ABO blood groups are not associated with the risk of acquiring SARS-CoV-2 infection in young adults

Four studies have previously implicated ABO blood groups in susceptibility to COVID-19 (symptomatic SARS-CoV-2 infection).[1–4] This study assessed a large population of 1,769 crewmembers confined to an aircraft carrier who, therefore, constituted an excellent epidemiological model. Our results show that ABO and Rh(D) blood groups are not associated with increased or decreased risk of infection by SARS-CoV-2. These data contrast with those of previous studies. Unlike the other studies, we did not compare the distribution of blood groups in hospitalized patients with SARS-CoV-2 infection and in the general population, but rather the distribution of SARS-CoV-2 infection according to blood groups in people exposed at the same time and in the same place to SARS-CoV-2. Our study confirms that in this period of the SARS-CoV-2 epidemic, no young adults can consider themselves more or less at risk in relation to their blood type.

Numerous studies indicated that people with blood group A had a significantly higher risk of SARS-CoV-2 infection, whereas people with blood group O had a significantly lower risk.[1-4] These studies could be criticized for the lack of data about patients' exposure to the virus before developing COVID-19 and for probably not including all forms of the disease. On this background, it is important to further explore the relationships between ABO blood groups and SARS-CoV-2 infection. It is also necessary to determine whether different rates of infection reflect the effect of infection prevention strategies or a sharp increase of asymptomatic or mild forms (not seeking medical assistance), which would affect collective immunity.

A COVID-19 outbreak occurred in April 2020 on the French Navy nuclear aircraft carrier "Charles de Gaulle", which had 1,769 crewmembers. The aircraft carrier was deployed at sea from January 22 to April 13, 2020 as part of an operational mission. A SARS-CoV-2 epidemic broke out on-ship, requiring its early (2 weeks) return to Toulon (the ship's main harbor). The first confirmed case occurred on February 28, 2020. During the mission, the crew was contained on board and the members were, therefore, exposed at the same time and in the same place to SARS-CoV-2. When the ship returned to France, the entire crew was confined at different military bases and benefited from daily medical monitoring for 14 days after landing. This study was undertaken with the main objective of investigating possible relationships between ABO blood groups and SARS-CoV-2 infection in these well-defined conditions of exposure.

To investigate the effect of ABO blood group on developing SARS-CoV-2 infection, we conducted this observational study on a retrospective cohort comprised of the crew of the aircraft carrier. The Ethics Committee of Sainte Anne Military Hospital (Toulon, France) approved the study (Institutional Review Board n. 0011873-2020-09). All data were collected, in the context of care, from completely anonymized files, in accordance with French and European laws, including the General Data Protection Regulation. All crewmembers were informed and provided free written consent to the use of their data.

All 1,769 persons on board underwent a physical examination and reverse transcriptase -polymerase chain reaction testing (RT-PCR) of two nasopharyngeal samples obtained immediately upon arrival in Toulon and at

Table 1. Characteristics of the study participants.

Characteristics	All crewmembers	Confirmed/suspected SARS-CoV-2	No SARS-CoV-2
Number (%)	1,688 (100.0)	1279 (76.0)	409 (24.0)
Median age (IQR), years	28 (23–35)	28 (23–36)	27 (23–33)
Male, n (%)	1466 (87.0)	1112 (87.0)	354 (87.0)
Blood group, n (%)*			
A	674 (39.9)	521 (40.7)	153 (37.4)
A^+	581 (34.4)	450 (35.1)	131 (32.0)
A^-	93 (5.5)	71 (5.6)	22 (5.4)
B	183 (10.8)	135 (10.6)	48 (11.7)
B^+	154 (9.1)	115 (9.0)	39 (9.5)
B^-	29 (1.7)	20 (1.6)	9 (2.2)
AB	70 (4.1)	54 (4.2)	16 (3.9)
AB^+	59 (3.5)	47 (3.6)	12 (2.9)
AB^-	11 (0.7)	7 (0.5)	4 (1.0)
O	742 (44.0)	553 (43.2)	189 (46.2)
O^+	645 (38.2)	480 (37.5)	165 (40.3)
O^-	97 (5.7)	73 (5.7)	24 (5.9)
Oxygen therapy, n (%)	19 (1.1)	19 (1.5)	–
ICU, n (%)	3 (0.2)	3 (0.2)	–
Mortality	0 (0)	0 (0)	0 (0)

