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Association of SARS-CoV-2 and ABO Blood Types: A Systematic Review

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Abstract

Coronavirus Disease 2019 pandemic caused huge burden on health care systems throughout the world. Studies outcomes are undebate regarding the association between ABO blood groups and Coronavirus Disease 2019.The aim of the current study was to determine the association between Coronavirus Disease 2019 and ABO blood grouping. For this study Published articles were searched on pubmed and google scholar by using several medical subject headings. All retrieved published articles screened properly from December 2019 to May 2021. All published original articles were included in the study. General information and frequency of ABO blood groups and Rh-D were gathered. Data was analyzed through Microsoft-Excel sheet 2020. Out Of 118 literatures, 59 studies met our desired outcome and arranged year-wise and continent-wise. Among total studies, 30 and 29 reports were published in year 2020 and 2021 respectively. Highest number of published reports were retrieved from Asia (31 reports), followed by South and North America (n=13). Among ABO blood groups, A blood group patients were found more vulnerable to Coronavirus Disease 2019 infection in Asia and Europe continents while patients with O blood groups were susceptible to Coronavirus Disease 2019 infection in Africa, South and North America. Coronavirus Disease 2019 infection was also observed more in Rh-D positive patients than Rh-D negative patients.It is concluded that both A blood group and O blood group patients are more prone to Coronavirus Disease 2019 infection. This study will serve to elaborated the link of phenotypic ABO blood types and Coronavirus Disease 2019 diseases.

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Keywords: ABO, Blood Group, Coronavirus, COVID-19, Rh-D, SARS–CoV-2

Introduction

The pandemic of Coronavirus Disease 2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). First time, it was emerged from China and spread throughout the globe.[1] Respiratory droplets formed during coughing, sneezing, breathing, and speaking serve as the transmission route. Dry cough, fever, and fatigue are the mild symptoms of COVID-19. Furthermore, if the disease is serious, it can lead to even death.[2]SARS-CoV-2 caused a global public health pandemic, with a high mortality and morbidity rate that rapidly overwhelmed the healthcare system. Patients with COVID-19 can be identified using radiological and laboratory tests.[3] Age, smoking, co-morbidities, innate traits, and suppress immune system are all risk factors for many infectious diseases, including COVID-19 infection. Furthermore, COVID-19 infection could be influenced by genetic factors.[3] The Rh-D factor and ABO blood type are both considered risk factors in a few infectious illnesses. Researcher studied the host susceptibility association with the ABO blood groups to infectious diseases.[4] Several research from diverse parts of the world (Asia, Europe, the Middle East, and America) found a link between blood phenotype and SARS-CoV-2. According to recent findings, there is a significant link (P-value 0.006) between COVID-19 and phenotypic blood type A.[2] Likewise, some other investigation indicates that people also with blood group A phenotypic are more reactive to COVID-19 unlike people with the phenotypic O blood group.[1] Nonetheless, researchers noted no statistically meaningful interaction between phenotypic ABO blood type and Rh-D blood group with COVID-19 conditions.[5] Additionally, a genome-wide association findings suggest that individuals with the phenotypic A blood type are often like to be infected than persons with some other phenotypic blood type. As a result, those with blood group A have a much high incidence of infection as patients with certain other blood groups.[6] Based on study, individuals with phenotypic blood type B seem to be more likely to get infected, whilst individuals with phenotypic blood type AB become less prone. There was no definitive link between ABO blood group phenotypes and the risk of occuring infection in patients.[7] Some other evaluation revealed that blood group A phenotypic persons had quite a substantially larger chance of illness when compared to controls, however blood group O phenotypic infected participants had a vastly lower risk.[3] SARS-CoV-2 infection and phenotypic blood type have such a contradictory interaction as each geography does indeed have a diverse outcomes, just like indicated in a work by Bhandari et al, whose claimed that those have phenotypic blood type O are just more likely to get infections followed by those having phenotypic Rh-D positive of A, B, and AB blood types.[4] In a published study from Lebanon, it's shown that infection occurrences were widespread phenotypic A blood group patients.[7]According to a Boston study, SARS-CoV-2 infection had also been found in a wide range of sick people with phenotypic blood type A, preceded by phenotypic blood group B, AB, and O. Also, no correlation has been found among any phenotypic blood type and other inflammatory indicators, including the intensity of the clinical outcome. It is often shown that phenotypic blood types B and AB, instead of phenotypic blood types A and O, have such a stronger connection with infection. In addition, Rh-D positive status was linked to infection in a substantial way.[8] As shown in a survey performed in Turkey, the number of infected was higher among individuals with phenotypic blood type A and AB, and smaller in people with phenotypic blood type O. A statistically meaningful link between phenotypic blood type A and infection was established.[9]
In a study conducted in Peshawar, Pakistan, persons with the phenotypic B blood type are far more prone to infection than those with phenotypic A, AB, and O blood groups, with the AB blood type being the less affected. Rh-D positive participants were shown to be less vulnerable to COVID-19 infections in the same study.[10]Some other study from Peshawar city of Pakistan, the infection was most usually diagnosed in medical practitioners with phenotypic A blood group, followed by phenotypic B blood type, O blood group, and AB blood type. Additionally, the people with Rh-D positive were being shown less resistant against COVID-19.[11] COVID-19 illness in young children is

