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ABO Blood Group and RhD Antigen Relationship to COVID-19 Infections in Duhok-Iraq: A Retrospective Study

Authors Mervan Yousif Huseyin

Affiliation *Medical Microbiology Department, Health Sciences College, Cihan University-Duhok, Iraq*

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Abstract

Background: Since the World Health Organization declared the Coronavirus a pandemic, various studies have suggested that blood group antigens might influence COVID-19 infection susceptibility. This research aims to assess the relationship between the ABO blood group system, RhD factors, and COVID-19 infection symptoms, considering age and gender variables in Duhok province, Iraq.

Method: This retrospective study analyzed data from 578 individuals who attended several hospitals and medical centers in Duhok province from September 2023 to February 2024. The cohort comprised 308 males and 270 females.

Results: The distribution of blood groups A, B, AB, and O among the participants was 22.1%, 26.3%, 18.5%, and 33.1% respectively. Blood type O was predominant in mild and severe COVID-19 cases. Statistical analysis revealed no significant differences ($p > 0.05$) between the observed and expected frequencies of blood groups and RhD antigens. However, significant differences ($p < 0.01$) were found in the age distribution of COVID-19 symptom severity between the genders, indicating varying symptomatology across different age groups. The comparison between genders did not show significant differences in age distribution ($p > 0.05$).

Conclusion: The study concludes that there are no statistically significant associations between the ABO and RhD antigen groups with the frequency of COVID-19 infections. However, age appears to play a critical role in the severity of symptoms, with significant variations noted between different age groups within both sexes. Further research is recommended to explore these variations' mechanisms and assess potential vulnerabilities among specific demographic groups.

What is already known about the topic?

- Since the onset of the COVID-19 pandemic, researchers have investigated potential biological factors influencing susceptibility and severity, including the role of blood group antigens.
- Some studies suggest that individuals with blood type O may have a lower risk of infection or severe symptoms. In contrast, blood type A has been associated with a higher susceptibility to severe COVID-19 outcomes.

*** Corresponding author.**
Mervan Yousif Huseyin
E-mail address: mervan.huseyin@duhokcihan.edu.krd

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Authors, 2024, College of Nursing, University of Mosul.

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Introduction

Coronavirus disease 2019 (COVID-19), first detected in Wuhan, China, was declared a global pandemic by the World Health Organization in March 2020 (Adhiah et al., 2022; Sahu et al., 2020). COVID-19 infections present a range of clinical manifestations, from asymptomatic carriers to critically ill patients exhibiting severe symptoms (Pereira et al., 2022). Hospitalized patients, especially those in intensive care units, have experienced significant morbidity and mortality, characterized by acute kidney injury, the need for inpatient dialysis, prolonged intubation, and a bimodal distribution of time from symptom onset to intubation (Agenziano et al., 2020). The pandemic has spurred numerous studies worldwide exploring various facets of the disease, including the severe respiratory distress associated with a cytokine storm (Huang et al., 2020) and an inverse correlation between vitamin D levels and SARS-CoV-2 infection rates (Padhi et al., 2020). Research has also examined the relationship between ABO and Rh blood groups and the risk of SARS-CoV-2 infection and severity in both adults and children (Ray et al., 2021), as well as the incidence of complicated appendicitis during the pandemic at Jordan University Hospital (Amarin et al., 2024). Studies have identified diabetes mellitus and chronic diseases as significant predictors of mortality among hospitalized COVID-19 patients (Hwaiz et al., 2022). Recent global data indicates over 160 million confirmed cases, with the majority presenting mild-to-moderate symptoms; however, approximately 10%-15% of cases progress to severe illness, and 5% become critically ill (Aiyegbusi et al., 2021). Additionally, epidemiological evidence suggests that females with blood type A may be more susceptible to COVID-19 (Fan et al., 2020). Given the emerging evidence linking the ABO blood group, D-dimer, CRP, and ferritin levels with COVID-19 severity, progression, and susceptibility (Zyara et al., 2023), further regional studies are essential due to the complex interplay of factors influencing COVID-19 outcomes.

Aim

This research project aims to investigate the relationship between the ABO and RhD blood group systems and the presentation of symptomatic and asymptomatic COVID-19 infections across different ages and genders in the Duhok province of Iraq.

