Original article

Blood Group and COVID-19 Transmission and Mortality in Patients With Malignant Disease

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Abstract

Aim: The study aimed to investigate risk factors affecting the transmission of and mortality from COVID-19 in patients diagnosed with a malignant disease. In this context, ABO blood groups, gender, age, type of malignant disease, type of anti-tumoral agents, comorbidities and stage were examined.

Materials and Methods: Files of 1,256 patients who presented to our clinic between March and December 2020 were retrospectively reviewed. Patients diagnosed with a malignant disease who became infected with COVID-19 and those who did not were compared with regard to demographic, clinical characteristics and laboratory results (status of having been infected with COVID-19, ABO blood groups).

Results: Of 1256 patients in total, 72 (5.7%) were diagnosed with COVID-19. Median age of cancer patients infected with COVID-19 was 53 years (18-80). The most common types of cancer included gastrointestinal cancer (22.2%), breast cancer (20.8%), genitourinary cancer (20.8%) and lung cancer (16.7%). Of the patients diagnosed with COVID-19, 18.1% (n=13) died. Multivariate analysis identified disease stage as an independent prognostic factor for the risk of mortality [HR: 0.07, 95% CI (0.007-0.74), (p=0.02)]. A comparison of patients who became infected with COVID-19 and those who did not with regard to ABO blood groups (p=0.39) showed no statistically significant differences between the two groups. There was also no correlation between ABO blood groups and the risk of COVID-19-related mortality (p=0.83).

Conclusion: In patients suffering from malignant diseases, the ABO blood type exhibited no correlation with the risk of COVID-19 transmission and mortality. This study determined the presence of metastatic disease as a negative prognostic factor. Patients suffering from a metastatic malignant disease represent a high risk group for COVID-19 and should be treated using all necessary precautions.

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Introduction

SARS-CoV-2 infection, the first cases of which were reported in the People's Republic of China in late 2019, spread rapidly within a short period of time, marking the beginning of the COVID-19 pandemic. During this period, which has impacted almost all populations, patients diagnosed with a malignant disease were included among high-risk patient groups (1,2). Besides cancer, conditions such as immunosuppression, presence of comorbidities and advanced age resulted in these patients being included in groups impacted more severely by the infection (3). Frequent hospital visits are also among the factors elevating the risk of COVID-19 transmission in this population (4).

The genetically coded ABO blood group system is a phenotypic reflection of a genetic makeup. These antigens may serve as a protective factor against certain diseases and as a predisposing factor for others. Furthermore, the ABO blood group system was found to be associated with multiple infectious diseases. In some studies, it has been reported that anaemia is more common in A blood group in plasmodium falciparum and that HIV ag/ab is more common in A blood group (5, 6). Relationships between many infectious pathogens and blood group antigens and Anti-A/B antibodies have been investigated in extensive analyses (7). For example, some human immunodeficiency virus (HIV) and Gp120 isolates can react with blood group active monoclonal antibodies and lectins (8). Many studies have been conducted to evaluate the relationship between COVID-19 infections and the ABO blood group system. Some studies have found that women with A blood group are more susceptible to COVID-19 infections, while much lower COVID-19 infection rates were found in those with O blood group (9). In a study conducted during the Hong Kong epidemic, it was argued that O blood group is more resistant to the transmission of severe acute respiratory syndrome coronavirus (SARS-CoV) and that the risk of transmission is higher in A, B and AB blood groups (10). Like HIV, SARS-CoV targets the host cell via adhesion glycoproteins. It has been suggested that SARS-CoV targets the respiratory and gastrointestinal mucosa with its spike (S) protein and that high-titre Anti-A monoclonal antibody can block the S protein (11). Based on this information, the status of blood groups in the transmission of and mortality from COVID-19 was examined in patients suffering from malignant diseases.

