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ORIGINAL PAPER

Transfusion profile, clinical characteristics, comorbidities and outcomes of 3014 hospitalized patients diagnosed with COVID-19 in Brazil

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Abstract

Background The novel coronavirus disease-2019 (COVID-19) caused a sudden and unexpected increase in the number of hospital admissions and deaths worldwide. The impact of social distancing on blood stocks was significant. Data on the use of blood products by patients with COVID-19 are scarce.

Material and methods A retrospective observational study was conducted by analysing the medical records of 3014 hospitalized COVID-19 patients in 16 Brazilian hospitals. Individual data related to clinical, laboratory and transfusion characteristics and outcomes of these patients were collected. Patients characteristics association with mortality and transfusion need were tested independently by logistic regression models.

Results Patients mean age was 57·6 years. In 2298 (76·2%) patients, there was an underlying clinical comorbidity. A total of 1657 (55%) patients required admission to intensive care unit (ICU), and 943 (31%) patients required ventilatory support and orotracheal intubation (OTI). There was a total of 471 (15·6%) deaths among all patients. 325 patients (10·7%) required blood transfusion; 3187 blood products were transfused: 1364 red blood cells in 303 patients, 1092 platelet units in 78 patients, 303 fresh frozen plasma in 49 patients and 423 cryoprecipitates in 21 patients. The mortality among patients who received transfusion was substantially higher than that among the total study population.

Conclusion Need for transfusion was low in COVID-19 patients, but significantly higher in patients admitted to ICU and in those who needed OTI. Knowledge of the transfusion profile of these patients allows better strategies for maintaining the blood stocks of hospitals during the pandemic.

Key words:
COVID-19, transfusion, SARS-COV-2, mortality, SARS.

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Introduction

In December 2019, a new disease (COVID-19) caused by a novel coronavirus called SARS-CoV-2 appeared in the city of Wuhan, Hubei Province, China [1,2]. The disease spread rapidly around the world, leading the World Health Organization (WHO) to declare a pandemic on 11 March 2020 [3]. Brazil declared national public health emergency in February 2020 [4].

According to WHO data, up to 14 January 2021, more than 91 million people were infected worldwide, of whom more than 1 970 000 died from complications of the

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disease [5]. In Brazil, the Ministry of Health confirmed the first case of COVID-19 in the city of São Paulo on 26 February 2020. Since then, more than 8·3 million cases and more than 207 000 deaths have been recorded [6]. International authorities have focused their efforts on social isolation measures and detection of new cases of COVID-19, in addition to the search for effective treatments to combat the most severe effects of this disease.

The clinical presentation of COVID-19 ranges from mild and self-limited upper airway inflammation (dry cough, fever, dyspnoea, fatigue, anosmia, ageusia) to severe pneumonia, sepsis, multiple organ failure and death [1,2]. The clinical and epidemiological characteristics, risk factors, laboratory presentation, diagnostic techniques and outcomes have been exhaustively investigated worldwide [7,8]. Many aspects of COVID-19 still need to be elucidated, and advances in its prevention and treatment depend on a greater understanding of its clinical and pathophysiological aspects.

It has been shown that RNA from SARS-COV-2 can be found in the blood of infected patients [9] and even in blood donors [10]. However, there is no evidence to date that it can be transmitted through blood transfusion [11]. With the travel restrictions and recommendations for social isolation, there was a significant and worrying decrease in blood donations and, consequently, in the blood stocks available during the first months of the pandemic. Worldwide, it was necessary to implement additional strategies to attract donors, who were often in social isolation and working from home [12].

The use of blood products in patients hospitalized with COVID-19 also needs to be better investigated and elucidated. The data in the literature on the need for transfusion of blood products in these patients are scarce. Our study describes the transfusion needs, clinical characteristics and outcomes of 3014 patients with COVID-19 in 16 hospitals that serve different regions of Brazil in six states of the country.

Materials and Methods

We conducted a retrospective observational study by analysing data collected by manual extraction from the medical records of hospitalized patients with a confirmed diagnosis of COVID-19. Diagnosis was made by nucleic acid testing by reverse transcription polymerase chain reaction (RT-PCR) of the sample collected from the nasopharynx/oropharynx or by a reactive antibody result in a blood sample. Infection was considered confirmed if the initial test result was positive or if it was confirmed in a repeated new sample collection. Repeat testing was performed whenever there was a high clinical probability of COVID-19 or if the initial test was considered a probable false-negative due to inadequate sample collection. The patients were admitted to 16 Brazilian hospitals where our transfusion service operates, in six states of Brazil, in the period from 03/01/2020 to 06/30/2020. Individual data related to epidemiological, clinical and laboratory characteristics, treatments performed (including admission to the intensive care unit (ICU) and need for orotracheal intubation (OTI) and mechanical ventilation) and outcome (discharge and death) were collected in 3014 adult patients over 18 years old.

