Impact of Variations in ABO Blood Groups on the Clinical Presentation and Hospital Outcome of COVID-19 Patients

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INTRODUCTION

Since it first showed up in late 2019, the new coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread around the world, creating a global pandemic that is still going on (1,2). As of December 2022, there have been over 635 million confirmed cases and over 6.6 million deaths attributed to COVID-19 worldwide(3). Saudi Arabia has not been spared from the devastation of this disease, with over 825,000 confirmed cases and over 9,300 deaths as of November 2022 (4).

There is significant variation in the severity and outcomes of COVID-19 between infected individuals(5). While some develop no or mild symptoms, others progress to critical illness with respiratory failure, septic shock, and multiorgan dysfunction requiring intensive care and having high mortality (6). Age and comorbidities like diabetes, obesity, and heart disease are known risk factors for severe COVID-19, but do not fully account for differences in disease manifestation (7). There is growing evidence that genetic factors also influence COVID-19 susceptibility and clinical outcomes.

One genetic factor that may modulate COVID-19 severity is the ABO blood group. The ABO gene encodes glycosyltransferases that add carbohydrate antigens to the extracellular surface of red blood cells and various other human cells and tissues (8,9). This results in expression of ABO blood types A, B, AB, and O in the population(10). Crucially, ABO antigens are also expressed on the surface membranes of cells lining the airway and alveolar epithelium that SARS-CoV-2 initially targets, leading to speculation that ABO blood type may affect viral binding and entry as well as subsequent immune responses (11,12).

Multiple studies globally have reported associations between ABO blood type and COVID-19 susceptibility, severity, and mortality (13,14). Some studies found blood groups A and AB to be associated with an increased risk of acquiring COVID-19 compared to groups O and B, while other studies found no relationship between ABO blood type and COVID-19 infection rates (14–16). Several meta-analyses consolidating data from dozens of studies around the world consistently demonstrate that blood groups A and AB are associated with a modest but significantly increased risk of severe COVID-19 illness compared to blood groups O and B (17–19).

Conversely, people with blood groups O and B appear less prone to respiratory failure, thrombogenic complications, and mortality due to COVID-19(20,21). A systematic review of over 150,000 COVID-19 patients reported mortality rates of 9.06% for blood group A, 6.08% for B, 6.57% for AB, and 5.63% for O (22,23). This indicates a more than 50% higher relative risk of mortality for blood group A compared to group O(24). The reasons for these observed ABO blood type-dependent differences in susceptibility and clinical trajectory of COVID-19 are not fully elucidated but may relate to ABO antigen expression on target cells for SARS-CoV-2 as well as ABO-associated variations in immune function, coagulation, and vascular biology pathways (25,26).

While global findings point towards blood groups A and AB bearing higher risk, region- and population-specific genetic differences may mean associations between ABO blood type and COVID-19 outcomes manifest differently across geographies(27). Data specific to Saudi Arabia and the Middle East remain quite limited thus far. Three studies from Saudi Arabia, Qatar, and Iran investigating links between ABO blood groups and COVID-19 severity and mortality have had inconsistent findings (28,29). Further research localized to the Saudi and broader Middle Eastern context is warranted to clarify if and how ABO blood group may be predictive of disease outcomes in this population(30,31)

Additionally, the relationship between ABO blood type and clinical presentation of COVID-19 in terms of specific symptoms, hospital course, and complications has been less studied(32). Chest imaging studies suggest more severe lung parenchymal injury and abnormal computed tomography findings in COVID-19 patients with blood groups A and AB compared to groups B and O (33). Blood groups A and AB have also been associated with higher rates of hospitalization, thromboembolic complications like deep vein thrombosis and pulmonary embolism, acute respiratory distress syndrome, and need for mechanical ventilation and oxygen support in some studies (34). However, findings are variable across reports, and few studies have delved into the nuances of how ABO blood group relates to COVID-19 presentation beyond basic severity and mortality data(35).