Methods

Study Design and Participants This cross-sectional study was conducted from September 2023 to February 2024 and included 578 participants. Individuals were recruited from several hospitals and medical centers across Duhok province, Iraq. Participants of various ages and genders who presented with symptomatic or asymptomatic COVID-19 were included in the study. The inclusion criteria were confirmed COVID-19 diagnosis via PCR testing. Exclusion criteria included individuals who declined to participate or had incomplete medical records.

Data Collection Data were collected using structured questionnaires administered by trained healthcare professionals. The questionnaires gathered detailed information on demographic characteristics (age, gender), medical history, symptoms of COVID-19 at the time of testing, and known blood group type (ABO and RhD factors).

Statistical Analysis The data were analyzed using the SPSS software version 2019 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarize the participants' demographic variables and clinical characteristics. Frequencies and percentages were used to describe categorical variables, while means and standard deviations were calculated for continuous variables.

The Chi-square test was used for inferential statistics to examine the association between categorical variables such as blood group type and COVID-19 symptoms. Independent t-tests were conducted to compare means of continuous variables between two groups (symptomatic vs. asymptomatic). One-way ANOVA was performed to analyze differences among more than two groups. Subsequently, pairwise comparisons were conducted using Duncan’s Multiple Range Test (Duncan, 1955) to determine significant differences between means.

Additionally, Spearman’s correlation coefficients were calculated to assess the strength and direction of association between age, gender, and other key study variables with the severity of COVID-19 symptoms.

Ethical Considerations This study was approved by the local ethics committee of Duhok Medical University, and informed consent was obtained from all participants. All procedures followed were according to the ethical standards of the committee responsible for human experimentation and the Helsinki Declaration of 1975, revised in 2000.

Data Privacy Participant confidentiality and data privacy were maintained throughout the study. Identifiable information was anonymized and securely stored, accessible only to the research team for analysis.

Results

Five hundred seventy-eight participants were enrolled in this study, including 308 males and 270 females, with ages ranging from under 20 to over 60. This distribution is detailed in Table 1.

Symptom Severity Across Age and Gender Figures 1 and 2 depict the distribution of COVID-19 cases by severity across different age groups for both genders. Notably, severe cases were predominantly higher among older age groups (>61 years), whereas mild cases were more common in younger age groups across both sexes.

Blood Group Distribution and Association with COVID-19 Severity Table 2 presents the distribution of ABO blood groups and RhD antigens among the participants. The blood groups were represented as follows: Type A (22.1%), Type B (26.3%), Type AB (18.5%), and Type O (33.1%). Among these, Type O+ had the highest frequency of severe cases (27%), followed by Type A+ (18.3%). The distribution of Rh-positive cases was higher in both mild (67.5%) and severe (70.6%) cases compared to Rh-negative cases.

Statistical analysis revealed no significant differences in the frequency of blood groups or RhD antigen between simple and severe cases ($p > 0.05$), suggesting that neither the ABO blood group nor RhD antigen significantly impacts COVID-19 symptom severity. These findings are illustrated in Figure 3, where the Chi-square test indicated no significant differences across all blood groups ($p > 0.05$).

Symptom Severity According to Age and Gender Table 3 shows the proportions of mild and severe cases categorized by age and gender. The rate of severe infection increased significantly with age in both males and females. Specifically, severe infections in males over 61 years were 67.3%, significantly higher than in younger age groups (9.8% in 21-40 years and 18.6% in 41-60 years). Females showed a similar trend, with severe cases at 53.7% in those over 61, compared to 10.4% and 11.1% in the younger age brackets. The observed significant difference ($p < 0.01$) confirms that age is critical to COVID-19 severity.

Blood Group Distribution Across Age Categories Further analysis was conducted to explore the distribution of blood groups across different age categories (Table 7). The

results showed no significant differences ($p > 0.05$) between observed and expected frequencies of blood groups among the age categories, indicating an even distribution of blood groups across ages in the study population.

Association Between Variables A Spearman correlation analysis was performed to ascertain the relationships between the study variables (Table 8). The correlation between age and symptom severity was significant ($r = 0.33$, $p < 0.01$), suggesting that age predicts COVID-19 severity. However, correlations between other variables, such as blood group and symptom severity, were not statistically significant ($p > 0.05$), reinforcing the findings that blood type does not influence the severity of COVID-19 symptoms.

