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The Correlation between ABO Blood Groups and the IFN-Γ Levels in COVID 19 Infected Patients

MSc. Oday Jawad Jasim, Dr. Wisam Basim Al-Tmemy,
BSc. Marwa sadiq Husain Meshary
Department of Medical Laboratory Technologies, AL KUT University College, Wasit, Iraq

Abstract: This investigation was conducted in the Iraqi province of Wasit in collaboration with the microbiology units of Fairouz Hospital and Alzahraa Hospital. This study's objectives were to assess interferon (IFN)-γ serum levels and this cytokine's protective role based on the ABO blood types among SARS-CoV-2 infected individuals. Samples were gathered in the province of Wasit from various locations. It had 22 healthy individuals as a control group and 66 blood samples from Iraqi patients suffering with COVID-19. The study was carried out between January and April of 2024, with both groups' ages ranging from 14 to 72. There were three patient classifications: mild (22 patients), moderate (22 patients), and severe (22 patients). All participants' serum samples were taken, and ELISA (enzyme-linked immunosorbent assay) was used to measure the levels of cytokines using monoclonal antibodies (Anti-A, B, and D). All of these tools are easily accessible in a blood test tool set. (AntiSera ABD Blood Grouping Reagent BIOLAB-India). The ANOVA test shows that mean level was statistically not significant difference(p-value 0.649) for concentration of interferon gamma according to the blood groups.

Keywords: SARS-CoV-2, Respiratory Coronavirus, blood groups, Interferon gamma.

Introduction

A number of pneumonia cases with an unclear cause surfaced in Wuhan, Hubei, China in December 2019. The new betacoronavirus known as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) was identified as the cause of these infections (1). The virus known as SARS-CoV-2 is the cause of the severe respiratory illness known as coronavirus disease 19 (COVID-19), which the World Health Organization (WHO) proclaimed to be a pandemic on March 11, 2020. (2,3,4).Genomic sequencing of viral isolates from five pneumonia patients admitted between December 18 and December 29, 2019, identified the presence of a hitherto unidentified CoV2 strain in those patients (5). The majority of countries in the world are currently affected by COVID-19. As of June 1, 2020, there were more than 6.1 million confirmed cases of COVID-19 worldwide. In China, the virus has caused serious illness in about 16–21% of cases, with a 2–3% fatality rate. According to the most recent estimates, the average number of individuals to whom an infected person will spread the virus in a community that is fully immune is approximately 3.77 (6). Based on the source of the first COVID-19 case, it is highly probable that the virus was transmitted from animal to human (7). The genus Coronavirus includes coronaviruses (CoV), which are members of the family Coronaviridae. Contagious viruses (CoVs) are pleomorphic RNA viruses that have unique crown-shaped peplomers that range in size from 80 to 160 nM and a 27–32 kb genomic size (8).Consequently, enclosed (CoV) viruses are some of the largest known RNA viruses.

Coronaviruses can infect a variety of hosts, such as humans and other animals. They can also cause dangerous diseases in domesticated animals, such as upper respiratory tract infections in humans (9). Numerous studies, ranging from epidemiological to experimental, have been published on COVID-19 patients in an effort to better understand the immunological mechanisms of the virus and potential therapeutic options. CD3+,CD4+, and CD8+ lymphocytes count are usually decreased according to disease stages (10). Besides it, cytokine storm is also present in severe patients due to elevation of interleukins such as TNF-α, IL-6, IL-8, and IL-10 (11,12). Thus, the differences among host immune responses play a major role in COVID-19 severity.

The A and B antigens and the antibodies that match them make up the majority of the ABO blood group system. A gene that codes for an antigen can be found on chromosome 9q34.1–34.2. There are four genetic phenotypes (A, B, O, and AB blood types) that are made up of the A, B, and O alleles (13). Host susceptibility to several illnesses can be increased or decreased by variations in blood group antigen expression. Through their roles as receptors and/or co-receptors for microbes, parasites, and viruses, blood type antigens can directly contribute to infection. In addition, numerous blood type antigens use the structure of membrane micro-domains to aid intracellular absorption, signal transduction, or cell adhesion. Blood group antigens can alter the body's natural defenses against illness (14). Since the start of the SARS-CoV-2 epidemic, several studies have been done on this topic. The blood group O was less common in severe COVID-19 patients who needed prolonged hospitalization and the blood group A was much more prevalent in individuals with symptomatic COVID-19 infections in comparison to the general population, according to a research on 265 COVID-19 patients (15). Additionally, two investigations have shown that blood type O may have some protective properties (16).