Materials and Methods

Files of patients diagnosed with a malignant disease who presented to our Medical Oncology Clinic between March 2020 and December 2020 were retrospectively reviewed. Demographic, clinical characteristics of the patients, data about their treatment and laboratory results (status of having been infected with COVID-19, COVID-19 PCR test results, ABO blood group results) were obtained from the hospital records system. Patients in whom the presence of a SARS-CoV-2 infection was confirmed clinically and by laboratory results (positive PCR test) were considered COVID-19 cases. Patients diagnosed with COVID-19 were defined as the case group and patients not diagnosed with COVID-19 were defined as the control group. Clinical and laboratory characteristics of the groups and their survival outcomes were evaluated. Information about the blood group of 1,256 patients who presented to our clinic during the pandemic was available. Of these patients, 72 contracted COVID-19 and 13 patients in the patient group that contracted COVID-19 died. All statistical analyses were performed based on the specified numbers of patients. Patients were categorised based on age, gender, presence of comorbid diseases, type of cancer diagnosis, disease stage (metastatic/non-metastatic), treatment agents they received (chemotherapy, immunotherapy, tyrosine kinase inhibitors, anti-hormonal therapies) and blood groups (ABO, Rh). The case and control groups were compared according to these parameters. Also, the case groups were further categorised as survivors and non-survivors.

Mann-Whitney U test and logistic regression analysis were used for the analyses of non-normally distributed or non-parametric variables. A 95% confidence interval and significance value of p<0.05 were used.

Table 1. Mortality risk for patients with Covid 19 + according to disease and treatment characteristics

	N (%)	Non-survivor (N,%)	Survivor (N,%)	P value
All patients	72	13 (18.1%)	59 (81.9%)	
Age (median, yrs)	53 (18-80)	46 (18-80)	55 (18-75)	0.23**
Gender				0.41*
Male	37 (51.4%)	8 (61.5%)	29 (49.2%)	
Woman	35 (48.6%)	5 (38.5%)	30 (50.8%)	
Comorbidities				0.79*
Yes	30 (41.7%)	5 (38.5%)	25 (42.4%)	
No	42 (58.3%)	8 (61.5%)	34 (57.6%)	
Diagnosis				0.65*
Brain	3 (4.2%)	0 (0%)	3 (5.1%)	
GUS	15 (20.8%)	1 (7.7%)	14 (23.7%)	
Gİ	16 (22.2%)	5 (38.5%)	11 (18.6%)	
Soft tissue	5 (6.9%)	1 (7.7%)	4 (6.8%)	
Breast	15 (20.8%)	2 (15.4%)	13 (22%)	
Lung/pleura	12 (16.7%)	3 (23.1%)	9 (15.3%)	
Head and Neck	2 (2.8%)	0 (0%)	2 (3.4%)	
Others	4 (5.6%)	1 (7.7%)	3 (5.1%)	
Stage				**0.01***
Metastatic	46 (63.9%)	12 (92.3%)	34 (57.6%)	
Non-metastatic	26 (36.1%)	1 (7.7%)	25 (42.2%)	
Anti Tumoral agents (n:61)				0.79*
Chemotherapy	36 (59%)	5 (50%)	31 (60%)	
TKİs	9 (14.8%)	2 (20%)	7 (13%)	
İmmunotherapy	3 (4.9%)	1 (10%)	2 (3.9%)	
Hormonal therapy	13 (21.3%)	2 (20%)	11 (21.6%)	

*TKİ: Tyrosine kinase inhibitors, GUS: genitourinary system, Gİ: gastrointestinal truct, * chi-square test, ** independent samples T test.*

Statistical Anaylsis

Data were statistically analysed using the SPSS 18.0 package program. Descriptive statistics were used to evaluate patient characteristics and the frequencies of the parameters. Student's t-test was used for normally distributed numeric variables. A chi-squared test, Fisher's exact test,

Results

The study included 1,256 patients whose data could be obtained. During the pandemic, 72 (5.7%) patients were diagnosed with a COVID-19 infection. General characteristics of the patients are presented in Table 1.