The results underscore the influence of age on COVID-19 severity, with older individuals experiencing more severe symptoms. However, ABO blood groups and RhD antigens do not appear to have a significant impact on the course of the disease. This study contributes to understanding demographic factors in COVID-19 severity and supports the need for targeted interventions in older populations.

Table 1. The overall frequency and percent of infected COVID-19 cases according to the gender and age category.

Factors		Frequency	Percent	Valid Percent	Cumulative Percent
Gender	Male	308	53.3	53.3	53.3
	Female	270	46.7	46.7	100.0
	Total	578	100.0	100.0	
Age Category	<20	83	14.4	14.4	14.4
	21-40	219	37.9	37.9	52.2
	41-60	167	28.9	28.9	81.1
	>61	109	18.9	18.9	100.0
	Total	578	100.0	100.0	

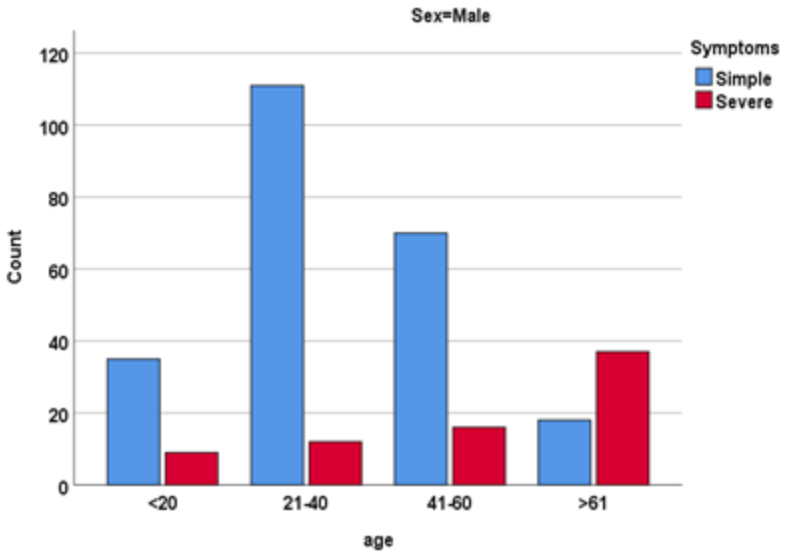

Figure 1. The distribution of symptoms among males from different age groups

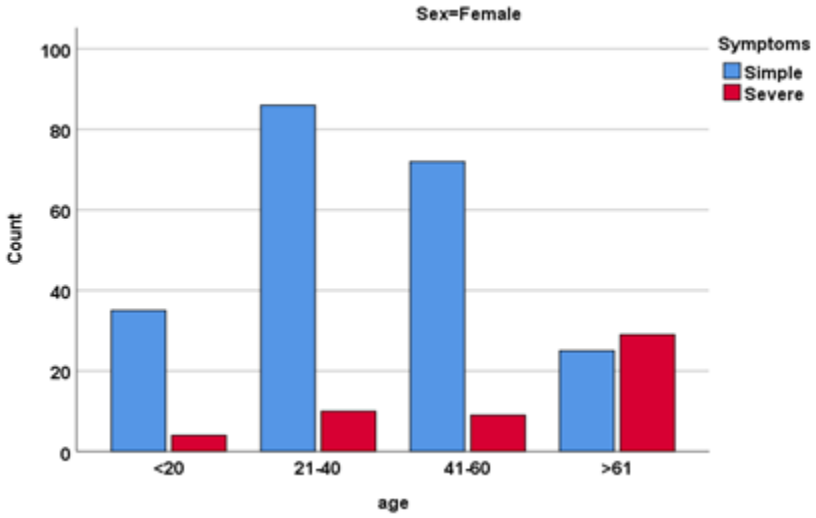

Figure 2. The distribution of symptoms among females with different age groups.

Table 2. The distribution of blood groups among infected individuals according to their symptoms.