significantly connected with phenotypic blood type A patients, according to a study conducted from Lahore, Pakistan, when compared to the control group with those other blood types.[12] The infection is somewhat more likely in phenotypic blood type B persons, according to a research from Muzaffargarh, Pakistan, followed by phenotypic blood type O, blood type A, and blood group AB.[13] According to a research conducted from Rawalpindi, individuals with phenotypic blood group A are more exposed to COVID-19 infection and have a higher severity rate, whilst patients with phenotypic blood group O are the least vulnerable.[14] While the prevalence of COVID-19 illness was greater in phenotypic blood type B persons, the severity and fatality rate substantially greater in phenotypic blood group A individuals, according to another study conducted from Rawalpindi.[15]. The main purpose of this paper was to compile the significant findings of the studies on Rh-D and phenotypic ABO blood group relation with SARS-CoV-2 reported by researchers all around the world. It's still up for argument whether any of those with vulnerable phenotypic blood groups are at greater risk of infections. This study aimed to investigate different studies to verify the presence of ABO group association with COVID-19.

Materials and Methods

Preferred reporting item for systematic review and meta-analysis protocol (PRISMA) was used for this literature review and analysis.

Data Search Sources and Strategy

An online available literature search was performed by using different keywords including “COVID-19 and blood group”, “COVID-19 and ABO blood group”, “COVID-19 and blood types”, “COVID-19 and Rh-D”, “SARS-CoV-2 and blood group”, “SARS-CoV-2 and ABO blood group”, and “SARS-CoV-2 and blood types” on NCBI Pubmed, and Google Scholar. The identified research studies were screened with abstracts and research paper title. Data published from December 2019 to May 2021 was searched and retrieved.

Inclusion and Exclusion Criteria

The retrieved papers were in English irrespective of study design, sample size, study duration, study location and country. Moreover, the control group was excluded and only data of COVID-19 infected subjects were extracted. All simple review, systematic, and meta-analysis published papers were exculded from the study.

Data Extraction

The searched articles were further analyzed to retrieve the data. The data was categorized in two sections (General and Participants data). General information related to paper such as title of paper, first author last name, year of publication, and study participants country. Participant’s characteristics including the sample size of COVID-19 infected patients, proportions of A blood group, B blood group, AB blood group, O blood group and Rh-D (Positive) were determined.

Statistical Analysis

All published data were retrieved and entered in Microsoft Excel Sheet 2020. The relation between ABO blood types and COVID-19 infection was assessed by computing the percentage of parameters.

