Distribution of ABO Blood Groups and Their Association With Low Risk of Severe COVID-19 Infection in Patients

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Abstract

Background: To date, only few studies have focused on the correlation between ABO blood groups and COVID-19 infection risk, especially gender differences in infection risk. Our study aimed to describe the ABO blood group distribution and its association with risk of severe COVID-19 infection for effective identification of the susceptible population.

Method From January 21 to February 20, 2020, we compared the ABO blood group distribution and gender distribution and performed a correlation analysis in severe, non-severe, and non-COVID-19 patients.

Results The results showed that the laboratory indices were significantly different between blood type O and non-blood-type-O COVID-19 patients. This indicated that patients of the type O blood group had a relatively lower risk of severe COVID-19 infection than patients of other blood types; in particular, females with blood type O had a lower risk of severe COVID-19 infection than males.

Conclusion: Herein, we report a potentially simple prediction decision system to minimize the risk of severe COVID-19 infection based on blood type. Special attention should be paid to patients with blood types other than type O to minimize their risk of severe COVID-19 infection.

Highlights

We described the ABO blood group distribution and its association with risk of severe COVID-19 infection.

We compared the ABO blood group distribution and gender distribution and performed a correlation analysis in severe, non-severe, and non-COVID-19 patients.

Females with blood type O had a lower risk of severe COVID-19 infection than males.

Introduction

With the spread of the coronavirus disease (COVID-19) pandemic worldwide, how to quickly know whether people around us are infected with COVID-19 remains a challenge, especially in the large recovery of working and studying. As not every country can afford to test nucleic acids to confirm the COVID-19 infection. In addition, some study tried to detect SARS-CoV-2 in unextracted oro-nasopharyngeal specimens[1]. In China, the first wave of COVID-19 has abated due to aggressive non-pharmaceutical interventions [2]. However, a second wave of COVID-19 transmission is possible, particularly from overseas importations [3]. Great efforts are being made to understand the factors that predispose to COVID-19 disease progression to find a window of opportunity for intervention [4]. The ABO blood group system is the most extensively investigated erythrocyte antigen system, which influences host susceptibility and is widely used in clinical practice. ABO blood groups have already been biologically associated with many chronic diseases such as cancer [5, 6, 7]. Previous studies indicated

that the ABO blood type influenced the long-term outcomes of Japanese patients with pancreatic cancer, presumably due to its impact on disease onset and tumour behaviour. In contrast, other studies showed that blood type showed no significant effect on the clinicopathological parameters of gastric cancer. However, the blood type O may be a prognostic factor for patients with gastric cancer. The ABO blood group is also linked to the prognosis of various diseases [8, 9, 10, 11], and prospective studies showed that the ABO blood group is associated with other diseases, which may be clinically significant [12, 13, 14]. Hence, we hypothesized that the ABO blood group would be associated with the risk of COVID-19 infection.

The association between the ABO blood group and COVID-19 infection risk in the Zhejiang province has rarely been reported. In this study, we set out to definitively describe the ABO blood group distribution and evaluate its correlation with the COVID-19 infection risk.

Materials And Methods

Demographic data and clinical diagnosis of patients

This retrospective study was conducted at Public Hygiene Center in the Taizhou Hospital of Zhejiang province between January 21, 2020, and February 20, 2020. The study flowchart is shown in Fig. 1. We included 138 COVID-19-diagnosed patients and 82 non-COVID-19 patients. We compared the ABO blood group distribution and gender distribution of severe and non-severe COVID-19 patients with those of non-COVID-19 patients, and we also compared these two distributions between blood-type-O and non-blood-type O COVID-19 patients. At the same time, we analysed and compared the laboratory indices of type-O and non-type-O COVID-19 patients. The results were followed up until March 11, 2020. The study was approved by the institutional review board and the Ethics Committee of Taizhou Hospital of Zhejiang province affiliated to the Wenzhou Medical University (K20200112). Informed written consent was obtained from all the participants. The majority of the suspected patients were diagnosed as COVID-19-positive on computerized tomography (CT) scans and reverse transcription polymerase chain reaction (RT-PCR) tests. The confirmed patients were then divided into the severe and non-severe groups.

The clinical diagnosis and classification criteria were in accordance to the novel “Coronavirus Pneumonia Diagnosis and Treatment Plan” (trial version 6) formulated by the National Health Commission General Office of Health Guidelines [15]. In this study, we included both severe and non-severe patients. Severe COVID-19 patients had the following three symptoms: respiratory distress characterized by a respiratory rate of $\geq$ 30 times/min, mean oxygen saturation of $\leq$ 93% in the resting state, and arterial blood oxygen partial pressure/oxygen concentration of $\leq$ 300 mmHg (1 mmHg = 0.133 kPa). The non-severe patient group consisted of mild (mild symptoms without pneumonia) and typical (fever or respiratory tract symptoms with pneumonia) COVID-19 patients.

Study population

Positive and negative stereotypes were detected automatically using an AutoVue automatic blood group analyser (Johnson & Johnson, USA). We collected a total of 220 ABO blood group data between January 21, 2020, and February 20, 2020, in Taizhou Hospital of Zhejiang province; the patients were divided into three groups: severe COVID-19 patients, non-severe COVID-19 patients, and non-COVID-19 patients.