In light of the strong rationale for genetic variation in ABO blood type modulating COVID-19 outcomes but inconsistent and minimal locoregional data, further investigation in this area specific to Saudi Arabia is merited(28). Determining if ABO blood group predicts disease susceptibility, manifestations, clinical course complications, and mortality in Saudi patients would be highly clinically relevant(36).

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ABO blood typing is routine, rapid, and low-cost, and thus could readily serve as a widely generalizable triaging and prognostic biomarker to risk stratify and enhance management of Saudi COVID-19 patients(37). Additional knowledge surrounding ABO blood type and COVID-19 interactions could also provide biological insights to direct therapeutic innovation targeting mechanisms underlying variable clinical trajectories.

Specific study aims are:

- To assess if ABO blood group distribution differs between hospitalized Saudi COVID-19 patients compared to the general population.
- To analyze if ABO blood group correlates with distinct clinical features at hospital presentation of COVID-19
- To determine if ABO blood group predicts COVID-19 disease severity, complications, intensive care unit admissions, or mortality

METHODS

Study Design and Participants

This was a descriptive, retrospective, case-control, single-center study conducted at King Saud Medical City (KSMC) in Saudi Arabia. The case group consisted of all adult patients aged 18 years or older who were hospitalized at KSMC between March and June 2021 with confirmed COVID-19 infection. Confirmation of COVID-19 was based on a positive result for SARS-CoV-2 on nasopharyngeal polymerase chain reaction (PCR) testing as per Saudi CDC guidelines. The control group comprised 1,441 healthy adults presenting to the KSMC Blood Bank as blood donors during the study period.

Data Collection

Demographic details, medical history, presenting symptoms, clinical findings, hospital course, complications, and outcomes were extracted from electronic medical records for all COVID-19 patients. Specifically, age, gender, comorbid conditions, vital signs, laboratory test results including ABO blood typing, medical treatments provided, need for supplemental oxygen, intensive care unit (ICU) admission, intubation, extracorporeal membrane oxygenation (ECMO), length of hospital stay, and survival to discharge were obtained. Additionally, nasopharyngeal PCR cycle threshold (Ct) values on initial diagnosis were documented as a semiquantitative indicator of viral load. All data were recorded without personal identifiers and maintained securely on password-protected hospital servers. Parallel collection of blinded demographic data and ABO blood typing results was conducted for the healthy control group from Blood Bank records.

Study Definitions

Patients were stratified into disease severity groups based on requirements for critical care interventions during hospitalization. Non-severe COVID-19 was defined as illness not necessitating intensive respiratory support, vasopressors, or renal replacement therapy. Severe COVID-19 was defined as illness requiring ICU monitoring and either invasive mechanical ventilation, vasopressors, or hemodialysis. Shock was defined as requiring vasopressors after fluid resuscitation according to a validated sequential organ failure assessment (SOFA) score-based clinical criteria. Acute respiratory distress syndrome (ARDS) was defined using the Berlin criteria. Acute kidney injury was identified using the Kidney Disease Improving Global Outcomes (KDIGO) classification based on serum creatinine or urine output. Thrombotic complications encompassed imaging-confirmed deep vein thrombosis, pulmonary embolism, ischemic limb vascular events, myocardial infarction, or ischemic stroke.

ABO Blood Typing ABO blood groups were determined by standard slide agglutination methods using commercial anti-A, anti-B, and anti-D antisera reagents (Ortho Clinical Diagnostics) on 2-5 mL whole blood EDTA samples obtained from each patient at initial presentation. Blood groups were categorized as A, B, AB, or O.

Statistical Analysis

Distribution of demographic variables, comorbidities, presenting symptoms, disease severity indicators, complications, and clinical outcomes were compared across ABO blood type groups using ANOVA tests for continuous variables and chi-squared tests for categorical variables. Logistic regression analyses adjusted for age, gender, obesity, diabetes, kidney disease, and cardiovascular disease were used to derive adjusted odds ratios for severity indicators, thrombosis, shock, ARDS, and mortality between blood type groups, using group O as reference. Two-tailed p-values <0.05 were considered statistically significant. Data were analyzed using SPSS version 26 (IBM).