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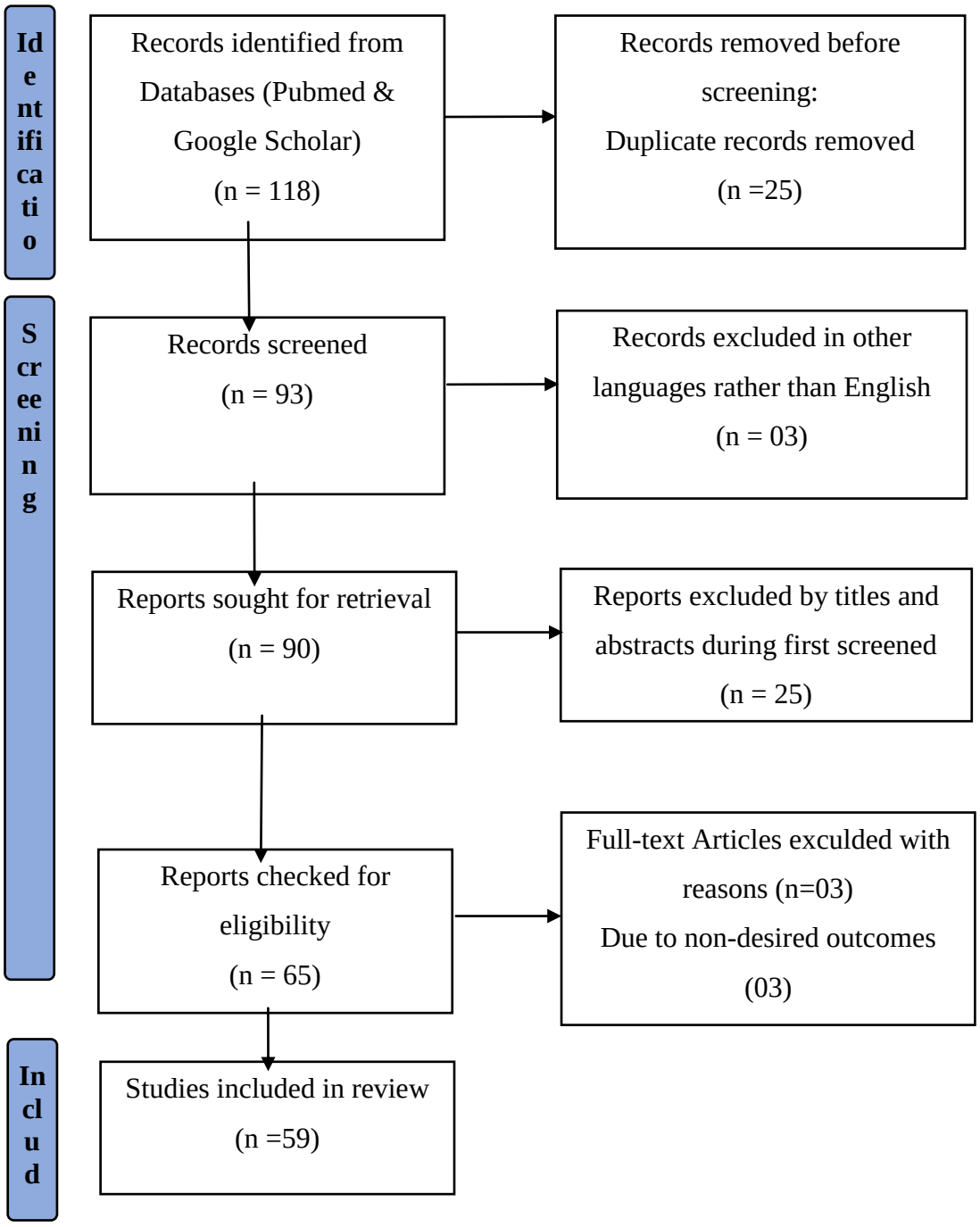

Figure 1: Study Selection for Systematic Review

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Result

Literature Search

A wide range of literature search yielded 118 relevant published research studies from databases (Pubmed and Google Scholar). Among total, 25 duplicates records were removed and remaining studies (n=93) were subsequently processed for further proper filtered based on language. As per our inclusion criteria, all remaining (n=93) reports were checked appropriately for languages, then removed three (n=03) studies due to language barrier. All articles in English language were thoroughly examined for titles and abstract admissible to our topic. Among total 90 articles, 25 literatures studies were excluded due to inappropriate abstracts and title. We reviewed the full text of remaining 65 studies, in which 59 studies met our desired criteria for a systematic review (Figure 1).