Statistical methods

We performed statistical analyses using SPSS version 25.0 (IBM, US). We expressed the categorical variables as frequencies and percentages and continuous variables as medians and interquartile ranges (IQRs) or means ± standard deviations (SDs). We compared the continuous variables using the Mann-Whitney U test and the categorical variables using the chi-square test; $p < 0.05$ was considered to indicate statistical significance. We used 95% confidence intervals (95% CIs) of odds ratios (ORs) as common measures to assess relative risk. The figures were plotted using GraphPad Prism version 8.0.

Results

Characteristics of patients

The complete demographic information of the study population is shown in Table 1. Between January 21, 2020, and February 20, 2020, a total of 200 patients with findings suggestive of COVID-19 underwent real-time RT-PCR tests, CT radiographies, and assessments of clinical symptoms. This resulted in 138 COVID-19-diagnosed patients and 82 non-COVID-19 patients. The median age was 50 years. Of the total patients, 74 (53.6%) were male, 70 (50.7%) had a history of return from Wuhan, and 31 (22.5%) had contact with people returning from the epidemic area. The clinical symptoms in the patients were fever (70.3%), cough (57.2%), expectoration (31.9%), pharyngula (10.1%), fatigue (22.5%), headache (10.9%), diarrhoea (8.0%), and chest tightness (8.7%). Comorbidities in the patients were diabetes (8.7%), hypertension (15.9%), chronic pulmonary disease (8.0%), digestive system disease (12.3%), and kidney disease (1.4%). Fourteen patients (10.1%) were habitual smokers. In addition, 82 patients who tested negative for SARS-CoV-2 nucleic acid had returned from Wuhan or had a history of contacting people who returned from the epidemic area.

Table 1
Clinical characteristics of and comorbidities in coronavirus disease (COVID-19)-diagnosed and non-COVID-19 patients.

Characteristics	Total (N = 220)	COVID19 (N = 138)	Non-COVID19 (N = 82)	Z / χ^2	*p* value
Sex — no. (%)					
Male	113 (51.4)	74 (53.6)	39 (47.6)	0.757	0.384
Female	107 (48.6)	64 (46.4)	43 (52.4)		
Age median (IQR), y	50 (40–56)	50 (40–56)	42 (32–56)	-5.935#	0.000*
Contact history— no. (%)					
Returned from Wuhan	124 (56.4)	70 (50.7)	54 (65.9)	4.844	0.028*
Contact with people returned from the epidemic area	59 (26.8)	31 (22.5)	28 (34.1)	3.517	0.061
Smoke — no. (%)	28 (12.7)	18 (13.0)	10 (12.2)	0.033	0.855
Symptoms — no. (%)					
Fever	151 (68.6)	97 (70.3)	54 (65.9)	0.468	0.494
Cough	133 (60.5)	79 (57.2)	54 (65.9)	1.607	0.205
Expectoration	80 (36.4)	44 (31.9)	36 (43.9)	3.184	0.074
Headache	23 (10.5)	15 (10.9)	8 (9.8)	0.069	0.793
Pharyngalgia	29 (13.2)	14 (10.1)	15 (18.3)	2.894	0.089
Fatigue	44 (20.0)	31 (22.5)	13 (15.9)	1.441	0.230
Diarrhea	15 (6.8)	11 (8.0)	4 (4.9)	0.811	0.368
Chest tightnes	17 (7.7)	12 (8.7)	5 (6.1)	0.502	0.478
Comorbidity — no. (%)					

Note: *p* values were obtained using the chi-square test or Mann-Whitney U test. *p* values indicate significant differences between COVID-19 and non-COVID-19 patients; *$p < 0.05$ was considered to indicate statistical significance. # represents the Z value.

Characteristics	Total (N = 220)	COVID19 (N = 138)	Non-COVID19 (N = 82)	Z / χ^2	*p* value
Diabetes	16(7.3)	12 (8.7)	4(4.9)	1.174	0.279
Hypertension	31(14.1)	22 (15.9)	9(11.0)	1.080	0.299
Chronic pulmonary disease	14(6.4)	11 (8.0)	3(3.7)	1.735	0.188
Digestive system disease	20(9.1)	17 (12.3)	3(3.7)	5.291	0.021*
Kidney disease	2 (0.9)	2 (1.4)	0 (0.0)	-	0.530

Note: *p* values were obtained using the chi-square test or Mann-Whitney U test. *p* values indicate significant differences between COVID-19 and non-COVID-19 patients; *$p < 0.05$ was considered to indicate statistical significance. # represents the Z value.

ABO blood group distribution

Table 2 shows the ABO blood group distribution in severe, non-severe, and non-COVID-19 patients. The blood group distributions in severe, non-severe, and non-COVID-19 patients were A = B > O > AB, O > A > B > AB, and O > B > A > AB, respectively (Fig. 2).

Table 2
ABO blood group distribution in Severe, Non-severe and Non-COVID19 patients.