All data regarding the transfusions performed were collected from blood component requests, duly completed and signed by the attending physician and validated by the hemotherapist, the specialist responsible for the transfusion service of the hospital. Written informed consent was obtained from all study participants or their legal representatives, and this study was approved by the ethics committees of the participating hospitals.

Statistical analysis was performed in software R 4.0.2 (R Core Team, Vienna, Austria, 2020). Patients baseline characteristics association with mortality and transfusion need during hospitalization outcomes were tested independently by logistic regression models. A multiple logistic regression model with all baseline variables, except sex (not significantly associated with the outcomes) and blood type (only available to a small subgroup of patients), was adjusted to identify independently associated variables, and adjusted odds ratios were presented with 95% confidence intervals. Area under the ROC curve (AUC) statistics were presented to evaluate predictive performance of the models.

Results

From March to June 2020, 3014 adult patients were hospitalized in 16 hospitals we evaluated, in six Brazilian states (São Paulo, Rio de Janeiro, Piauí, Pará, Manaus and the Federal District). From these patients, diagnosis was made by RT-PCR in 2951 (97·9%) or a reactive serological test in 63 (2·1%). Table 1 shows the baseline clinical and laboratory characteristics of these patients and compares their distribution between two groups: patients who died and patients discharged, as well as each *odds ratio* related to a specific characteristic. It is notable that the blood type, platelets count and haemoglobin value were not available to all patients. The mean age was 57·6 years (18 to 102) and the male:female ratio, 1·4:1·0 (with 1786 men and 1228 women). Clinical comorbidities were analysed in all patients. Hypertension, diabetes, cancer and pneumopathy were also analysed separately. Age, any comorbidity, hypertension, diabetes, cancer, pneumopathy, low platelets counts and low haemoglobin levels

Table 1 Patients characteristics and association with death

Baseline characteristics	Total (n = 3014)	Discharge (n = 2543)	Death (n = 471)	Odds Ratio (95% CI)	*P* value
Age, years, mean ± SD	57·6 ± 17·8	54·8 ± 16·8	73·0 ± 15·3	1·067 (1·060; 1·075)	<0·01
Age group					
18–40	595 (19·7%)	577 (97·0%)	18 (3·0%)	1	
41–60	1135 (37·7%)	1062 (93·6%)	73 (6·4%)	2·20 (1·30; 3·73)	<0·01
61–80	899 (29·8%)	693 (77·1%)	206 (22·9%)	9·53 (5·81; 15·62)	<0·01
Over 80	385 (12·8%)	211 (54·8%)	174 (45·2%)	26·43 (15·87; 44·03)	<0·01
Sex					
Female	1228 (40·7%)	1034 (84·2%)	194 (15·8%)		
Male	1786 (59·3%)	1509 (84·5%)	277 (15·5%)	0·98 (0·80; 1·20)	0·83
Blood type	(n = 340)				
A	137 (40·3%)	65 (47·4%)	72 (52·6%)	1	
AB	13 (3·8%)	4 (30·8%)	9 (69·2%)	2·03 (0·60; 6·91)	0·26
B	32 (9·4%)	12 (37·5%)	20 (62·5%)	1·50 (0·68; 3·32)	0·31
O	158 (46·5%)	75 (47·5%)	83 (52·5%)	1·00 (0·63; 1·58)	1
Any comorbidity					
No	716 (23·8%)	657 (91·8%)	59 (8·2%)		
Yes	2298 (76·2%)	1886 (82·1%)	412 (17·9%)	2·43 (1·84; 3·27)	<0·01
DM					
No	2358 (78·2%)	2031 (86·1%)	327 (13·9%)		
Yes	656 (21·8%)	512 (78·0%)	144 (22·0%)	1·75 (1·40; 2·17)	<0·01
HAS					
No	1812 (60·1%)	1582 (87·3%)	230 (12·7%)		
Yes	1202 (39·9%)	961 (80·0%)	241 (20·0%)	1·72 (1·42; 2·10)	<0·01
Cancer					
No	2861 (94·9%)	2438 (85·2%)	423 (14·8%)		
Yes	153 (5·1%)	105 (68·6%)	48 (31·4%)	2·64 (1·83; 3·74)	<0·01
Pneumopathy					
No	2812 (93·3%)	2388 (84·9%)	424 (15·1%)		
Yes	202 (6·7%)	155 (76·7%)	47 (23·3%)	1·71 (1·20; 2·39)	0·002
Platelets ($\times 10^9$/L)	(n = 2897)				
≥150 001	2243 (77·9%)	1937 (86·4%)	306 (13·6%)	1	
100 001 to 150 000	525 (18·2%)	415 (79·0%)	110 (21·0%)	1·68 (1·32; 2·14)	<0·01
≤100 000	111 (3·9%)	79 (71·2%)	32 (28·8%)	2·56 (1·67; 3·93)	<0·01
Haemoglobin (g/L)	(n = 2885)				
≥11·1	2483 (86·1%)	2182 (87·9%)	301 (12·1%)	1	
8·1–11·0	315 (10·9%)	206 (65·4%)	109 (34·6%)	3·84 (2·95; 4·98)	<0·01
≤8·0	87 (3·0%)	48 (55·2%)	39 (44·8%)	5·89 (3·8; 9·14)	<0·01