	Symptoms no (%)			
	Simple	**Severe**	**Total**	**P value**
	n=452	**n=126**	**n=578**	
Blood group				0.525
A+	62 (13.7)	23 (18.3)	85 (14.7)	
A-	32 (7.1)	11 (8.7)	43 (7.4)	
B+	85 (18.8)	18 (14.3)	103 (17.8)	
B-	37 (8.2)	12 (9.5)	49 (8.5)	
AB+	54 (11.9)	14 (11.1)	68 (11.8)	
AB-	33 (7.3)	6 (4.8)	39 (6.7)	
O+	104 (23)	34 (27)	138 (23.9)	
O-	45 (10)	8 (6.3)	53 (9.2)	
RhD antigen				
Positive	305 (67.5)	89 (70.6)	394 (68.2)	0.453
Negative	147 (32.5)	37 (29.4)	184 (31.8)	

The Chi-square test was performed.

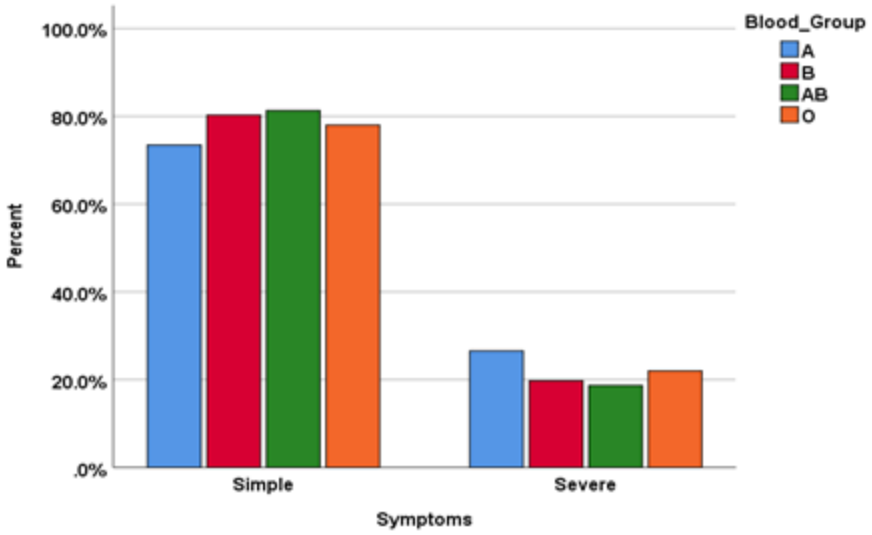

Figure 3. The distribution of blood groups among infected individuals according to their symptoms.

Table 3. Comparisons of age categories' frequency and proportion within gender between simple and severe symptoms of the infected people.

		Symptoms no (%)		
Sex	Age	Simple	Severe	**P value**
Male	<20	35 (79.5)	9 (20.5)	0.0001
	21-40	111 (90.2)	12 (9.8)	
	41-60	70 (81.4)	16 (18.6)	
	>61	18 (32.7)	37 (67.3)	
Female	<20	35 (89.7)	4 (10.3)	0.0001
	21-40	86 (89.6)	10 (10.4)	
	41-60	72 (88.9)	9 (11.1)	
	>61	25 (46.3)	29 (53.7)	
Total	<20	70 (84.3)	13 (15.7)	0.0001
	21-40	197 (90)	22 (10)	
(for both	41-60	142 (85)	25 (15)	
sexes)	>61	43 (39.4)	66 (60.6)	
	Total	452 (78.2)	126 (21.8)	

The Chi-square test was performed.

Table 4. Comparison among A, B, AB, and O blood groups for simple and severe symptoms.

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	2.693[a]	3	.441
Likelihood Ratio	2.645	3	.450
Linear-by-Linear Association	.572	1	.449
N of Valid Cases	578		
a. 0 cells (0.0%) have an expected count of less than 5. The minimum expected count is 23.33.			

