusion needs of patients positive for Covid-19. The SARS-CoV-2 infection is in fact often associated with multifactorial anaemia, coagulation disorders and multi-organ failure in the most severe cases.[3]

The Italian National Blood Centre (Centro Nazionale Sangue [CNS]) promoted an awareness campaign on the importance of donation[1,2] through the media at the national and local levels, highlighting all the adopted measures to mitigate the risk to blood, donor and staff safety. Volunteers of the blood donor associations were involved in contacting donors by telephone or through automatic messaging systems and social media. Following the recommendations of CNS, a triage with a check of body temperature was implemented in our hospital, and donors with a recent history (last 2 weeks) of body temperature over 37.5°C, symptoms of respiratory infection (cough, dyspnoea, sore throat, rhinorrhoea) or having had contact with a suspected or confirmed case of Covid-19 were not allowed to donate. To comply with the requirement of social distancing, donors were advised to make prior appointments in order to avoid waiting times and long duration of stay at donation venues. Rigid post-donation measures were also adopted to collect additional information regarding possible cases of infection in people who had made a donation; in such cases, blood components not yet used were discarded, and a close monitoring of transfused patients was put in place.

Despite all these activities, we documented a decrease of 32% in the number of donations compared to the same period of 2019. Following the national and regional awareness campaigns in the first 2 weeks of March 2020, in the third week of March, the total number of donations was close to that registered in the previous year. However, in the following weeks, the number of donations decreased markedly, in conjunction with the worsening of the pandemic outbreak. Despite the reduction in the availability of blood components, the parallel decrease in demand, mainly due to a drastic reduction in

the number of surgical procedures, made it possible to satisfy all the requests without major problems.

Haematological patients were fully supported during the pandemic, both those hospitalised in the ward and those admitted in the transplant unit. There was a slight decrease in the number of transfusions in outpatients (−16%), for whom online consultations were performed for non-urgent cases; if transfusion was deemed necessary, the patients were referred to the blood centre closest to their home. Patients with hemoglobinopathies such as sickle cell disease and thalassemia were regularly followed up and transfused at our centre.

The markedly lower number of transfusions in surgical and non-Covid-19 internal medicine wards was counterbalanced by the increase in demand associated with the SARS-CoV-2 infection in the ICU and infectious diseases department. Of note, one in five inpatients with Covid-19 overall, and one in three of those admitted to the ICU, required a transfusion during their hospital stay. In these patients, transfusions can help counteract hypoxia; furthermore, the anaemic status can worsen as a consequence of frequent blood sampling, inflammation, haemorrhagic episodes, acute respiratory distress syndrome or sepsis. The role of PBM in patients positive for Covid-19 has also been recently emphasised: The correction of anaemia during the early phases of the infection could be of benefit to avoid the most severe consequences of the respiratory infection.[4,5]

In our hospital, a restrictive transfusion threshold (Haemoglobin ≤ 7 g/L) is applied in stable patients, even those admitted to the ICU. In Covid-19-transfused patients, the threshold increased to an average of 7.8 g/L due to the severe, unstable clinical conditions. The average post-transfusion increment of 0.84 g/L was satisfactory; however, the increment was significantly lower for patients admitted to the ICU compared to those admitted in the IDD.

The dysfunction of endothelial cells induced by infection results in excess thrombin generation and fibrinolysis shutdown, which indicate a hypercoagulable state in patient with infection,[6] responsible for a poor prognosis.[7] In our case series, compared to patients admitted to the IDD, those in the ICU showed higher values of D-dimer, indicative of coagulopathy, and higher CRP levels, indicative of a more severe inflammatory status; on the other hand, no major differences between the two groups emerged as for other coagulation parameters. This can be at least partially related to the adoption in our hospital of protocols for the management of coagulopathy with low-molecular-weight heparin and for blocking the inflammatory cascade with tocilizumab.

We documented a high mortality rate among Covid-19-positive, transfused patients. About 60% of patients admitted to the ICU and one in three of those admitted to the IDD died during their hospital stay. Patients who died did not differ from those who survived in terms of age and gender distribution; however, markers of inflammatory activity, particularly PCT levels, were markedly higher in patients who died than in survivors, together with a more severe lymphopenia.

Based on the available current evidence, restrictive RBC transfusions are associated with decreased morbidity and mortality,[8,9] and a transfusion trigger of 7 g/L is clinically acceptable for most non-acutely bleeding critically ill patients. In certain groups of critically ill patients, such as those with septic shock, acute respiratory failure, severe or acute ischemic heart disease and brain injury, who may be at increased risk of the adverse effects related to anaemia, a trigger of 7–9 g/L is clinically acceptable. Although patients with Covid-19 in the ICU share many characteristics with patients admitted to the ICU for other reasons, at the moment, there are no studies demonstrating that transfusion per se in patients with Covid-19 has a negative effect on the evolution of the disease.

From an organisational point of view, the need to address both donations and patient care posed additional challenges to our hospital. In fact, active strategies had to be implemented to ensure the safety of donations and satisfy the demand for transfusions from one side and reduce the non-necessary procedures from the other side, thus ensuring the possibility to meet the needs of Covid-19 and non-Covid-19 patients. On the other hand, the existence of the blood donation centre within the hospital and the coordination of the activities of collection and distribution of blood components made it possible to better plan care and adapt the provision of services to the actual availability of units to be transfused. A multidisciplinary evaluation of the appropriateness of transfusion requests was also put in place, helping to meet the shortage of blood components. Overall, the tight coordination of the different activities and expertise represented a key factor in limiting the negative impact of the epidemics on the provision of care.

4.2 | Strengths and limitations

Several reports have described the impact of Covid-19 on transfusion services[1,10-13]; however, to our knowledge, this is the first report showing the impact of the Covid-19 pandemic not only on transfusion practices but also on outcomes. As such, it offers important information, particularly regarding the measures needed to face the increasing demand for transfusion support. The major limitation of our study is the origin of the data from a single, large hospital. Additional experiences will help to better define the burden posed by Covid-19 to transfusion services and the strategies that should be implemented to meet the needs of all patients.

5 | CONCLUSIONS

The Covid-19 epidemic has had a profound impact on transfusion activities. During the emergency phase, the important blood demand for Covid-19-positive patients was satisfied, despite the reduction in donations, because of the reduction in activities in the other hospital wards. However, in recent weeks, specific structures have been gradually created for people with Covid-19, freeing hospitals from caring for these patients. This has important implications in light of the new outbreak of the epidemic. In fact, in these circumstances, the request for transfusion support for Covid-19 patients would add to the routine requests of hospitals that would resume their usual care activities. All this could create a dramatic shortage of transfusion products,

which could be at least partially remedied by increasing the stocks of frozen blood cells, optimising PBM and promoting donor awareness campaigns.

CONFLICT OF INTEREST

The authors have no competing interests.

AUTHOR CONTRIBUTIONS

Anna Quaglietta: study design; acquisition, analysis or interpretation of data; drafting of the manuscript; approved the submitted version of the paper. **Antonio Nicolucci**: drafting of the manuscript; statistical analysis; approved the submitted version of the paper. **Raffaella Posata**: acquisition, analysis or interpretation of data; approved the submitted version of the paper. **Antonella Frattari**: acquisition, analysis or interpretation of data; approved the submitted version of the paper. **Giustino Parruti**: acquisition, analysis or interpretation of data; approved the submitted version of the paper. **Patrizia Accorsi**: acquisition, analysis or interpretation of data; approved the submitted version of the paper.

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