Percentages in the total column are variable distribution and in the death column are death incidence.

were associated with death. Sex and ABO blood type were not associated with increased risk of death.

Table 2 shows the events during hospitalization. Transfusion, intensive care unit (ICU) admission and need for orotracheal intubation (OTI) were associated with higher risk of death. There was need for transfusion of any blood component in 325 patients (10·8%). In total, 3187 blood products were transfused, including packed red blood cells (RBCs), random platelet concentrate (RPC), apheresis platelet concentrate (APC), fresh frozen plasma (FFP) and units of cryoprecipitate (CRYO) in 325 patients (mean 9·8 units/patient). A total of 1364 RBCs were transfused in 303 patients (10·0%), with a mean of 4·5 units/patient. A total of 1101 platelet units were transfused in 80 patients (2·6%). In addition, 303 FFPs were used in 49 patients (1·6%) (mean 6·2 units/patient), and 423 CRYO were used in 21 patients (0·7%) (mean 20·1 units/patient). The clinical or laboratory indications for transfusion were not available to most patients.

Table 3 describes patients' characteristics who were transfused and patients who were not transfused. Table 4 describes the need for transfusion based on hospitalization needs. Age (patients older than 60 years), any comorbidity, hypertension, diabetes, cancer, low platelets

Table 2 Events during hospitalization and outcome

Events	Total (n = 3014)	Discharge (n = 2543)	Death (n = 471)	Odds Ratio (95% CI)	*P* value
Transfusion					
No	2689 (89·2%)	2404 (89·4%)	285 (10·6%)		
Yes	325 (10·8%)	139 (42·8%)	186 (57·2%)	11·3 (8·8; 14·5)	<0·01
ICU					
No	1357 (45·0%)	1330 (98·0%)	27 (2·0%)		
Yes	1657 (55·0%)	1213 (73·2%)	444 (26·8%)	18·0 (12·4; 27·4)	<0·01
IOT					
No	2071 (68·7%)	2006 (96·9%)	65 (3·1%)		
Yes	943 (31·3%)	537 (56·9%)	406 (43·1%)	23·3 (17·8; 31·1)	<0·01

Percentages in total column are variable distribution and in death column are death incidence.

counts and low haemoglobin levels were associated with need for transfusion. Sex, ABO blood type and pneumopathy were not statistically significant to transfusion need. ICU admission and need for OTI were associated with higher risk for transfusion need.

A multiple logistic regression model with all baseline variables was performed, except sex (not significantly associated with the outcomes) and blood type (only available to a small subgroup of patients). Table 5 shows the results applied to risk of mortality and Table 6 to transfusion need. In this model, age, cancer, low platelets count and low haemoglobin level were independent risk factors for death. Diabetes, hypertension and pneumopathy were not. Considering risk for transfusion, age, hypertension, low platelets count and low haemoglobin level were statistically significant. Diabetes, cancer and pneumopathy were not.

Discussion

The COVID-19 pandemic brought hundreds of challenges to humanity in all sectors of society. As the number of cases has increased dramatically worldwide, great efforts have been made to better understand the pathophysiology of the disease, its forms of transmission, its clinical behaviour and the search for effective preventive or therapeutic actions were targets of a large part of the global scientific community.