Table 5. Comparison between both symptoms cases for age and gender of the studied sample

Variable	Simple (n= 452)	Severe (n= 126)	P value
Age (years) *a*	38.44 **b** ± 17.131	55.57 **a** ± 21.725	0.0001
Male *b*	(234). (76.0 %)	74 (24.0 %)	0.166
Female *b*	218 (80.7 %)	52 (19.3 %)	
	Male (n= 308)	Female (n= 270)	P value
Age (years) *a*	41.25 ± 19.65	43.23 ± 19.40	0.225

A *student t-test and a b Chi-square test were performed, and p < 0.05 = significant.*

Table 6. **Comparison among blood groups for age of sample cases**

Descriptive statistics for Age variable (years)									
Blood Group	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	P value
					Lower Bound	Upper Bound			
A	128	43.3594	19.73156	1.74404	39.9082	46.8105	10.00	88.00	0.527
B	152	42.2368	20.07824	1.62856	39.0191	45.4545	11.00	90.00	
AB	107	43.5047	20.13088	1.94613	39.6463	47.3631	13.00	89.00	
O	191	40.5864	18.65847	1.35008	37.9233	43.2495	11.00	89.00	
Total	578	42.1747	19.53858	.81270	40.5785	43.7709	10.00	90.00	

One-way ANOVA was performed; P<0.05 = significant.

Table 7. Comparison among age categories based on blood groups

Blood group	Age category no (%)					P value
	=<20	**21-40**	**41-60**	**>61**	**Total**	
	n= 83	**n= 219**	**n= 167**	**n= 109**	**n=578**	
A	18 (14.10)	42 (32.8)	44 (34.4)	24 (18.8)	128 (100)	0.69
B	25 (16.4)	54 (35.5)	43 (28.3)	30 (19.7)	152 (100)	
AB	15 (14.0)	39 (36.4)	30 (28.0)	23 (21.5)	107 (100)	
O	25 (13.1)	84 (44.0)	50 (26.2)	32 (16.8)	191 (100)	

A chi-square test was performed for this analysis.

Table 8. Correlation coefficients between the studied parameters (variables)

		Age Category	**Gender**	**RhD antigen**	**Symptoms**	**Blood Group**
Spearman's rho	Age Category	1.000	.034	.084	.33**	-.043
	Gender	.034	1.000	.067	-.058	.006
	RhD antigen	.084	.067	1.000	-.028	-.043
	Symptoms	.330**	-.058	-.028	1.000	-.031
	Blood Group	-.043	.006	-.043	-.031	1.000

. Correlation is significant at the 0.05 level (2-tailed).

****. Correlation is significant at the 0.01 level (2-tailed).***

Discussion

Since the coronavirus disease (COVID-19) started in 2019, rapidly regarded as a pandemic by the World Health Organization WHO after spreading over the world (Natarajan et al., 2023). The A, B antigen-encoding gene is located on chromosome 9q34.1–34.2, and there are four genetic phenotypes (A, B, O, and AB blood types) (Wu et al., 2020). The blood groups system referred to as ABO is very frequently investigated within the scope of medical treatment and extensively studied erythrocyte antigen system and is also known to be the most easily accessible factor that is present in an individual's genome (Hama et al., 2023). Blood group antigens can play a direct role in infection by serving as receptors and/ or coreceptors for microorganisms, parasites, and viruses (Wu et al., 2020; Nalbant *et al.,* 2021; Behal et al., 2010; Chakrani et al., 2018). Differences in blood group antigen expression can increase or decrease host susceptibility to many infections, such as Rotaviral gastroenteritis, Hepatitis B virus, cardiovascular diseases,

and Digestive system and vein diseases [(Groot et al., 2020; Jing et al., 2020; Al-amiri et al., 2022; Jiang et al., 2024). Some recent research suggested that ABO groups and Rh factors may play a role in susceptibility to Covid-19, particularly A and O (Deleers et al., 2021; Omer et al., 2022; Adhiah et al., 2022). Furthermore, COVID-19 continues to evolve with global health implications, and the world is racing to learn more about transmission, evolution, and sequelae (Narayanan et al., 2024). Also, there have been few studies investigating the association between the ABO System and Rh factors and susceptibility to Covid-19 in Iraq and the Middle East. Hence this study aimed to assess and identify the relationship between the ABO system and RhD factors with symptomatic and non-symptomatic COVID-19 infections with age and gender in Duhok province -Iraq.

Although Soares et al. (2023) and other studies suggested that blood group A may be a risk factor for COVID-19 infection and that blood group O may have a lower risk, in the current study, it could be observed that the frequency of type O was higher than that of other types in both simple and severe cases. This may be due to the fact that participants with type O had a higher rate of infection than those with A, B, or AB types.