Study Characteristics of Inclusion

Among total, we retrieved 59 studies that met our study criteria for a systematic review. Among total (n=59), 30 studies were published in year 2020 while 29 studies published in 2021 (1st January to 31st May). Of 30 reports published in 2020, 09 studies published in different regions of United States of America (USA), followed by China and Iran (03 Studies each), Italy (02 studies), Spain (02 studies), and Turkey (02 studies). Sample size of each study was varied from one another. Frequently, diagnosis were confirmed by RT-PCR test using nasopharyngeal specimens. On the other hand, 29 studies published in five months from January to May 2021. Among all published reports, four (04 studies) reported from Turkey, followed by Saudi Arabia, Pakistan and USA (03 studies each) published whereas two studies from China.

Association of COVID-19 infection and ABO Blood groups reports of year 2020

In the year 2020, 739390 COVID-19 infected individuals were included in this systematic study. The infected patients with the phenotypic A blood group were noticed to be the most vulnerable, with a total frequency of 37.8%, followed by the phenotypic O blood group with a proportion of 37.3%, while 18.5% COVID-19 infection in patients with the phenotypic B blood group, and the least in patients with the AB blood group (6.4%). Thirteen of the 30 studies found a connection between Rh-D and COVID-19 infection, indicating that Rh-D positive individuals are more infected than Rh-D negative individuals. In the year 2020, the frequency of "Rh-D" positive was found to be 90.6% in all previous papers (Table 1).

Association of COVID-19 infection and ABO Blood groups reports of year 2021

A total of 71387 patients were investigated in 29 published reports in 2021. According to studies published in the year 2021, phenotypic blood group A patients were found to be more prevalent than other blood groups, accounting for 38.4% of all participants, followed by the phenotype O blood type. In COVID-19 infected individuals, the O blood type was found in 33.7%. The percentage of B blood group and AB blood group was 19.8% and 8.0% respectively. Rh-D factor was also studied in overall 16 studies which shows 87.9% Rh-D positive COVID-19 patients (Table 2).

Association of COVID-19 infection and ABO Blood groups (Continental-wise distribution) of total 59 studies

Europe

A total of 12 studies reported from continent Europe in which seven (07) published in year 2020 while five (05) published in year 2021. Studies conducted in Spain (04), two each in England, France, and Italy, one each in Belgium and France. In all 12 studies, 6202 COVID-19patients were studied in which A blood group patients were found more prone than other blood groups. The proportion of A,

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O, B, and AB blood group were 46.7%, 36.3%, 12.6%, and 4.5% respectively. Rh-D factor was also studied in four (04) reports, that shows high level of COVID-19 infection in Rh-D positive patients with frequency of 82.0% (Table 3).

Africa

Of total (n=59) studies, fours reports published from Africa continent. Three (03) studies published in year 2020 while one (01) in year 2021. One study each published in Nigeria, Tunisia, Sudan, and Egypt. In all studies, 1260 patients were found infected with COVID-19. Blood group was examined to find the most susceptible blood group patients to COVID-19 infection. The O blood group was noted prevalent in COVID-19 infected patients. The frequency of O blood group was 39.8%, followed by A blood group with 33.9%, B blood group in 19.6% patients and AB blood group in 6.7% patients. Similarly, the Rh-D factor was examined which showed that Rh-D positive patients (92.4%) were more prone to COVID-19 infection rather than Rh-D negative patients (Table 4).

South and North America

Total of 13 studies were retrieved from both South and North America continents in which one study from Canada and remaining 12 reports published in different states of USA. Among all continents, highest number of patients were study in South and North America Continents. The COVID-19 patients were 728833 included in these 13 studies. It was found that O blood group patients are more vulnerable with a frequency of 48.7%, followed by A blood group patients (33.6%), B blood group patients (13.7%), and least infection were identified in patients of AB blood group (4.0%). Rh-D factor was also evaluated in COVID-19 patients. Seven studies (07) retrieved which determined the Rh-D factor and overall 91.5% patients were Rh-D positive (Table 5).

Asia

The majority of work presented from Turkey (06 studies), China (05 studies), Pakistan (05 studies), Iran (04 studies), Saudi Arabia (04 studies), and one study each from Afghanistan, Bahrain, Bangladesh, India, Iraq, Jordan, and Lebanon. The 31 studies reported from Asia comprised a total of 74482 patients. COVID-19 infection was diagnosed in the highest percentage of A blood group phenotypic patients (37.7%), followed by O blood group (28.6%), B blood group (24.1%), and AB blood type (9.6%). The Rh-D positive was detected in 89.6% COVID-19 infected patients (Table 6, 7).