The clinical progression of the disease is the main factor that correlates with the use of blood products. This study shows that the need for transfusions in hospitalized patients with COVID-19 is not high (10·4%). In general, studies show that patients with the disease have normal or slightly decreased haemoglobin and platelet values [13]. However, it has been shown that patients with more severe forms of COVID-19 have lower haemoglobin levels than those with mild forms of the disease [14]. Patients who are admitted to the ICU and/or need OTI have higher mortality rates and require larger amounts of blood products. Our study showed that the main type of blood product used is red blood cells (9·5% of patients), followed by platelets (2·4%), fresh frozen plasma (1·6%) and cryoprecipitate (0·7%).

A previous study showed a higher risk of disease severity for individuals in blood group A and a protective effect in individuals in blood group O [15]. Our study did not observe any effect on mortality related to the ABO blood group. Maybe, one reason for this is the low number of transfused patients and the low percentage of patients with ABO typing available for analysis.

Previous studies have reported that advanced age is an important independent predictor of mortality, both in SARS, MERS and COVID-19 [16-18]. Our study confirms that increasing age is associated with deaths in patients with COVID-19, corroborating other studies that identified this predictor. Age-related defects in T- and B-cell function and excess production of type 2 cytokines can lead to a deficiency in the control of viral replication and to pro-inflammatory activity with longer responses, leading to worse outcomes [19]. Also, laboratory results that indicate more severe clinical conditions, such as low platelet counts and low haemoglobin levels, were also associated with higher mortality rates. Dysregulated inflammation, vascular injury and hypercoagulability are conditions related to COVID-19 pathophysiology that can correlate to these laboratory findings.

Our study identified as risk for transfusion many factors, such as age, clinical underlying comorbidities, low platelet counts, low haemoglobin levels, admission to ICU and OTI need. This is similar to a previous published study, with a lower cohort [20].

It has been previously demonstrated that hospitalized patients with COVID-19 have lower blood transfusion utilization rates than hospitalized patients without COVID-19 [21]. Our study, which included a large number of patients, also found that these patients had low rates of

Table 3 Patient characteristics and association with transfusion

Baseline characteristics	Total (n = 3014)	No transfusion (n = 2699)	Transfusion (n = 325)	Odds Ratio (95% CI)	*P* value
Age, years, mean ± SD	57·6 ± 17·8	56·6 ± 17·7	65·6 ± 17·1	1·03 (1·02;1·04)	<0·01
Age group					
18–40	595 (19·7%)	555 (93·3%)	40 (6·7%)	1	
41–60	1135 (37·7%)	1065 (93·8%)	70 (6·2%)	0·91 (0·61; 1·36)	0·65
61–80	899 (29·8%)	755 (84·0%)	144 (16·0%)	2·65 (1·83; 3·82)	<0·01
Over 80	385 (12·8%)	314 (81·6%)	71 (18·4%)	3·14 (2·08; 4·73)	<0·01
Sex					
Female	1228 (40·7%)	1099 (89·5%)	129 (10·5%)	1·05 (0·83;1·33)	0·68
Male	1786 (59·3%)	1590 (89·0%)	196 (11·0%)		
Blood type	(n = 340)				
A	137 (40·3%)	18 (13·1%)	119 (86·9%)	1	
AB	13 (3·8%)	2 (15·4%)	11 (84·6%)	0·83 (0·17; 4·06)	0·82
B	32 (9·4%)	1 (3·1%)	31 (96·9%)	4·69 (0·60; 36·50)	0·14
O	158 (46·5%)	16 (10·1%)	142 (89·9%)	1·34 (0·66; 2·75)	0·42
Any comorbidity					
No	716 (23·8%)	682 (95·3%)	34 (4·7%)	2·92 (2·05;4·26)	<0·01
Yes	2298 (76·2%)	2007 (87·3%)	291 (12·7%)		
DM					
No	2358 (78·2%)	2125 (90·1%)	233 (9·9%)	1·49 (1·14;1·92)	<0·01
Yes	656 (21·8%)	564 (86·0%)	92 (14·0%)		
HAS					
No	1812 (60·1%)	1657 (91·4%)	155 (8·6%)	1·77 (1·40;2·22)	<0·01
Yes	1202 (39·9%)	1032 (85·9%)	170 (14·1%)		
Cancer					
No	2861 (94·9%)	2573 (89·9%)	288 (10·1%)	2·86 (1·91;4·17)	<0·01
Yes	153 (5·1%)	116 (75·8%)	37 (24·2%)		
Pneumopathy					
No	2812 (93·3%)	2516 (89·5%)	296 (10·5%)	1·42 (0·93;2·12)	0·09
Yes	202 (6·7%)	173 (85·6%)	29 (14·4%)		
Platelets ($x10^9$/L)	(n = 2897)				
≥150 001	2243 (77·9%)	2035 (90·7%)	208 (9·3%)	1	
100 001 to 150 000	525 (18·2%)	456 (86·9%)	69 (13·1%)	1·48 (1·11; 1·98)	0·01
≤100 000	111 (3·9%)	80 (72·1%)	31 (27·9%)	3·79 (2·45; 5·88)	<0·01
Haemoglobin (g/L)	(n = 2885)				
≥11·1	2483 (86·1%)	2320 (93·4%)	163 (6·6%)	1	
8·1 to 11·0	315 (10·9%)	231 (73·3%)	84 (26·7%)	5·18 (3·85; 6·96)	<0·01
≤8·0	87 (3·0%)	24 (27·6%)	63 (72·4%)	37·36 (22·75; 61·37)	<0·01