Materials and Methods:

Samples collection

This study was conducted in the Wasit provincial cities of Alzahraa Hospital and Fairouz Hospital. 88 blood samples were drawn for this investigation from different locations across the province of Wasit between January and April of 2024. Blood samples from COVID-19 patients who visited Fairouz and Alzahraa Hospitals as well as a few private labs were obtained. The current study has been approved by the local ethics council at the scientific research ministry of health, higher education, and scientific research in Iraq. All patients who participated in the study were previously told of its purpose and provided their agreement by signing a consent form. Prior to the blood sample, each patient's name, age, gender, smoking status, and family history were collected.disease duration and the type of therapy regime. The serum was separated into aliquots in Eppendorf tubes and kept in the freezer at -80°C. The serum levels (IFN-γ) in the samples were measured by Enzyme Linked Immunosorbent Assay (ELISA) using The Kits From (CUSABIO, CHINA) at a wavelength of 450 nm. All blood samples were placed in a cool-box under aseptic conditions.

Study Groups

Eighty-eight individuals, both men and women, participated in the study in total. The study groups comprised the following:

Group 1: sixty-six individuals who have COVID-19 Their samples were taken from Fairouz Hospital and al Zahraa Teaching Hospital, and they were diagnosed using (R T-PCR). Their files contained the clinical data that was gathered.

Group 2: Twenty-two individuals who appeared to be in good health were assigned to the control group.

Statistical analysis

Version 26 of the statistical package for social sciences (SPSS) software was used to enter, code, and analyze data. Several tests were used to analyze the data. The categorical variables were described using frequency and percentages. The continuous variables were described using the mean and standard deviation. The evaluation of the relationship between categorical variables involved the use of both Fisher's exact test and Chi-square analysis. Regarding the variations in means among continuous variables, The appropriate tests were the independent sample t-test, one-way ANOVA, two-way ANOVA, and Mann-Whitney test. To determine whether correlation exists between variables that are not regularly distributed, the Spearman correlation coefficient was employed. P-values of 0.05 or less were regarded as significant. The graphical display of the data also made use of pie and bar charts.

Results and Discussion

For this study, 88 participants were included in order to evaluate the impact of IFN-γ on the severity of COVID-19 infection. Twenty-two of the subjects had negative RT-PCR results (mean no COVID-19). The remaining 66 individuals who tested positive for the PCR were split into three equal groups, totaling 22, and were categorized as severe, moderate, and mild instances. Of the 88 participants in the study, the mean age and standard deviation (SD) were 49.55±17.11 years (lowest age = 14 and maximum age = 72 years old).

Additional sociodemographic characteristics provided by the respondents were displayed in (Table 1). The majority of them (83%) lived in cities, and more than half of them (53.4%) were female. A+ (33%) was the most common blood group in the sample, followed by O+ (29.5%). Of the 66 COVID-19 patients who were chosen, 42 (63.6%) were receiving steroid treatment, and only 18 (27.3%) were receiving Remdesivir, an antiviral medication. Five individuals (7.6%) experienced a subsequent bacterial illness. Out of the COVID-19 patients, only 4 (6.1%) died (table 2). Regarding age and sex distribution, there was no discernible difference between the patient and control groups. (Table 1) displays sociodemographic characteristics, while (Table 2)displays the frequency distribution of patients' COVID-19 disease history.

(Table1): Frequency distribution of the sociodemographic features of 88 participants.

Variables	Categories	Frequency	Percent
Gender	Female	47	53.4%
	Male	41	46.6%
Place of living	Rural	15	17.0%
	Urban	73	83.0%
Smoking status	Non-smoker	70	79.5%
	Smoker	18	20.5%
Job-status	Governmental	23	26.1%
	Self-employer	23	26.1%
	Housewife	37	42.0%
	Retired	4	4.5%
	Student	1	1.1%
COVID-19 vaccination	Non-vaccinated	76	86.4%
	Vaccinated	12	13.6%
Blood group	AB+	10	11.4%
	AB-	2	2.3%
	A+	29	33.0%
	A-	1	1.1%
	B+	18	20.5%
	B-	2	2.3%
	O+	26	29.5%

(Table 2): Frequency distributions of COVID-19 disease history among 66 infected patients.

Variables	Categories	Frequency	Percent
COVID-19 disease severity	Severe Moderate Mild	22 22 22	33.3% 33.3% 33.3%
Steroid drugs	No steroid Steroid	24 42	36.4% 63.6%
Antiviral drugs	No-remdesivir Remdesivir	48 18	72.7% 27.3%
Secondary bacterial growth	No bacterial growth Bacterial growth	61 5	92.4% 7.6%
Disease outcome	Cure Death	62 4	93.9% 6.1%

The results in the present study (Table 3), showed that non-significant differences between health status groups of samples regarding their blood group (*P*-value=0.505). Near half of the patients 45.5% suffering from severe COVID-19 were from blood group A. Also moderate cases showed a higher percentage 40.9% in group A.