This study showed that there are statistically significant differences among blood groups and also the RhD antigen group ($p>0.05$) between observed and expected frequencies; on the other hand, this study found that the observed and expected proportions are significantly different ($p<0.01$) for simple and severe cases for age categories within both sexes; in addition, the total observations in an average of both sexes also, differed significantly ($p<0.01$). These results ensure that the symptoms may differ between males and females and according to the age of infected people. In the same way, in the study of Amin et al. (2021), there was a significant difference between symptoms in males and females where the infection rate was higher in males than in females and also suggested that the hospitalizing rate increased for older patients (>40 years). Our results illustrate a highly significant difference ($p<0.01$) between simple and severe symptoms based on the age of participants, where the higher ages recorded severe symptom cases. While comparing both genders, there was no significant difference ($p>0.05$) between male and female ages. Similarly, the results of Omer et al. (2022) showed that there were no significant differences in ABO and RhD antigen distributions between the COVID-19 cases and non-COVID controls. Also, no ABO group was associated with the risk of hospitalization as a marker of the severity of infection. Also, Hama et al. (2023) found

that there was no significant difference in COVID-19 severity for ABO blood groups A, O, B, and AB. However, the results of Adhiah et al. (2020) indicated that blood group A may be associated with an increased risk of developing COVID-19, particularly in males. Besides this study, Wu et al. (2020) found that the patients with blood group A had an increased risk for infection with SARS-CoV-2, whereas blood group O was associated with a decreased risk. Additionally, it was found that blood group A was associated with an increased risk of infection. In contrast, group O was associated with a decreased risk (Zhao et al., 2021). Again, the most frequently seen blood type among COVID-19 patients was A+, and the Rh+ blood group was found in all cases admitted to the intensive care unit (Yaylaci et al., 2020). Likewise, the study of Mustafa et al. (2023) concluded that the decreased susceptibility of individuals with blood group O and the increased susceptibility of individuals with blood group A to COVID-19 could be linked to the presence of natural anti-blood group antibodies, particularly anti-A antibodies, in the blood. Further, Blood group A positivity was frequent (40%) in severe COVID-19 disease, and the positive blood group was frequent in moderate COVID-19 disease (34.62%) (Thakkar et al., 2024). Also, A, B, and Rh+ are found to be more susceptible to COVID-19 infection. In contrast, blood groups O, AB, and Rh- are at a lower risk of COVID-19 infection, and no association was found between blood groups and susceptibility to severity of disease and mortality (Rana et al., 2021). Conversely, the study of Al-amiri et al. (2022) showed that patients with blood group O had a higher risk of COVID-19 infection, although having milder cases, those with blood group O present more frequently with cough and fever, while patients with blood group AB do not experience any severe cases. Zyara et al. (2023) found that the frequencies of blood types A, B, AB, and O were 25.33, 38.00, 31.33, and 5.33%, respectively, and proved that age is an important factor in the COVID-19 infection's development.

Furthermore, according to Talukder et al. 2022, fever (88.47%) was the most prevalent symptom among the patients, followed by cough (64.65%). Meanwhile, significant differences were observed. Thus, the consequence is that the evidence illustrates that these differences among human beings may be due to genetic factors, the variety of proteins in the blood, or other reasons that have not been known yet. Therefore this research suggests doing more studies on the relationships between the ABO blood group and Covid-19 diseases and other infections.

Conclusion

In conclusion, this study found that the observed and expected proportions are significantly different ($p<0.01$) for simple and severe cases of COVID-19 for age categories within both sexes. In addition, there are no significant differences ($p>0.05$) among the blood groups for infections.

Conflict of interest

I declare that there are NO conflicts of interest

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Funding: This research received no external funding.

Institutional Review Board Statement: This study was approved by the local ethics committee of Duhok Medical University, and informed consent was obtained from all participants. All procedures followed were according to the ethical standards of the committee responsible for human experimentation and the Helsinki Declaration of 1975, revised in 2000.

Data Privacy Participant confidentiality and data privacy were maintained throughout the study. Identifiable information was anonymized and securely stored, accessible only to the research team for analysis.

Informed Consent Statement**:** Not applicable.

Data Availability Statement: Available from the corresponding author upon reasonable request.

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