Patients		Gender	Type A	Type B	Type AB	Type O	Non-Type O
COVID19 (N = 138)	Severe (N = 32)	total	11(34.4%)	11(34.4%)	4 (12.5%)	6 (18.8%)	26(81.2%)
		male	7(36.8%)	4(21.1%)	2 (10.5%)	6 (31.6%)	
		female	4(30.7%)	7(53.8%)	2 (15.4%)	0 (0.0%)	
	Non-severe (N = 106)	total	30(28.3%)	29 (27.4%)	12(11.3%)	35(33.0%)	71(67.0%)
		male	16(29.1%)	15(27.3%)	5(9.1%)	19(34.5%)	
		female	14(27.5%)	14(27.5%)	7 (13.7%)	16(31.4%)	
Non-COVID19 (N = 82)		total	22(26.8%)	23(28.0%)	6(7.3%)	31(37.8%)	51(62.2%)
		male	7(17.9%)	9(23.1%)	4(10.3%)	19(48.7%)	
		female	15(34.9%)	14(32.6%)	2(4.7%)	12(26.1%)	

Blood type O correlation analysis

Compared with severe, non-severe COVID-19 patients to non-COVID-19 with the blood group of type A, type B, type AB, and type O in COVID19 and non-COVID19 patients. Our results indicated that patients

with blood type O had a lower risk of severe COVID-19 infection than those with other blood types (χ^2 = 4.066, p = 0.044, OR = 0.380 ,95%CI : 0.141–1.025) (Table 3, Fig. 3)

Table 3
ABO blood group distribution and correlation analysis in Severe, Non-severe and Non-COVID19 patients.

Patients	Type A	Type B	Type AB	Type O
Severe (N = 32)	11(34.4%)	11(34.4%)	4 (12.5%)	6 (18.8%)
Non-COVID19 (N = 82)	22(26.8%)	23(28.0%)	6(7.3%)	31(37.8%)
χ^2	0.625	0.433	-	4.066
p value	0.429	0.510	0.463	0.044*
OR	1.429	1.344	1.810	0.380
95%CI	0.594–3.437	0.561–3.221	0.475–6.892	0.141–1.025
Non-severe (N = 106)	30(28.3%)	29 (27.4%)	12(11.3%)	35(33.0%)
Non-COVID19 (N = 82)	22(26.8%)	23(28.0%)	6(7.3%)	31(37.8%)
χ^2	0.050	0.011	0.876	0.464
p value	0.823	0.916	0.349	0.496
OR	1.077	0.966	1.617	0.811
95%CI	0.564–2.054	0.507–1.839	0.580–4.509	0.444–1.482
	Non-type O			Non-type O
COVID19 (N = 138)	97(70.3%)			41(29.7%)
Non- COVID19 (N = 82)	51(62.2%)			31(37.8%)
χ^2	1.518			
p value	0.218			
OR	0.695			
95%CI	0.391–1.238			

Note: *p* values were obtained by a Chi-square test. * $p < 0.05$ was considered statistically significant. OR, odds ratio. CI, confidence interval.

Gender distribution and correlation analysis

We evaluated gender distribution in and performed a correlation analysis of the ABO blood groups of severe, non-severe, and non-COVID-19 patients. This indicated that there was a significant difference between female patients with severe COVID-19 and blood group type O blood group and female non-

COVID-19 patients (p = 0.049,, OR = 0.721,95%CI : 0.599–0.868) (Table 4, Fig. 4); thus, females with blood group type O had a lower risk of severe COVID-19 infection.

Table 4
Gender distribution and correlation analysis in ABO blood group of Severe, Non-severe and Non-COVID19 patients.

Patients	Sex	Type A	Type B	Type AB	Type O
Severe (N = 19)	Male	7(36.8%)	4(21.1%)	2 (10.5%)	6 (31.6%)
Non-COVID19 (N = 39)	Male	7(17.9%)	9(23.1%)	4(10.3%)	19(48.7%)
χ^2		-	-	-	1.559
P **value**		0.189	1.000	1.000	0.212
OR		2.667	0.889	1.029	0.486
95%CI		0.772–9.215	0.235–3.364	0.171–6.188	0.153–1.539
Non-severe (N = 55)	Male	16(29.1%)	15(27.3%)	5(9.1%)	19(34.5%)
Non-COVID19 (N = 39)	Male	7(17.9%)	9(23.1%)	4(10.3%)	19(48.7%)
χ^2		1.572	0.213	-	1.899
P **value**		0.210	0.654	1.000	0.168
OR		1.875	1.250	0.875	0.556
95%CI		0.687–5.117	0.482–3.240	0.219–3.492	0.244–1.285
Severe (N = 13)	Female	4(30.7%)	7(53.8%)	2 (15.4%)	0 (0.0%)
Non-COVID19 (N = 43)	Female	15(34.9%)	14(32.6%)	2(4.7%)	12(26.1%)
χ^2		-	-	-	-
P **value**		1.000	0.201	0.227	0.049*
OR		0.830	2.417	3.727	-
95%CI		0.218–3.151	0.683–8.548	0.470-29.534	-
Non-severe (N = 51)	Female	14(27.5%)	14(27.5%)	7 (13.7%)	16(31.4%)
Non-COVID19 (N = 43)	Female	15(34.9%)	14(32.6%)	2(4.7%)	12(26.1%)
χ^2		0.603	0.290	-	0.134
P **value**		0.437	0.590	0.173	0.714
OR		0.706	0.784	3.261	1.181
95%CI		0.293-1.700	0.323–1.901	0.640-16.613	0.484–2.879

Note: *p* values were obtained by a Chi-square test. * $p < 0.05$ was considered statistically significant. OR, odds ratio. CI, confidence interval.

COVID-19 infection risk factors

There was no significant difference in the distribution and comorbidity between the type O blood group and other non-type-O blood groups (Tables 3 and 5), but there were significant differences in the laboratory indices. The blood group type O patients had lower laboratory indices except for MCV (mean corpuscular volume) and MCH (mean corpuscular hemoglobin) (Fig. 5).