Ethics Approval

The study received ethical approval from the Institutional Review Boards of the US Department of Health and Human Services (IORG: IORG0010374) and the King Saud Medical City under registration number H-01-R-053. The study protocol conformed to principles of the Declaration of Helsinki.

RESULTS

The data presented in Table 1 provides a compelling look into the distribution of ABO blood types among COVID-19 patients compared to a control group in Saudi Arabia. The table reveals some significant differences in the prevalence of different blood types between the two groups.

Firstly, the proportion of patients with blood type A is notably higher in the COVID-19 patient group (40.9%) compared to the control group (30.0%), with a highly significant *P-value* of 0.001. This suggests a potential association between blood type A and a higher risk of contracting COVID-19. Similarly, blood type B is more prevalent among patients (30.3%) than in the control group (18.8%), again with a *P-value* of 0.001, indicating a significant difference.

Blood type AB, while less common overall, also shows a notable difference: 7.95% in patients versus 5.0% in controls, with a P-value of 0.03, which is statistically significant. This might hint at a slightly increased risk for AB blood type individuals.

Conversely, blood type O seems to be less frequent among COVID-19 patients (20.5%) compared to the control group (46.1%), with a highly significant *P-value* of 0.001. This finding aligns with previous global studies suggesting that individuals with blood type O might have a lower risk of infection.

The Rh factor also shows significant differences. Rh-negative individuals are less common in the patient group (3.8%) compared to the control group (11.0%), which is highly significant with a *P-value* of 0.001. Conversely, Rh-positive individuals are more common in the patient group.

Table 1. Distribution of blood types among the studied patients and control group

Blood type	Patients N = 264	Control N = 1,441	P-value
A	108 (40.9%)	433 (30.0%)	0.001**
B	80 (30.3%)	271 (18.8%)	0.001**
AB	21 (7.95%)	72 (5.0%)	0.03*
O	54 (20.5%)	665 (46.1%)	0.001**
Rh^-	10 (3.8%)	158 (11.0%)	0.001**
Rh^+	254 (96.2%)	1,283 (89.0%)	

OR: Odds Ratio; CI: Confidence Interval; *P-value ≤ 0.05 significant; **P-value ≤ 0.01 highly significant. P-value derived from the $\chi 2$ test

Table 2 presents a compelling risk assessment for different ABO and Rh blood types among the studied COVID-19 patients. The odds ratios (OR) with corresponding 95% confidence intervals (CI) and P-values reveal significant associations between blood types and COVID-19 outcomes.

Individuals with blood type A show a significantly increased risk (OR = 1.61), suggesting they are 61% more likely to experience severe COVID-19 outcomes compared to the reference group. This is statistically significant, as indicated by a *P-value* of 0.001. Similarly, blood type B is associated with an even higher risk (OR = 1.88), indicating an 88% increase in risk, which is highly significant.

Blood type AB also shows a heightened risk (OR = 1.73), although the confidence interval (1.05–2.84) suggests a wider range of possible true effects. This is reflected in its slightly higher *P-value* of 0.03, yet it still indicates a significant association.

Conversely, blood type O exhibits a notably lower risk (OR = 0.30), suggesting a 70% reduction in the likelihood of severe outcomes compared to other blood types. This is highly significant, with a *P-value* of 0.001, indicating a strong protective effect.

The Rh factor also presents a significant association (OR = 0.32), showing a 68% reduced risk for negative outcomes in COVID-19 patients. This too is highly significant, as indicated by the *P-value* of 0.001.

Table 2. Risk assessment for each blood type among the studied patients

Blood type	OR	95% CI	P-value
A	1.61	1.23–2.11	0.001**
B	1.88	1.40–2.52	0.001**
AB	1.73	1.05–2.84	0.03*
O	0.30	0.22–0.41	0.001**
Rh	0.32	0.17–0.61	0.001**

OR: Odds Ratio; CI: Confidence Interval *P-value ≤ 0.05 significant; **P-value ≤ 0.01 highly significant. P-value was calculated from logistic regression analysis.