Table 2: Covid-19 transmission and mortality status according to blood groups

		All patients	Blood groups (A-B-O)	O	A	B	AB	Rh group	Positive	Negative
All patients	N	1256		430 (34.2%)	488 (38.9%)	222 (17.7%)	116 (9.2%)		1092 (86.9%)	164 (13.1%)
	Covid(+)	72 (5.7%)		28 (38.8%)	21 (29.1%)	15 (20.8%)	8 (11.1%)		59 (81.9%)	13 (18.1%)
	Control	1184 (94.4%)		402 (33.9%)	467 (39.4%)	207 (17.4%)	108 (9.1%)		1033 (87.2%)	151 (12.8%)
	X^2		0.38					0.19		
	HR (95%CI)			reference	0.64 (0.36-1.15)	1.04 (0.54-1.99)	1.06 (0.47-2.40)	0.66 (0.35-1.23)		
	p*		0.39		0.14	0.90	0.88	0.19		
Covid-19 +	N	72		28 (38.9%)	21 (29.2%)	15 (20.8%)	8 (11.1%)		59 (81.9%)	13 (18.1%)
	Non-survivor	13 (18%)		6 (46.2%)	3 (23.1%)	4 (30.7%)	0 (0%)		11 (84.6%)	2 (15.4%)
	Survivor	59 (82%)		22 (37.3%)	18 (30.5%)	11 (18.6%)	8 (13.6%)		48 (81.4%)	11 (18.6%)
	X^2		0.40					0.78		
	HR (95%CI)			reference	0.61 (0.13-2.79)	1.33 (0.31-5.72)	0.00	1.26 (0.24-6.51)		
	p*		0.83		0.52	0.69	0.99	0.78		

*X2:chi-square test, *Binary logistic regression*

Median age of patients who contracted COVID-19 was 56 years. Male patients comprised 51.4% (n=37) of the cases. The most common types of cancer in COVID-19-positive patients included gastrointestinal cancer (22.2%), breast cancer (20.8%), genitourinary cancer (20.8%) and lung cancer (16.7%). Univariate and multivariate analyses showed that age, gender, comorbidity status and type of primary diagnosis had no effect on mortality in the patients infected with COVID-19. Of 61 patients in active treatment, 59% (n=36) received chemotherapy, 21% (n=13) received hormonal therapies, 14.8% (n=9) received tyrosine kinase inhibitor and 4.9% (n=3) received immunotherapy agents. A comparison of patients with regard to treatment they received showed no statistically significant differences between treatment agents in terms of mortality rates (p=0.79).

Of 1,256 patients evaluated with regard to ABO and Rh blood groups, 72 patients diagnosed with COVID-19 were defined as the case group and 1,184 COVID-19-negative patients were defined as the control group. In the case group, the rates of O, A, B and AB blood groups were 38.8% (n=28), 29.1% (n=21), 20.8% (n=15) and 11.1% (n=8), respectively. Regarding the case group, 81.9% of the patients (n=59) were Rh-positive and 18.1% (n=13) were Rh-negative. Meanwhile, in the control group, the rates of O, A, B and AB blood groups were 33.9% (n=402), 39.4% (n=467), 17.4% (n=207) and 9.1% (n=108), respectively. In the control group, 87.2% (n=1,033) of patients were Rh-positive and 12.8% (n=151) were Rh-negative. There was no statistically significant difference arising from ABO and Rh groups between the case and control groups with regard to the risk of COVID-19 transmission or among COVID-19-positive patients with regard to the risk of mortality. Details regarding blood groups are specified in Table 2.

The evaluation of COVID-19-positive patients in multivariate analyses according to the stage of disease showed that patients had a higher mortality risk in the metastatic stage compared with the non-metastatic stage [mortality rate of 26% in the metastatic stage, 3.8% in the non-metastatic stage (HR: 0.07, 95% CI (0.007-0.74), (p=0.02)]. Results of multivariate analysis are presented in Table 3.

Table 3. Multivariate analysis for mortality risk in patients with Covid 19 (+)

	Multivariate analysis	
	HR (95% CI)	**P value***
Age	0.93(0.87-1.00)	0.59
Comorbidities (no/yes)	1.76(0.23-13.0)	0.57
Stage (metastatic/non-metastatic)	**0.07(0.007-0.74)**	**0.02**
Blood groups (A-B-O)		0.80
O	Reference	
A	0.42(0.07-2.34)	0.32
B	0.76(0.15-3.90)	0.74
AB	0.99(0.00--)	0.99
Rh group (negative/positive)	1.66(0.25-10.7)	0.59

**Binary logistic regression.*

Discussion

It is known that patients diagnosed with a malignant disease are predisposed to infections due to immunosuppression arising from comorbidities and treatment they receive. During the COVID-19 pandemic, many unknown factors have become subjects of research, including, among other things, how and to what degree susceptible populations, such as those

suffering from malignant diseases, are affected by the pandemic and what the factors affecting disease transmission and mortality are. This study aimed to investigate the risk factors affecting the transmission of and mortality from COVID-19 in patients diagnosed with a malignant disease. The risk factors analysed included ABO blood groups, gender, age, type of malignant disease, type of anti-tumoral agents, comorbidities and stage.