Table 5
The Comorbidity of Type O and Non-Type O COVID-19 patients.

	N (%)				
Comorbidity	**Total (N = 138)**	**Type O(N = 41)**	**Non-type O(N = 97)**	**χ^2**	***p* value**
Diabetes	12 (8.7)	4 (9.8)	8 (8.2)	-	0.750
Hypertension	22 (15.9)	5 (12.2)	17 (17.5)	0.638	0.425
Chronic pulmonary disease	11 (8.0)	5 (12.2)	6 (6.2)	-	0.302
Digestive system disease	17 (12.3)	3 (7.3)	14 (14.4)	1.474	0.225
Kidney disease	2 (1.4)	0 (0.0)	2 (2.1)	-	1.000
Note: *p* values were obtained by a Chi-square test. *p* values indicate the differences of comorbidity between Type O and Non-Type O COVID-19 patients, $p < 0.05$ was considered statistically significant.					

Note

The data are presented as mean ± SD, and *p* values were obtained using the Mann-Whitney U test. *p* values indicate significant differences between type O and non-type-O COVID-19 patients; $p < 0.05$ was considered to indicate statistical significance. *$p < 0.05$, **$p < 0.01$.

Discussion

The results of this study showed that the blood group distributions in severe, non-severe, and non-COVID-19 patients were A = B > O > AB, O > A > B > AB, and O > B > A > AB, respectively. The distribution of blood type O in the severe COVID-19 group was significantly different from that in the non-COVID-19 group. There was a negative correlation between blood type O and the risk of severe COVID-19 infection, but there were no significant differences between the distributions of other blood groups and severe COVID-19 infection risk. The number of female patients with blood type O with severe COVID-19 was significantly different from that in the non-COVID-19 group, and there were no significant differences in

other blood groups. This study is different from ones conducted earlier[16, 17] as the gender and the blood type distribution make association with risk of severe COVID-19 patients.

The gene encoding the ABO blood group system is very stable and is located on the long arm of chromosome 9 at the band 9q34. It is closely associated with many diseases [10, 18, 19]. Glenda et al. [20] found the blood group antigen expression to be different across regions and populations because of natural selection and the effect of an external factor. Liao et al. [21] suggested that the A, B, and AB blood types might be susceptible to norovirus infection; however, blood type O appeared to be more susceptible to norovirus infection. Jing et al. [22] performed a meta-analysis to investigate whether the ABO blood groups were associated with hepatitis B virus (HBV) infection. They found a correlation between the ABO blood groups and the incidence of eight types of cancers [23].

In this study, the blood group results of COVID-19 patients were analysed retrospectively. The non-COVID-19 patients who all returned from Wuhan or had a history of contact with people who returned from Wuhan contact were significantly different between the 'Wuhan returners' and 'contact history with people from Wuhan' groups. This may be due to the variations in epidemic situations in different areas of Wuhan and the different frequency of personal protective activities, but the electronic medical records did not contain this information in detail. We found that patients with COVID-19 were generally older than non-COVID-19 patients, and there was a significant difference in the comorbidity of gastric disease between the COVID-19 and non-COVID-19 patients (12.3% vs. 3.7%, respectively; $\chi^2 = 5.291$, $p = 0.021$).

Blood group antigens can modify the innate immune response to infection [24]. Patients with blood type A had an increased risk of infection with SARS-CoV-2, whereas those with blood type O had a decreased risk, indicating that certain ABO blood groups were correlated with SARS-CoV-2 [18], and the distribution ratio of blood types A and O across various ages and genders was almost consistent with the trend in value found in other studies [25].

We divided the COVID-19 patients into type O and non-type-O blood groups and analysed the comorbidity data and laboratory indices in the two groups. The results indicated that there were no significant differences in the comorbidity data, and there is currently no literature showing that diabetes, hypertension, chronic pulmonary disease, gastric disease, kidney disease, or hepatitis increases the risk of infection of SARS-CoV-2. However, we found that ALT (alanine aminotransferase), LDH (Lactate dehydrogenase), and TBCD19 (Total $CD19^+$B cell ratio) were lower in type O COVID-19 patients, while their MCV had a higher value. MCH values showed significant differences between the type O and non-type-O COVID-19 patient groups. ALT is mainly distributed in the liver, followed by the skeletal muscle, kidneys, heart muscle, and other tissues. It is one of the most sensitive indicators of liver damage. LDH is an enzyme found in the cytoplasm of nearly all cells in the human body and is used to detect cell necrosis and tissue destruction [26]. One study [22] indicated that the relationship between LDH and in-hospital mortality in patients with acute aortic dissection was non-linear. LDH was positively associated with in-hospital mortality when it was more than 557 U/L. Another study showed that idiopathic pulmonary arterial hypertension patients with high LDH levels had a low cumulative survival rate [27].

CD19 is a common surface marker of all B cells. B cells mainly mediate humoral immunity such as anti-infection, MCV, MCH, and mean corpuscular haemoglobin concentration (MCHC). They often declared the pathological changes of red blood cells from different sides, which had a value for the diagnosis of anaemia, which suggested that the damage to the liver and myocardium in COVID-19 patients with blood type O was less serious than that in patients with non-type O.

Limitations

Some limitations of our study were the lack of generalizability of our findings to other populations (as our patients were only from China) and the small sample size. To date, the association between the ABO blood group and COVID-19 remains a challenge to determine accurately; further gene hereditary and large-scale population studies should be conducted to analyse all polymorphic blood groups and to explore blood group genomics in COVID-19 patients to verify this hypothesis.