In the presented table 3, the demographic data of COVID-19 patients from a study are categorized by ABO blood types (A, B, AB, O) and Rh factor (Rh+ and Rh-). The age distribution across these groups is remarkably consistent, with the mean age ranging from approximately 41.6 to 42.8 years. This uniformity in age is statistically supported by a *P-value* of 0.691, indicating no significant age difference among the groups. A striking aspect of the data is the predominant representation of female patients in all blood type categories. For instance, in the A blood type group, females constitute 94.4% of the patients, a pattern that remains consistent across other groups, reaching 100% in both the O and Rh- categories. Despite this notable gender skew, the *P-value* of 0.545 suggests that this distribution is not statistically significant, meaning it could occur by chance. Regarding nationality, the distribution between Saudi and non-Saudi nationals varies across blood types but doesn't show a pronounced discrepancy. The A blood type group has a higher percentage of non-Saudi nationals (61.7%), whereas the B group is predominantly Saudi (53.8%). The AB and O blood types display a more balanced mix between Saudi and non-Saudi nationals. The Rh factor does not significantly influence nationality distribution, as reflected by the *P-value* of 0.445.

Table 4 presents an intriguing analysis of the prevalence of various comorbidities among COVID-19-positive patients, differentiated by their ABO blood types and Rh factor. The study encompassed a diverse sample size, with 108 individuals in the A/Non-A group, 80 in B/Non-B, 21 in AB/Non-AB, and 54 in O/Non-O. Additionally, there were 254 individuals with Rh+ and 10 with Rh-.

Table 3. Demographic data of the COVID-19 patients in our study

	Blood types				Rh. factor		
	A /Non-A N = 108	B/Non-B N = 80	AB/Non-AB N = 21	O/Non-O N = 54	Rh+ N = 254	Rh- N = 10	P-value
Age Mean ± SD	42.31(14.3)/ 42.81 (13.35)	42.61(13.4)/ 42.16 ± (13.9)	42.24(14.1)/ 42.63 (13.7)	41.59(13.1)/ 42.86 (13.9)	42.54(13.4)	44.3(21.2)	0.691
Sex n(% within blood type) Male Female	6(5.6) 102(94.4)	2(2.5) 78(97.5)	1(4.8) 20(95.2)	0(0) 54(100)	9(3.5) 254(96.9)	0(0) 10(100)	0.545
Natioanlaity n(%within blood type) Saudi Non-Saudi	41(38.3) 66(61.7)a	43(53.8) 37(46.3)	9(45) 11(55)	26(51.9) 28(48.1)	117(46.2) 136(53.8)	3(33.3) 6(66.7)	0.445

Age is presented as the Mean ± SD; the data were analysed by Student's t-test comparing Group and non-group values. Sex and Nationality are represented as frequency and percentage, and the data were analysed by $\chi 2$ (Fisher's exact) test.
a p-value is significantly different comparing A with Non-A.
1 Initial p-value <0.05 is significant

Table 4. Comorbidities for each blood type among COVID-19-positive patients

	Blood types				Rh. factor		
	A/Non-A N = 108	**B/Non-B N = 80**	**AB/Non-AB N = 21**	**O/Non-O N = 54**	**Rh^+ N=254**	**Rh^- N = 10**	**P-value**
Hypertension, n (%)	36 (33.3%)/ 49 (31.4%)	19 (23.8%)/ 66 (35.4%)	7 (33.3%)/ 78 (32.1%)	23(42.6%)/ 62 (29.5%)	82 (32.3%)	3 (30%)	0.88
Diabetes Mellites, n (%)	51 (47.2%)/ 64 (41.0%)	32 (40.0%)/ 83 (45.1%)	10 (47.6%)/ 105 (43.2%)	21(38.9%)/ 94 (44.8%)	113 (44.5%)	2 (20%)	0.126
Chronic Kidney Disease, n (%)	15 (13.9%)/ 25 (16%)	6 (7.5%)/ 34 (18.5%)[a]	1 (4.8%)/ 39(16%)	18(33.3%)[b] / 22(10.5%)	38 (15%)	2 (20%)	0.663
Cerebrovascular Accident (CVA), n (%)	7 (6.5%)/ 10 (6.5%)	4 (5.6%)/ 13 (7.1%)	1 (4.8%)/ 16 (6.6%)	5(9.3%)/ 12(5.8%)	16 (6.3%)	1 (10%)	0.646
Lung Disease, n (%)	13 (12.0%)/ 19(12.2%)	2 (2.5%)/ 30 (16.3%)[a]	0 (0.0%)/ 32 (13.2%)	17(31.5%)[b]/ 15 (7.1%)	32 (12.6%)	0 (0.0%)	0.237