Overall summary of 59 published studies

In all, 810777 people were infected with COVID-19 in 59 investigations, with the A blood type being detected in 38.1% of cases, followed by the O blood type in 35.5%, the B blood type in 19.2%, and the AB blood group in 7.2%. Furthermore, 89.1% of the patients tested positive for Rh-D. Phenotype A blood group patients were shown to be more vulnerable to infection than other blood types in the European and Asian continents. On the other hand, patients of the O blood type were more susceptible in three continents: Africa, South America, and North America. Furthermore, Rh-D positive people were 89.1% more likely than Rh-D negative blood type individuals to acquire COVID-19.

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Table 1: Characteristics of studies included in a systematic review published in year (2020)

Authors	Country	COVID-19 Cases	A Blood Group (%)	B Blood Group (%)	AB Blood Group (%)	O Blood Group (%)	Rh-D +ive (%)
Wu et al., (2020)2	China	187	36.9	33.7	21.9	7.5	
Bhandari et al., (2020)4	USA	825	26.7	13.6	3.3	56.4	95.1
Abdollahi et al., (2020)5	Iran	397	40.3	22.4	9.3	28	89.9
Latz et al., (2020)8	USA	1289	34.2	15.6	4.7	45.5	90.1
Fan et al., (2020)9	China	105	42.8	26.7	8.6	21.9	
Noor et al., (2020)14	Pakistan	326	37.4	32.8	8	21.8	
Khalil et al., (2020)16	Lebanon	146	40.4	17.1	6.8	35.7	
Hoiland et al., (2020)17	Canada	398671	34.7	11.8	3.9	49.6	
Li et al., (2020)18	China	265	39.2	25.3	9.8	25.7	
Ahmed et al., (2020)19	England	86	40	22	14	24	
Boudin et al., (2020)20	France	1257	41.3	10.6	4.2	43.9	85.4
Chegni et al., (2020)21	Iran	76	44.7	22.4	5.3	27.6	
Sedighinejad et al., (2020)22	Iran	249	27.7	23.3	8.8	40.2	92
Valenti et al., (2020)23	Italy	505	44.6	10.5	7.3	37.6	
Gamal et al., (2020)24	Italy	1601	43.3	9.5	3.8	43.4	86.9
Kotila et al., (2020)25	Nigeria	297	19.5	25.9	5.7	48.9	
Higazy et al., (2020)26	Saudi Arabia	1775	38	26	10	26	
Marcos et al., (2020)27	Spain	226	44	8.4	4.4	43.2	
Tonon et al., (2020)28	Spain	134	40	18	2	40	
Tahaet al., (2020)29	Sudan	557	32.3	18.3	6.1	43.3	91.7
Yalaoui et al., (2020)30	Tunisia	51	49.1	13.7	3.9	33.3	
Solmaz et al., (2020)31	Turkey	14701	39.7	18.6	8.1	33.6	88.4
Yaylac et al., (2020)32	Turkey	397	50.6	13.9	5.3	30.2	90.4
Szymanskiet al., (2020)33	USA	4968	29.6	17	4.1	49.3	
Zietz et al., (2020)34	USA	13051	32.9	15.6	4.3	47.2	90.8
Niles et al., (2020)35	USA	276536	33.9	13.1	3.7	49.3	90
Barnkob et al., (2020)36	USA	7422	44.4	12.1	5.1	38.4	
Zietz et al., (2020)37	USA	13051	32.9	15.6	4.3	47.2	90.8
May et al., (2020)38	USA	165	34	18	5	43	96
Deleers et al., (2020)39	USA	74	37.9	24.3	0	37.8	
Grand Total		**739390**	**37.8**	**18.5**	**6.4**	**37.3**	**90.6**

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Table 2: Characteristics of studies included in a systematic review published in year (2021)