Conclusions

In summary, the laboratory indices were significantly different between blood type O and non-blood-type-O COVID-19 patients, which indicated that patients with the blood type O had a relatively lower risk of severe COVID-19 infection. In particular, females with blood type O had a lower risk of deteriorating, severe COVID-19 infection. Special attention should be given to patients with blood types other than type O to minimize their risk of severe COVID-19 infection.

Abbreviations

MCV
mean corpuscular volume
MCH
mean corpuscular hemoglobin
ALT
alanine aminotransferase
LDH
Lactate dehydrogenase
TBCD19
Total CD19 + B cell ratio
OR
odds ratio.
CI
confidence interval

Declarations

Availability of data and materials

Not applicable

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Author Contributions

Conceptualization, M.P. and S.H.; methodology, M.P.; software, Q.L.; validation, C.C., J.Q. and M.H.; formal analysis, J.Y.; investigation, S.C.; resources, M.P.; data curation, M.P.; writing—original draft preparation, M.P.; writing—review and editing, S.H.; visualization, Q.Z.; supervision, M.P.; project administration, M.P.; funding acquisition, M.P. All authors have read and agreed to the published version of the manuscript

Ethics approval and consent to participate

The study was approved by the institutional review board and the Ethics Committee of Taizhou Hospital of Zhejiang province affiliated to the Wenzhou Medical University (K20200112)

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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Figures

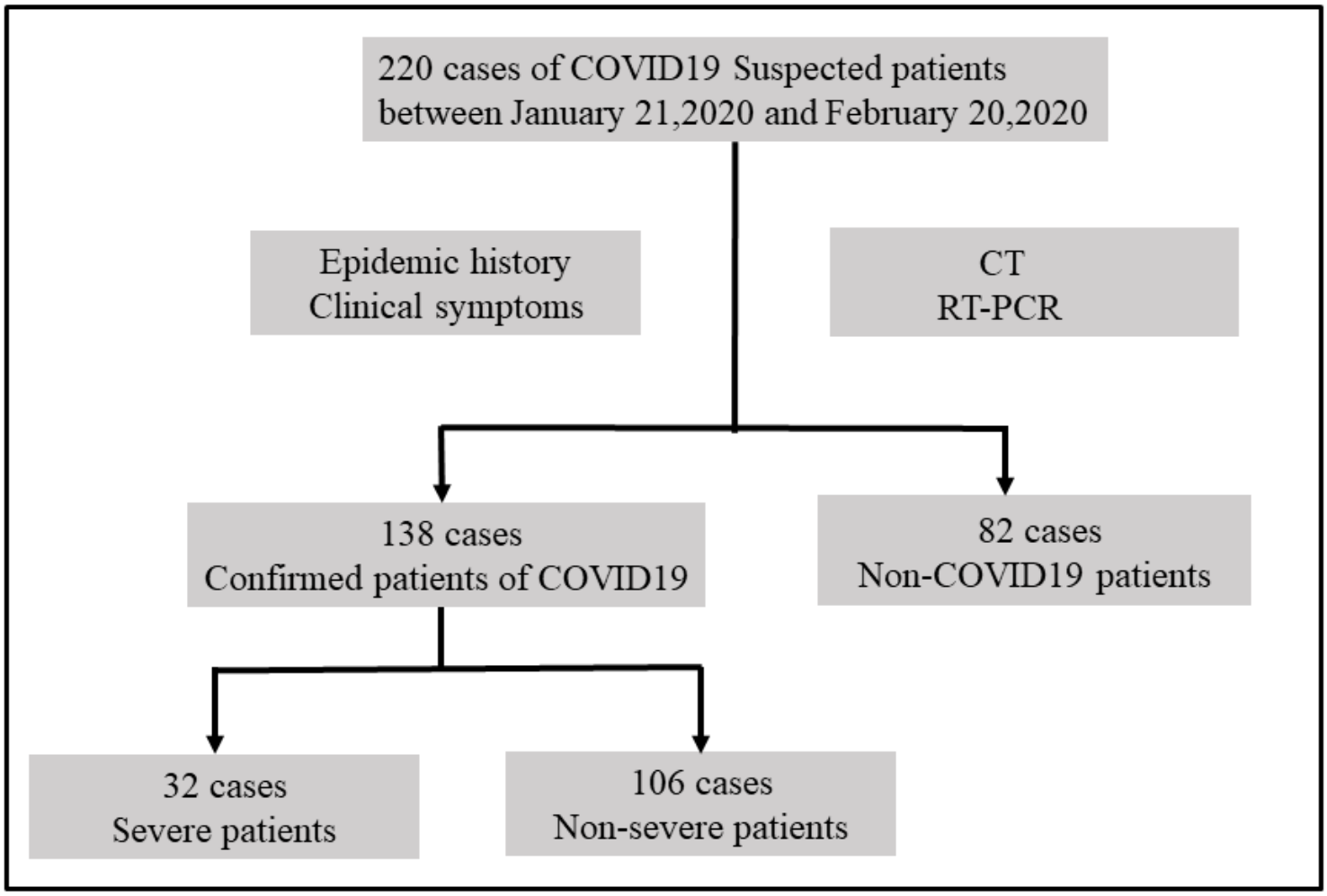

Figure 1

Flowchart for the selection of the coronavirus disease (COVID-19)-diagnosed and non-COVID-19 patient cohort.