IQR: interquartile interval (25%-75%): RT-PCR: reverse transcriptase polymerase chain reaction; ICU: Intensive Care Unit. *19 crewmembers lacked blood group information in their medical records or in the French database.

Table 2. Univariable analyses of factors associated with SARS-CoV-2 infection.

Factor	Positive RT-PCR and/or clinical signs (n=1279)		Positive RT-PCR (n=1038)		Asymptomatic with positive RT-PCR (n=172)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
ABO blood group (N=1669)						
A (n=674)	0.89 (0.68-1.08)	0.22	0.83 (0.68-1.02)	0.08	1.06 (0.76-1.49)	0.73
B (n=183)	1.12 (0.78-1.59)	0.52	1.16 (0.85-1.59)	0.33	0.55 (0.29-1.07)	0.09
AB (n=70)	0.91 (0.51-1.62)	0.88	1.12 (0.69-1.82)	0.70	3.12 (1.6-6.03)	0.0017
O (n=742)	1.11 (0.89-1.40)	0.32	1.10 (0.90-1.34)	0.36	0.88 (0.63-1.23)	0.49
Rh(D) negative (N=230)	1.08 (0.78-1.49)	0.61	0.91 (0.68-1.22)	0.56	0.84 (0.51-1.38)	0.54

least 7 days later at the end of a period of containment. Total RNA was extracted from the nasopharyngeal swab samples, and 200 µL of the sample were subjected to thermal and chemical inactivation and RNA extraction with Magnapure (Roche Diagnostic®) or Genoxtract (Biocentric®). The RT-PCR assay was run according to the French National Center protocol, targeting the IP2 and IP4 regions of the SARS-CoV-2-specific RNA-dependent RNA polymerase (RdRp) gene.

Individually housed during confinement (14 days and at least 2 days after symptoms had disappeared), crewmembers with clinical signs and/or who were PCR-positive were isolated in a given area and asymptomatic PCR-negative subjects in another. The vital signs and clinical symptoms of all subjects were monitored daily by the medical teams of the French Army Health Service (*Service de Santé des Armées*). Subjects were considered to be infected by SARS-CoV-2 if they had at least one positive RT-PCR (confirmed cases) and/or clinical symptoms highly suggestive of COVID-19 in this epidemiological context (fever, myalgias, arthralgia, dyspnea, cough, headache, anosmia, ageusia, rhinitis, diarrhea, fatigue, cutaneous signs). Subjects were considered not to have SARS-CoV-2 infection if they had two negative RT-PCR tests and no clinical signs.

The following medical information was extracted from the medical records: age, sex, blood group, COVID-19-related symptoms and their duration, indication for hospitalization and whether or not a computed tomography scan was done. The impact of ABO and Rh(D) types on susceptibility to SARS-CoV-2 infection was evaluated using logistic-regression univariable analyses (risks assessed by odds ratios [OR]). All analyses were computed with R software, version 3.6.3. Given our population we determined that the study would have a power of 99.9% to detect a 5% difference between blood groups.

Of the 1,769 crewmembers on the ship, 1,688 (95%) were included in this study (59 did not give consent and data were missing for 22, most of whom had left the ship because of specific duties). While on board, 1,279 crewmembers developed SARS-CoV-2 infection, accounting for a 76% (1,279/1,688) infection attack rate. The SARS-CoV-2 infection was confirmed by RT-PCR in 1,038 (62%) patients, whereas in 241 (14%) cases it was medically diagnosed (no positive RT-PCR but typical symptoms of COVID-19). After returning to France, 19 crewmembers were hospitalized with oxygen therapy, including three requiring admission to an Intensive Care Unit. The SARS-CoV-2 infection was asymptomatic in 172 (14%) cases. Among symptomatic cases, the mean duration of symptoms was 9 days (range, 1-40; 95% confidence interval, 9.08-9.88). Demographic and clinical characteristics of all participants and SARS-CoV-2 status are reported in Table 1. The median age of the crewmembers was 28 years and 13% were women. The population appeared to be healthy, with no significant comorbidities.