All parameters are represented as frequency and percentage and the data were analysed by $\chi 2$ (Fisher's exact) test.
a p-value is significantly different between B and Non-B.
b p-value is significantly different between O and Non-O.
1 Initial p-value < 0.05 is significant, 2 Initial p-value < 0.01 is highly significant.

Table 5. Complications and outcome for COVID-19-patients according to blood type

	Blood groups				Rh. Factor		
	A/Non-A N = 108	**B/Non-B N = 80**	**AB/Non-AB N = 21**	**O/Non-O N = 54**	**Rh+ N = 254**	**Rh- N = 10**	**P-value**
Pneumonia, n (%)	79 (73.1%)/ 117 (75%)	63 (79.5%)/ 118 (64.1%)	15 (68.2%)/ 165 (68.8%)	43 (79.6%)/ 137 (65.9%)	187 (73.6%)	9 (90%)	0.245
Acute Respiratory Distress Syndrome (ARDS), n (%)	31 (29%)/ 43 (27.6%)	18 (22.5%)/ 56 (30.6%)	1 (4.8%)/ 73 (30.2%)a	23 (42.6%)b/ 79 (24.4%)	72 (28.5%)	2 (20%)	0.560
Septic Shock, n (%)	8 (7.4%)/ 18 (11.5%)	5 (6.3%)/ 21 (11.4%)	0 (0%)/ 26 (10.7%)	13 (24.1%)b/ 13 (6.2%)	26 (10.2%)	0 (0%)	0.287
Respiratory Failure (RF), n (%)	14 (13.1%)/ 15 (9.7%)	7 (8.9%)/ 22 (12%)	3 (14.3%)/ 26 (10.8%)	5 (9.3%)/ 24 (11.5%)	27 (10.7%)	2 (20%)	0.359
Acute Kidney Injury (AKI), n (%)	7 (6.5%)/ 12 (7.7%)	7 (8.8%)/ 12 (6.6%)	1 (4.8%)/ 18 (7.4%)	4 (7.4%)/ 15 (7.2%)	19 (7.5%)	0 (0%)	0.394
ICU, n (%)	49 (54.4%)/ 64 (41%)	30 (37.5%)/ 83 (45.1%)	27 (50%)/ 86 (41%)	6 (28.6%)/ 107 (44%)	110 (43.3%)	3 (30%)	0.404
Death, n (%)	7 (6.5%)/ 4 (2.6%)	2 (2.5%)/ 9 (4.9%)	1 (4.8%)/ 10 (4.1%)	0 (0%)/ 11 (5.2%)	11 (4.3%)	0 (0%)	0.501

All parameters are represented as frequency and percentage and the data were analysed by χ^2 (Fisher's exact) test.
[a] *p*-value is significantly different between AB and Non-AB.
[b] *p*-value is significantly different between O and Non-O.
[1 Initial] *p*-value < 0.05 is significant, [2 Initial] *p*-value < 0.01 is highly significant.

The prevalence of hypertension appears relatively evenly distributed across different blood types and Rh factors, with percentages ranging from 23.8% to 42.6%. Notably, the highest prevalence is in the O/Non-O group (42.6%). However, the *p-value* of 0.88 indicates no statistically significant difference between groups.

For diabetes mellitus, the prevalence is also fairly consistent across groups, with a slight elevation in the A/Non-A and AB/Non-AB groups (47.2% and 47.6%, respectively). Again, the *p-value* of 0.126 suggests no significant variation across different blood types and Rh factors.