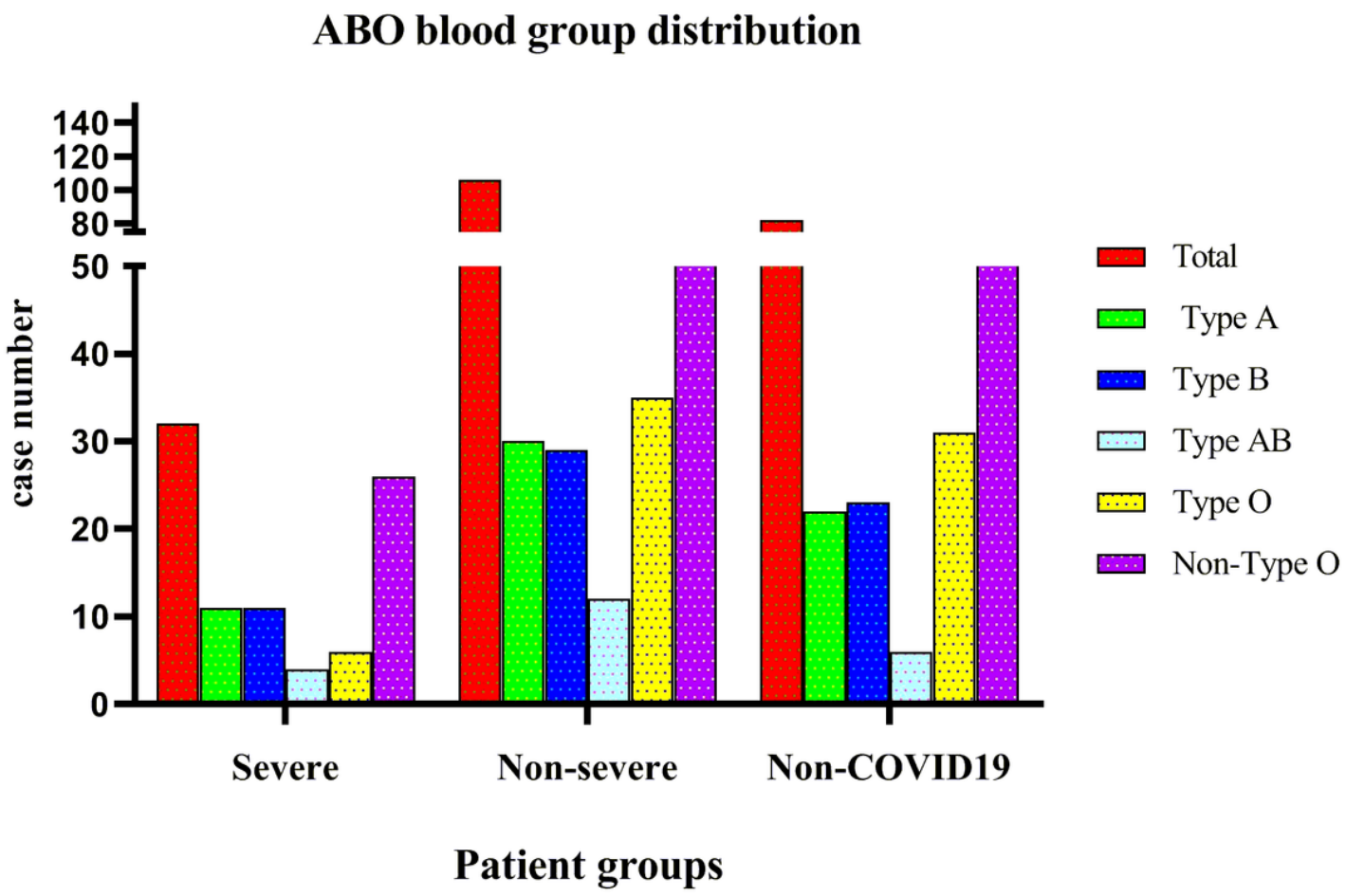

Figure 2

ABO blood group distribution in severe, non-severe and non-coronavirus disease (COVID-19) patients.