Authors	Country	COVID-19Cases	A Blood Group (%)	B Blood Group (%)	AB Blood Group (%)	O Blood Group (%)	Rh-D +ive (%)
Zhao et al., (2021)1	China	1775	37.8	26.4	10	25.8	
Almadhi et al., (2021)3	Bahrain	2334	22	27.6	5	45.4	
Bari et al., (2021)12	Pakistan	66	25.7	34.9	1.5	37.9	
Saify et al., (2021)40	Afghanistan	1036	31.8	23.5	8.3	36.4	92.2
Badsha et al., (2021)41	Bangladesh	185	34.6	39.5	5.4	20.5	98.9
Nauffal et al., (2021)42	Brigham	1114	29.6	14.9	6.4	49.1	
Peng et al., (2021)43	China	32	34.4	34.4	12.5	18.7	
Shamikh et al., (2021)44	Egypt	355	34.9	20.6	11	33.5	93.2
Lehrer et al., (2021)45	England	720	44.9	9.2	3.2	42.7	
Kibler et al., (2021)46	France	22	81.8	0	0	18.2	68.8
Pandey et al., (2021)47	India	1191	24.8	35.2	9	31	93.2
Nasiriet al., (2021)48	Iran	329	39.2	20.1	6.4	34.3	90.3

Majeed et al., (2021)49	Iraq	3691	27.7	33.2	11.4	27.7	90.8
Sughayer et al., (2021)50	Jordan	292	28.8	18.7	11.2	41.3	87.5
Rahim et al., (2021)51	Pakistan	1935	27	35.9	11.8	25.3	93.3
Malik et al., (2021)52	Pakistan	1067	18.9	27.6	48.9	4.6	
Covali et al., (2021)53	Romania	46	52.2	21.7	6.5	19.6	87
Samra et al., (2021)54	Saudi Arabia	507	75.1	3.5	2.2	19.2	
Ansari et al., (2021)55	Saudi Arabia	57	26	18	4	52	
Shitany et al., (2021)56	Saudi Arabia	726	35	25	12	28	81.4
G´omez et al., (2021)57	Spain	566	45	7	5	43	
Diaz et al., (2021)58	Spain	965	45.6	9.5	3.1	41.8	
Goker et al., (2021)59	Turkey	186	57	10.8	7.4	24.8	86
Dal et al., (2021)60	Turkey	39850	39.4	14.7	10.9	35	79.6
Coluk et al., (2021)61	Turkey	144	47.9	13.9	3.5	34.7	86.8
Kirisci et al., (2021)62	Turkey	455	44.4	19.3	6.6	29.7	89.7

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Ibrahim et al., (2021)63	USA	46	27.3	10.6	1.5	60.6	87.4
Anderson et al., (2021)64	USA	11468	39.6	9	3.2	48.2	
Mullins et al., (2021)65	USA	227	36.6	11	3.1	49.3	
Grand Total		**71387**	**38.4**	**19.8**	**8**	**33.7**	**87.9**

Table 4: COVID-19 infection and ABO blood group association in Africa

Authors	Country	COVID-19 Cases	A Blood Group (%)	B Blood Group (%)	AB Blood Group (%)	O Blood Group (%)	Rh-D +ive (%)
Kotila et al., (2020)25	Nigeria	297	19.5	25.9	5.7	48.9	
Taha et al., (2020)29	Sudan	557	32.3	18.3	6.1	43.3	91.7
Yalaoui et al., (2020)30	Tunisia	51	49.1	13.7	3.9	33.3	
Shamikh et al., (2020)44	Egypt	355	34.9	20.6	11	33.5	93.2
Grand Total		**1260**	**33.9**	**19.6**	**6.7**	**39.7**	**92.4**

Table 5: COVID-19 infection and ABO blood group association in South and North America

Authors	Country	COVID-19 Cases	A Blood Group (%)	B Blood Group (%)	AB Blood Group (%)	O Blood Group (%)	Rh-D +ive (%)
Bhandari et al., (2020)[4]	USA	825	26.7	13.6	3.3	56.4	95.1
Latz et al., (2020)[8]	USA	1289	34.2	15.6	4.7	45.5	90.1
Hoiland et al., (2020)[17]	Canada	398671	34.7	11.8	3.9	49.6	