Percentages in total column are sample distribution and in transfusion column are transfusion need during hospitalization.

Table 4 Events during hospitalization and transfusion need

Hospitalization variables	Total (n = 3014)	No transfusion (n = 2699)	Transfusion (n = 325)	Odds Ratio (95% CI)	*P* value
ICU					
No	1357 (45·0%)	1328 (97·9%)	29 (2·1%)		
Yes	1657 (55·0%)	1361 (82·1%)	296 (17·9%)	9·97 (6·87;15·00)	<0·01
IOT					
No	2071 (68·7%)	1992 (96·2%)	79 (3·8%)		
Yes	943 (31·3%)	697 (73·9%)	246 (26·1%)	8·94 (6·84;11·69)	<0·01

Percentages in total column are sample distribution and in transfusion column are transfusion need during hospitalization.

Table 5 Multiple logistic regression model for mortality

Coefficient	Estimate	Std. Error	Odds Ratio (95% CI)	*P* value
Age, years	0·06	0·003	1·06 (1·05; 1·07)	<0·01
DM	0·25	0·13	1·28 (0·99; 1·66)	0·06
HAS	-0·01	0·12	0·99 (0·78; 1·26)	0·94
Cancer	0·42	0·22	1·52 (0·99; 2·33)	0·05
Pneumopathy	0·12	0·21	1·12 (0·74; 1·70)	0·58
Platelets (100 001 to 150 000 × 10^9/L)	0·53	0·14	1·70 (1·30; 2·24)	<0·01
Platelets (<100 000 × 10^9/L)	0·45	0·25	1·57 (0·96; 2·58)	0·07
Haemoglobin (8·1–11·0 g/L)	0·85	0·15	2·33 (1·74; 3·13)	<0·01
Haemoglobin (<8·0 g/L)	1·41	0·26	4·11 (2·48; 6·81)	<0·01
AUC: 81·3%				

Table 6 Multiple logistic regression model for transfusion need

Coefficient	Estimate	Std. Error	Odds Ratio (95% CI)	*P* value
(Intercept)	–4·03	0·26	1	-
Age, years	0·02	0·004	1·02 (1·01; 1·03)	<0·01
DM	0·08	0·16	1·09 (0·80; 1·48)	0·59
HAS	0·42	0·14	1·53 (1·15; 2·03)	<0·01
Cancer	0·34	0·26	1·41 (0·85; 2·33)	0·18
Pneumopathy	0·13	0·25	1·14 (0·70; 1·85)	0·61
Platelets (100 001 to 150 000 × 10^9/L)	0·53	0·16	1·71 (1·25; 2·34)	<0·01
Platelets (<100 000 × 10^9/L)	0·64	0·28	1·90 (1·10; 3·27)	0·02
Haemoglobin (8·1–11·0 g/L)	1·43	0·16	4·17 (3·05; 5·69)	<0·01
Haemoglobin (<8·0 g/L)	3·40	0·27	30·04 (17·83; 50·59)	<0·01
AUC: 77·1%				

blood utilization. With the pandemic and the consequent suspension of elective surgeries, the number of transfusions also naturally drops in hospitals. Thus, with these two factors, the impact caused by the pandemic on the low rates of blood donations with a consequent decrease in blood stocks is lower. Future studies that better elucidate the pathophysiology of the disease may guide us better regarding the use of blood products by patients with COVID-19 and aid in outlining specific strategies for blood stock maintenance in this new hospital scenario.

Conflict of Interest

The authors have no conflict of interest.

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