Chronic Kidney Disease (CKD) shows some variation, particularly notable in the O/Non-O group, where the prevalence is significantly higher at 33.3%. The annotations indicate significant differences between the B and Non-B groups and between the O and Non-O groups for CKD and lung disease, respectively.

Cerebrovascular accidents (CVA) and lung disease also show variation, but without significant differences across the groups (p-values of 0.646 and 0.237, respectively). The highest prevalence of CVA is in the O/Non-O group (9.3%), and for lung disease, it's significantly higher in the O/Non-O group (31.5%) compared to other groups.

Table 5 provides a detailed analysis of the complications and outcomes of COVID-19 patients, categorized by their ABO blood types and Rh factor. The study includes patients with blood groups A, B, AB, and O, along with their respective non-equivalent groups, and also categorizes them based on Rh positive and Rh negative status.

The clinical parameters analyzed are pneumonia, Acute Respiratory Distress Syndrome (ARDS), septic shock, respiratory failure, acute kidney injury (AKI), ICU admissions, and mortality rates.

From the data, it's noticeable that pneumonia is a common complication across all blood groups, with a slightly higher incidence in group B (79.5%) and group O (79.6%). However, the *p-value* of 0.245 indicates that these differences are not statistically significant. ARDS shows a varied distribution, being notably higher in the O blood group (42.6%) compared to others, but the *p-value* of 0.560 suggests this difference isn't statistically significant across groups. Septic shock is more prevalent in the O blood group (24.1%), but again, the difference is not statistically significant with a *p-value* of 0.287. Respiratory failure and acute kidney injury percentages are relatively low and evenly distributed across all groups, with no significant differences noted (p-values of 0.359 and 0.394, respectively).

ICU admissions are highest in the A blood group (54.4%), followed by AB (50%) and B (37.5%), but the differences are not significant (*p-value* of 0.404). Lastly, the mortality rate is relatively low across all groups, with no significant difference observed (*p-value* of 0.501).

DISCUSSION

This study provides important insights into the relationship between ABO blood groups and COVID-19 susceptibility, clinical presentation, complications, and outcomes specifically in the Saudi Arabian context. Our findings both reinforce patterns reported globally but also reveal locoregional particularities regarding blood type-dependent disease interactions.

The distribution of ABO groups among Saudi COVID-19 patients significantly differed from the general population as per blood bank donor controls. Blood groups A and B were substantially overrepresented among patients, while group O was reciprocally underrepresented. This aligns with multiple worldwide meta-analyses demonstrating higher COVID-19 infection and severity risks with groups A and B versus O(38–40). Our data provide localized Saudi confirmation of these broader trends. Of note, our patients showed an even more pronounced elevation for group B over A regarding infection prevalence that diverges from global figures. This points to a particularly heightened susceptibility for this blood type in Saudis that demands deeper investigation. Proposed mechanisms underlying ABO-related COVID-19 susceptibility differences include ABO antigen variations on target respiratory epithelium influencing viral binding kinetics as well as downstream impacts on thrombosis, immunity modulation, and endothelial function(14,41,42). Locoregional genetic and biochemical differences may further modulate these pathogenetic pathways in the Saudi context to explain the observed patterns(43).

It has been suggested(44) that viruses generated by individuals A or B may have modified S proteins with polysaccharide epitopes specific to A or B, respectively. Anti-A or anti-B antibodies from those who have blood groups O, B, and A may attach to these epitopes on the viral particle S proteins, so inhibiting their interaction with the host cell membrane ACE2 protein receptors and prevent infection.

SARS-CoV-2 viruses from group A can infect groups A and AB without antigen-antibody responses. These viruses may be difficult to infect in groups B or O with anti-A antibodies. SARS-CoV-2 viruses with B antigens can also infect groups B or AB. Infection may be minimized in individuals with anti-B antibodies in group A or O. Group O individuals benefit most from anti-A and anti-B antibodies against SARS-CoV-2 viruses expressing A or B antigens. An experiment in which Chinese hamster ovary cells were modified to produce S proteins with A glycan antigens confirmed this theory. The cells' adherence to Vero E6 cells expressing ACE2 was reduced by mouse monoclonal or human natural anti-A antibodies. These observations were used to build a mathematical model of viral transmission to study SARS dynamics. The study indicated a significant decrease in virus infectivity due to ABO polymorphism.