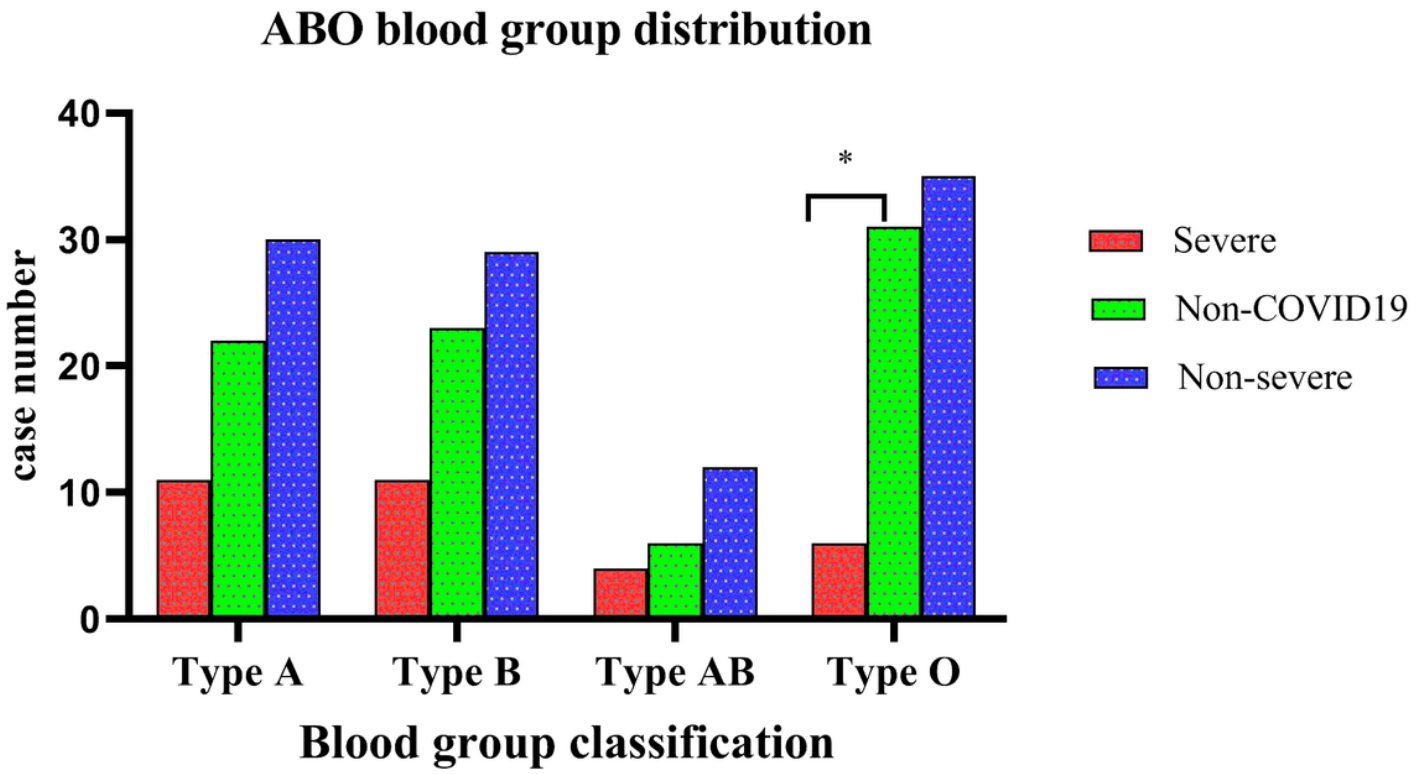

Figure 3

ABO blood group distribution in and correlation analysis of severe, non-severe and non-coronavirus disease (COVID-19) patients. p values were determined using a chi-square test; *p < 0.05 was considered to indicate statistical significance.