Of 1,256 patients who were examined and treated at our clinic and whose blood groups could be determined exactly, 5.7% (n=72) were diagnosed with COVID-19 during the pandemic. Since the pandemic period is a dynamic period, variability in this rate across regions and an increase over time are expected. Previous studies conducted on patients diagnosed with a malignant disease have reported that advanced age, presence of comorbidities and receiving chemotherapy as opposed to other antitumor agents increase COVID-19-related mortality (12-14). In the evaluation of factors affecting mortality in patients infected with COVID-19 in this study, age, gender, presence of comorbidities and treatment received by the patients (chemotherapy, immunotherapy, TKI, hormonal therapy) were found to not influence disease-related mortality. COVID-19 is thought to be associated with a poorer course in lung cancers. However, in this study, the diagnosis of primary malignancy did not have a significant correlation with mortality. However, metastatic stage was found to be an independent risk factor predicting COVID-19 infection-related mortality (mortality rate of 26% in metastatic patients, 3.8% in non-metastatic patients (HR: 0.07, 95% CI (0.007-0.74), (p=0.02)). This can be explained by damage to natural barriers caused by cancer invasion and the patients' relative vulnerability to secondary infections. ABO blood group antigens are expressed in various tissues and cells, such as the epithelial, platelet, vascular endothelial cells and neurons. It is suggested that this system affects the spread of many pathogens. ABO antibodies are also a component of the innate immune system (15,16). Previous studies have found that susceptibility to viral infections is associated with ABO blood group. For example, susceptibility to Norwalk virus and hepatitis B was reported to vary depending on ABO blood type (17,18). Furthermore, individuals with O blood group were reported to have a lower likelihood of contracting SARS coronavirus (19). Do differences in blood group antigen expressions influence the risk of COVID-19 transmission and COVID-19-related mortality? Multiple epidemiological studies have been performed on this topic. Some studies have found that the number of patients with type-A blood was higher among patients infected with SARS-CoV-2 compared with healthy controls, while the number of those with O blood group was much lower. Some studies have also identified a correlation with the risk of mortality (9,20-22). In the study conducted by Zhao J. and colleagues, it was reported that A blood group was associated with a predisposition to COVID-19 infection, whereas the rate of infection was lower and the course of infection milder in O blood type individuals (21). In the study by Solmaz I. and colleagues conducted on a healthy population, COVID-19-positivity was reported to be higher in A blood group and lower in O blood group. However, it was stated that the need for intensive care did not vary across the groups (22). In another study, Arac E. and colleagues reported that there were no significant differences across the ABO blood groups, but that a significant difference existed within the Rh system, with Rh positivity predisposing persons to COVID-19 infection and Rh negativity exerting protective effects against it (23). The present study did not include a healthy population. Among the patients diagnosed with a malignant disease, those who did not become infected with COVID-19 were considered the control group and those who became infected with COVID-19 were considered the case group. A comparison of the group that contracted COVID-19 and the group that did not revealed no significant differences in terms of ABO blood groups (p=0.39). Moreover, it was found that ABO blood groups did not affect mortality in patients who became infected with COVID-19 (p=0.83). Similarly, it was also found that Rh antigen positivity was not a factor affecting COVID-19 transmission (p=0.19) and associated mortality (p=0.78). In this study,

ABO/Rh blood groups were evaluated with regard to susceptibility to COVID-19 infection and the related risk of mortality. The results of this study showed that COVID-19 and ABO/Rh blood groups did not have a statistically significant correlation in terms of the risk of transmission or the risk of mortality. However, metastatic malignant disease was an independent risk factor for COVID-19-related death. Limitations of this study include its single-centre, retrospective design and heterogeneity of the study population.

Conclusion

This study found that metastatic malignant diseases increased COVID-19-related mortality, while ABO blood groups and the Rh antigen status had no correlation with the risk of COVID-19 transmission and COVID-19-related mortality. According to the results of this study, patients suffering from a metastatic malignant disease represent a high risk group for COVID-19 and should be treated using all necessary precautions.

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