Szymanski et al., (2020)[33]	USA	4968	29.6	17	4.1	49.3	
Zietz et al., (2020)[34]	USA	13051	32.9	15.6	4.3	47.2	90.8
Niles et al., (2020)[35]	USA	276536	33.9	13.1	3.7	49.3	90
Barnkob et al., (2020)[36]	USA	7422	44.4	12.1	5.1	38.4	
Zietz et al., (2020)[37]	USA	13051	32.9	15.6	4.3	47.2	90.8
May et al., (2020)[39]	USA	165	34	18	5	43	96
Nauffal et al., (2021)[42]	USA	1114	29.6	14.9	6.4	49.1	
Ibrahim et al., (2021)[63]	USA	46	27.3	10.6	1.5	60.6	87.4
Anderson et al., (2021)[64]	USA	11468	39.6	9	3.2	48.2	
Mullins et al., (2021)[65]	USA	227	36.6	11	3.1	49.3	
Grand Total		**728833**	**33.6**	**13.7**	**4.0**	**48.7**	**91.5**

Table 6: COVID-19 infection and ABO blood group association in Asia (2020)

Authors	**Country**	**COVID-19 Cases**	**A Blood Group (%)**	**B Blood Group (%)**	**AB Blood Group (%)**	**O Blood Group (%)**	**Rh-D +ive (%)**
Wu et al., (2020)2	China	187	36.9	33.7	21.9	7.5	
Abdollahi et al., (2020)5	Iran	397	40.3	22.4	9.3	28	89.9

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Fan et al., (2020)9	China	105	42.8	26.7	8.6	21.9	
Noor et al., (2020)14	Pakistan	326	37.4	32.8	8	21.8	
Khalil et al., (2020)16	Lebanon	146	40.4	17.1	6.8	35.7	
Li et al., (2020)18	China	265	39.2	25.3	9.8	25.7	
Chegni et al., (2020)21	Iran	76	44.7	22.4	5.3	27.6	
Sedighinejad et al., (2020)22	Iran	249	27.7	23.3	8.8	40.2	92
Higazy et al., (2020)26	Saudi Arabia	1775	38	26	10	26	
Solmaz et al., (2020)31	Turkey	14701	39.7	18.6	8.1	33.6	88.4
Yaylacı et al., (2020)32	Turkey	397	50.6	13.9	5.3	30.2	90.4
Grand Total		**18624**	**39.8**	**23.8**	**9.3**	**27.1**	**90.2**

Table 7: COVID-19 infection and ABO blood group association in Asia (2021)

Authors	**Country**	**COVID-19 Cases**	**A Blood Group (%)**	**B Blood Group (%)**	**AB Blood Group (%)**	**O Blood Group (%)**	**Rh-D +ive (%)**
Zhao et al., (2021)[1]	China	1775	37.8	26.4	10	25.8	
Almadhi et al., (2021)[3]	Bahrain	2334	22	27.6	5	45.4	
Rahim et al., (2021)[10]	Pakistan	1935	27	35.9	11.8	25.3	93.3

Bari et al., (2021)[12]	Pakistan	66	25.7	34.9	1.5	37.9	
Saify et al., (2021)[40]	Afghanistan	1036	31.8	23.5	8.3	36.4	92.2
Badsha et al., (2021)[41]	Bangladesh	185	34.6	39.5	5.4	20.5	98.9
Peng et al., (2021)[43]	China	32	34.4	34.4	12.5	18.7	
Pandey et al., (2021)[47]	India	1191	24.8	35.2	9	31	93.2
Nasiri et al., (2021)[48]	Iran	329	39.2	20.1	6.4	34.3	90.3
Majeed et al., (2021)[49]	Iraq	3691	27.7	33.2	11.4	27.7	90.8
Sughayer et al., (2021)[50]	Jordan	292	28.8	18.7	11.2	41.3	87.5
Malik et al., (2021)[52]	Pakistan	1067	18.9	27.6	48.9	4.6	
Samra et al., (2021)[54]	Saudi Arabia	507	75.1	3.5	2.2	19.2	
Ansari et al., (2021)[55]	Saudi Arabia	57	26	18	4	52	
Shitany et al., (2021)[56]	Saudi Arabia	726	35	25	12	28	81.4
Goker et al., (2021)[59]	Turkey	186	57	10.8	7.4	24.8	86
Dal et al., (2021)[60]	Turkey	39850	39.4	14.7	10.9	35	79.6
Coluk et al., (2021)[61]	Turkey	144	47.9	13.9	3.5	34.7	86.8
Kirisci et al., (2021)[62]	Turkey	455	44.4	19.3	6.6	29.7	89.7
Grand Total		**55858**	**35.7**	**24.3**	**9.9**	**30.1**	**89.1**