The lowest percentages among severe and moderate cases were from blood group AB (13.6% and 9.1% in the same order). Around 40.9% of those who didn't have COVID-19 were from blood group O in the appendices,These results agreed with study achieved by (17)in Turkey, who showed that blood group O may be slightly protective against the COVID-19 infection, while blood group A may have a role in increasing susceptibility to the illness. Also, revealed as compared to the control group, COVID-19 patients had a higher prevalence of blood group A and a lower prevalence of blood group O. The results in the present study were agreed with study achieved by (18), who showed that Patients with blood type O demonstrated a lower vulnerability to SARS-CoV infection. Also, agreed with (19), who showed that blood group O was connected to a reduced mortality risk when compared to non-O blood groups, whereas blood group A was linked to a greater mortality risk when it came to the case fatality rate.

(Table 3): Association of blood groups and the severity of COVID-19 among 66 infected patients.

Disease status	**Blood group**				***P*-value (Fisher's Exact Test)**
	AB	**A**	**B**	**O**	
Severe COVID-19	3 (13.6%)	10 (45.5%)	6 (27.3%)	3 (13.6%)	0.505
Moderate COVID-19	2 (9.1%)	9 (40.9%)	5 (22.7%)	6 (27.3%)	
Mild COVID-19	4 (18.2%)	7 (31.8%)	3 (13.6%)	8 (36.4%)	
No COVID-19	3 (13.6%)	4 (18.2%)	6 (27.3%)	9 (40.9%)	
Total	12 (13.6%)	30 (34.1%)	20 (22.7%)	26 (29.5%)	

(Table 4): Mean differences of interferon- γ among different blood groups in 88 participants.

Blood group	**N**	**Mean**	**Standard Deviation**	**95% Confidence Interval for Mean**		***P*-value (ANOVA test)**
				Lower Bound	**Upper Bound**	
AB	12	231.25	128.195	37.007	149.80	0.649
A	30	239.92	102.918	18.790	201.49	
B	20	197.13	130.271	29.130	136.16	
O	26	211.12	142.409	27.929	153.59	
Total	88	220.50	124.260	13.246	194.18	

The ANOVA test shows that mean level was statistically not significant difference for concentration of interferon gamma according to the blood groups (Table 4) the blood group O in mild covid 19 tended to high levels concentration (366-398pg/ml) of IFN gamma than that non-O groups A(306-319pg/ml), B(334-349pg/ml), AB(322-338pg/ml) and this result refers to activity of group O against the virus this result agreement with (20), who showed that higher levels of all statistically significant cytokines, with the exception of HGF (hepatocyte growth factor), at the first moment were associated with better prognosis in the O blood type, and a substantial decrease followed after six days in the hospital.

These findings would also explain the O blood group's early and efficient immune response, along with the crucial role that ACE2, SARS-CoV-2, and anti-A antibodies play in the pathogenesis of COVID-19. They would also suggest that the viral infection was cleared quickly. Despite the presence of anti-A antibodies in blood group B, no published research have demonstrated that this blood type is more resistant to SARS-CoV-2. This situation was explained by (21). IgM type anti-A antibodies are present in blood group B, whereas IgG type anti-A antibodies are present in blood group O. Also, (22), who was explained this status to Blood type B has much greater ACE2 activity than blood group O, which increases the risk of contracting the virus too much. This may account for the increased death and critical patient rates in blood group B compared to blood group O. (Table 5) displays differences in mean Interferon-γ amongst COVID-19 patient categories. P-value was less than 0.001. The lowest mean (229.88±56.310) was found in patients with severe COVID-19, while the mean for patients with mild COVID-19 was 355.95±21.346. This outcome concurs with a study conducted by (23). After ten days of symptoms, the increased IFN-γ levels that were found in early COVID-19 infection in Brazil were not maintained in comparison to healthy persons. The death rate rose in individuals whose IFN-γ levels remained elevated. concur with the study by (24). Researchers in Iran discovered that the mild group's IFN-γ levels were much greater than those of the control group, and both the severe and mild groups' IFN-γ levels were significantly higher than those of the healthy control group. however, the current study is at odds with (25).In Irbil, Iraq, researchers found that there was no significant difference in the IFN-γ concentrations between the control, mild, severe, and recovered from COVID-19 groups.

(Table 5): Mean differences and descriptive statistics of Interferon-γ among (66) COVID-19 patients.

COVID-19	Mean	Standard Deviation	95% Confidence Interval for Mean		*P*-value (One way ANOVA test)
			Lower Bound	Upper Bound	
Severe	229.88	56.310	204.91	254.84	<0.001
Moderate	266.03	29.208	253.08	278.98	
Mild	355.95	21.346	346.49	365.41	
Total	283.95	65.576	267.83	300.07	

A noteworthy (P-value <0.001) positive and robust connection (r=0.806) has been seen between the Interferon-γ level and the COVID-19 classes, namely severe, moderate, and mild. The results of the current study indicate that the mild group had higher levels of Interferon-γ than the control group, indicating a relationship between IFN-γ and viral load. This is consistent with a study by (26), which found a strong correlation between IFN-γ and viral load, indicating that the virus may increase these cytokines' secretion.

Conclusions

In view of the findings of the present study, this investigation shows the level of interferon gamma concentration was statistically not significant difference according to the blood groups in COVID 19 infected patients.

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