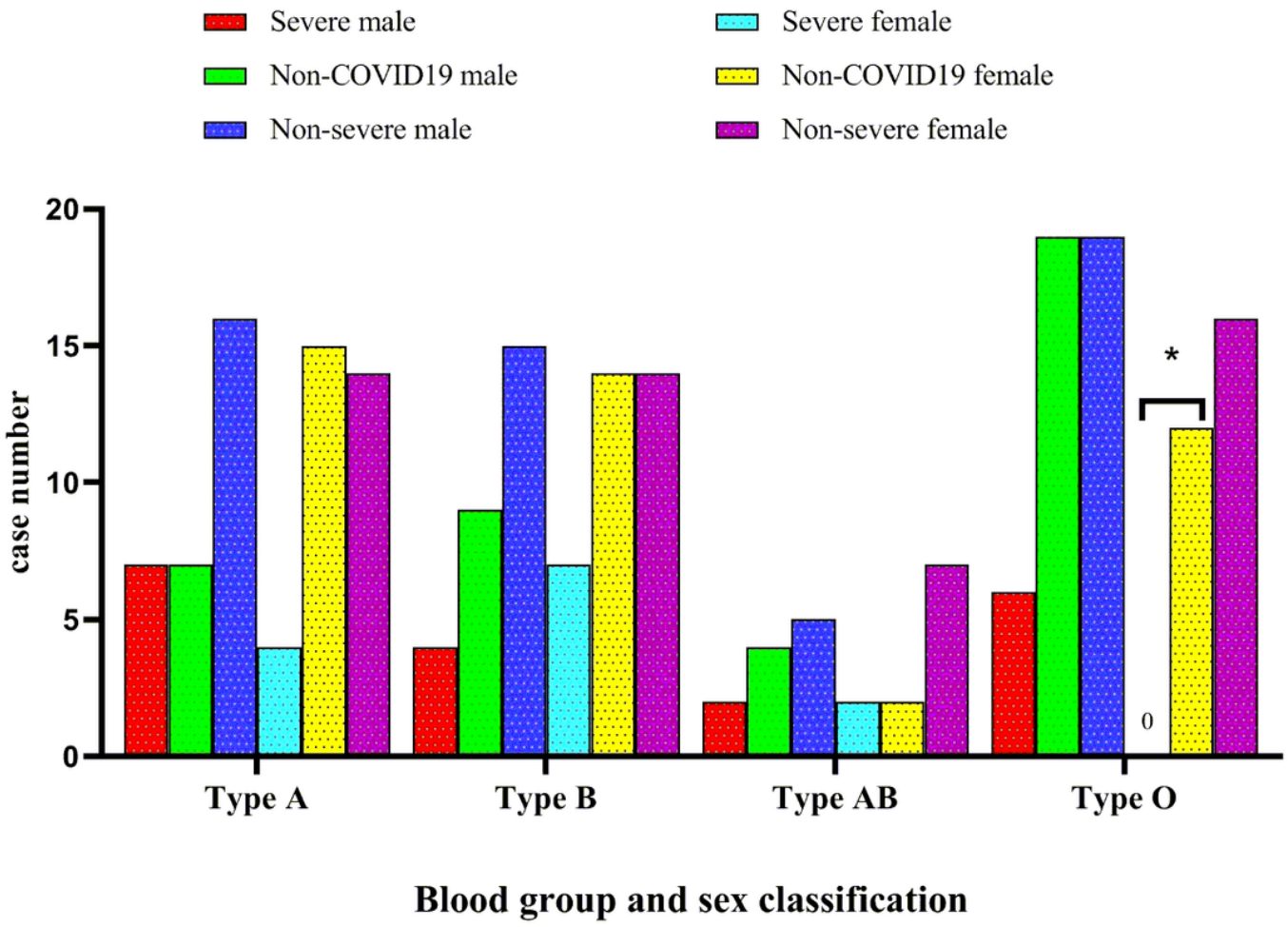

Figure 4

Gender distribution in and correlation analysis of ABO blood group of severe, non-severe, and non-COVID-19 patients. p values were determined using a chi-square test; *p<0.05 was considered to indicate statistical significance.

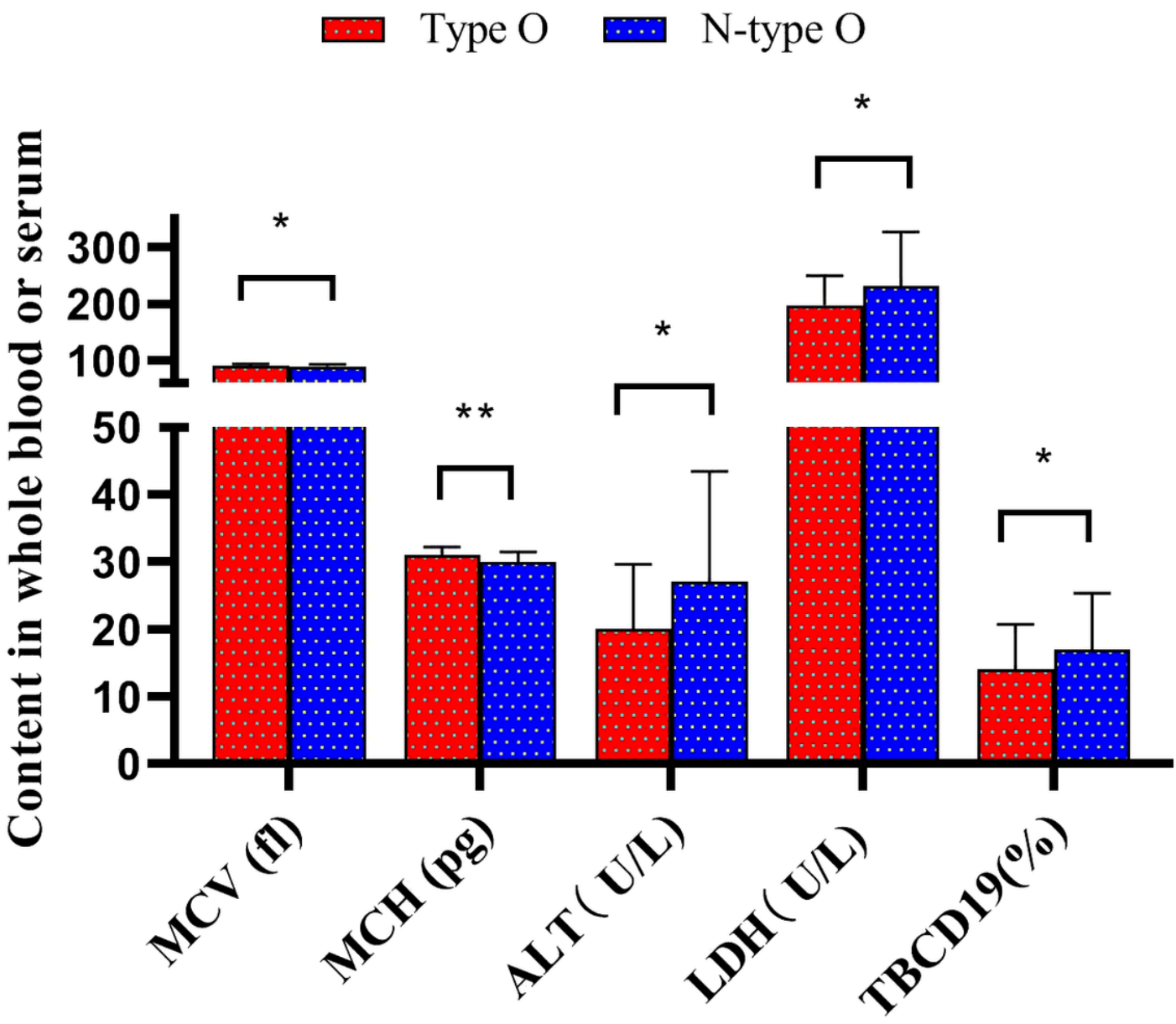

Figure 5

Comparison of laboratory indices between type O and non-type-O blood groups in coronavirus disease (COVID-19) patients. Note: The data are presented as mean ± SD, and p values were obtained using the Mann-Whitney U test. p values indicate significant differences between type O and non-type-O COVID-19 patients; $p<0.05$ was considered to indicate statistical significance. *$p<0.05$, **$p<0.01$.