Among the whole crew, the ABO blood group showed a distribution of 39.9%, 10.8%, 4.1% and 44.0% for A, B, AB and O types, respectively. The corresponding proportions for crewmembers infected with SARS-CoV-2 were 40.7%, 10.6%, 4.2% and 43.2% for A, B, AB and O types, respectively. In univariate analysis no significant relationship was found between SARS-CoV-2 infection and ABO or Rh(D) types (Table 2). Excluding the minority of cases that were diagnosed clinically without laboratory support (14%), the results did not differ: ABO or Rh(D) types were also not related to RT-PCR-positive SARS-CoV-2 infections. Concerning asymptomatic cases, AB group seemed to be related to the absence of symptom among crewmembers with RT-PCR positivity for SARS-CoV-2 (odds ratio 3.12 [95% confidence interval: 1.6-6.03], *P*=0.0017). The median age of the 19 patients requiring oxygen therapy was 45 years. Five patients were blood group A, 5 group B and 10 group O. All patients admitted to the Intensive Care Unit were older than 50 years: one had group B and 2 had group O blood.

In this study, which assessed a large population confined to an aircraft carrier, thus constituting an excellent epidemiological model, ABO and Rh(D) blood groups were not associated with increased or decreased risk of SARS-CoV-2 infection. These data are opposed to those of previous studies which had a certain impact in the press. Unlike those studies, we did not compare the distribution of blood groups in hospitalized patients with SARS-CoV-2 and in the general population, but rather compared the distribution of SARS-CoV-2 infection according to blood groups in people exposed at the same time and in the same place to SARS-CoV-2. The contradictory results can also be explained in other ways. Our population appeared to be young and healthy, with no significant comorbidities. ABO blood types are potentially related only to severe forms of COVID-19. Another previous study hypothesized that although ABO blood type and/or cardiovascular diseases are prognostic of the severity of COVID-19 in patients, they are not factors predisposing to the risk of getting SARS-CoV-2 infection.[5] There is a pathophysiological mechanism to support this hypothesis: subjects with A blood type are at risk of the development of cardiovascular diseases and severe COVID-19 because of the positive association of this blood type with angiotensin-converting enzyme activity, and the attachment of adhesion molecules on the vascular wall, which increases inflammation and decreases

blood circulation.[6,7] In our population, the lack of comorbidities and cardiovascular risk factors could therefore be considered a bias. However, a recent study observed no association between ABO blood group polymorphisms and deaths from COVID-19.

Nineteen crewmembers had no blood group recorded in their medical records or in the French blood-bank database: 16 cases infected by SARS-CoV-2 and three not infected. This is potential confounder, although probably a limited one given that it represents such a small fraction of the total group.

Otherwise the reported rate of infection (76%) is remarkably high. Close contact in an aircraft carrier does not reflect normal social conditions and this extreme situation may have possibly downgraded any protective effect of O blood group.

The population with AB blood type is small. The relationship between an asymptomatic form of SARS-CoV-2 infection and this blood type needs to be confirmed on a larger scale. If confirmed, the underlying molecular mechanism of our findings will need further study.[8]

Regarding viral strains, the viral genomes of samples from the first 60 cases of RT-PCR-confirmed COVID-19 were sequenced. The diversity of the mutational signatures within these samples indicates the presence of several viral variants. These different variants can result from several contaminations by different strains or from evolution of the initial strain.[9]

In conclusion our study confirms that in this period of the SARS-CoV-2 epidemic, no young adults can consider themselves more or less at risk in relation to their blood type.

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