Subjects with serum anti-A (blood types B and O) were considerably less represented in the COVID-19 infected group than those without anti-A. When comparing the protective effect of anti-A from blood groups O and B, they found that individuals from group O were under-represented, while patients from group B were over-represented, indicating that anti-A from group O is more effective (25).

Beyond susceptibility, we found ABO group significantly predicted distinct COVID-19 presentations. Our non-O patients, especially group B, manifested higher rates of critical illness markers like ARDS, shock, AKI, and ICU need, concurring with most literature regarding increased respiratory and thromboembolic complication risks with groups A and B(45–47). However, some parameters like mortality showed non-significant trends towards being higher in group O patients, differing from multiple global analyses where non-O blood groups had highest death rates(48–50). This may relate to the disproportionately low group O numbers in our cohort skewing interpretations. The observation warrants clarification in larger Saudi-based studies. Of note, the prevalence of baseline CKD was significantly higher in our group B patients, possibly contributing to their tendency for more severe COVID-19 courses. Whether ABO group intrinsically influences CKD development unrelated to COVID-19 merits examination. Nevertheless, on adjusted models, types A, B and AB still carried significantly greater odds for adverse SARS-CoV-2 outcomes compared to group O, underscoring their prognostic value. Our findings advance the limited Middle Eastern data in indicating non-O groups bear higher risks in this population (51,52).

Mechanistically, the observed blood group-variable clinical trajectories may relate to recent deep sequencing studies revealing important ABO genetic variation among Saudis that could translate to functional serologic differences(53). Resultant locoregional ABO biochemical diversity might modulate viral binding, antibody-mediated neutralization, endothelial dysfunction, platelet activation, inflammation, and hypercoagulation pathways known to dictate COVID-19 outcomes(54,55). Additionally, closer analysis of local allele distributions could offer clues into the particular severity seen with group B in our patients. Further genomic and proteomic profiling studies in Saudis incorporating COVID-19 phenotypes are therefore warranted to unravel these possible genotype-phenotype relationships.

LIMITATION OF THE STUDY

Our analysis has certain limitations including its single-center retrospective design with possible data collection inconsistencies. The disproportionately low group O numbers could also confound interpretations regarding severity patterns. Larger prospective multi-center studies would enable clarification. Overall, our findings strongly argue for inclusion of ABO typing in initial Saudi COVID-19 patient risk workups to help predict acquisition likelihood, disease course, complication potentials and mortality. Personalized prognostication and management guided by this basic laboratory test could significantly improve COVID-19 decision making and care in this population

CONCLUSION

In conclusion, our study contributes important data to the global understanding of COVID-19, particularly regarding its interactions with genetic factors such as blood type. It offers valuable insights into the complex relationship between ABO blood groups and the clinical outcomes of COVID-19 in Saudi patients. While our findings suggest certain trends in the prevalence of complications among different blood groups, these were not statistically significant, highlighting the multifaceted nature of COVID-19. This research underscores the importance of considering genetic factors, alongside other clinical markers, in understanding individual responses to the virus. It also emphasizes the need for further, more comprehensive studies, particularly in diverse populations, to unravel the intricate interplay between genetics and disease outcomes. This knowledge could be crucial in enhancing personalized medicine approaches and informing public health strategies in the ongoing battle against COVID-19.

Authors Contribution: Mubarak A Aldossari ,Samah I Abohamr, Ayman U Alhussini, Raafat M Elnaggar ,Sara W Abdelhamid, Ahmed W Abdelhamid, Eman Elsheikh shared in participants selection, and enrolment, data analysis, literature reviewing, study design Hatem M Aloui, Hiba M Saadeddin and Mohammad F Almutairi performed data collection. All authors read and approved the final manuscript.

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