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Discussion

The present systematic review provides comprehensive description of COVID-19 association with ABO blood group in different continents of the world. In this systematic review, 59 studies consisting of 810777 patients were studied. Among all patients, A blood group and O blood group patients were at higher risk than B blood group and AB blood group patients. In terms of the Rh-D factor, patients with Rh-D positive blood groups were more likely to acquire infection than those with Rh-D negative blood groups. We sorted all of the patients into two different groups, one by year and the other by continent. These classifications were quite useful in detecting COVID-19 infection in various populations. COVID-19 infection has been shown to be relatively common in phenotypic A blood groups in Europe and Asia than in non-A blood groups, according to this study. Furthermore, in Africa, South and North America, phenotypic O blood group patients were more vulnerable to infection than non-O blood group people. Although the mechanisms of infection are still unknown, several theories have been proposed in support of a link between blood types and SARS-CoV-2. The phenotypic ABO blood antigen-encoding genes are did find at 34.1-34.2, on the p-arm of chromosome 9.[66] Four (04) genetic phenotypes make up these antigens (A, B, AB, and O). Increases and decreases in blood group antigen expression might impact pathogen infection sensitivity, which might explain some of the differences in host susceptibility to COVID-19 infections.[67]

Additionally, the phenotypic ABO blood type antigen is expressed on the membrane of erythrocytes, but it is also found on other regions of the body, such as airway epithelial cells, alveolar epithelial cells, and bodily fluids.[68] The antigen-receptor interaction is further influenced by receptor mediated affinity, invasion ability, and hereditary susceptibility. There is evidence that antigens in blood groups operate as receptors for a variety of pathogenic microorganisms.[67]

Angiotensin-Converting Enzyme 2 (ACE-2) is thought to be a putative SARS-CoV-2 receptor since receptor binding domains are found on S-proteins.[69] Recent genetic investigations have demonstrated that natural anti-A antibodies can prevent the interaction between ACE-2 and the S-protein of SARS-CoV-2, implying that patients with phenotypic blood groups B and O are protected from COVID-19, while those with phenotypic blood groups A are more prone to SAR-CoV-2.[70] Additionally, those with phenotypic blood group O have a lesser number of ACE, whereas individuals with phenotypic blood group A have a higher amount. The ACE enzyme lowers blood pressure and is a risk factor for COVID-19.[71] Consequently, the ACE2/ACE1 ratio aids in the prevention of endothelium and vascular dysfunctions.[72] SARS-CoV-2 enters the human body through a particular transmembrane serine protease 2 receptor and ACE-2.[73] Polymorphisms in the ABO blood type can impact ACE blocker therapy response and may aid to reduce SARS-CoV transmission.[74] Individuals with phenotypic blood type O have a larger amount of interleukin 6 (IL-6) which is an important part of cell defence. As a result, the study discovered that IL-2 is linked to the severity of COVID-19. In the healing of the lungs, IL-6 may have a more protective function.[75]

According to one study, blood group is linked to several pulmonary and coagulation disorders, particularly in COVID-19 patients. Individuals with the phenotypic A blood type have a genetically higher rate of von willebrand factor (VWF) and are hence more prone to thrombosis.[76] Our comprehensive study also revealed that patients with phenotypic blood type A are at a significant risk of acquiring COVID-19infection. Few other meta-analysis studies have found that phenotypic blood group A is now more vulnerable to infection, whereas phenotypic blood group B is

the lesser prone.[77] Another meta-analysis supports our findings that the risk of infection increases with age in participants with phenotypic A blood type.[78]

There are various possible limitations to this systematic review. Despite the fact that we had a significant number of studies and a big sample size, we did not conduct statistical analysis (meta-analysis) to determine the p-value and odd ratio to assess the dependable outcome since we depended on data from scientific databases, which still need to be explored. Second, we can't include the control group for comparison with COVID-19 infected patients. In this investigation, gender, mortality, and other co-morbidities were not compared to ABO blood group. Because this research was confined to English literature, numerous other language publications were omitted. No study was found from continent of Australia.

Conclusion

In conclusion, this systematic review evaluated at multiple published studies from various countries to see whether there is a link between COVID-19 infection and phenotypic blood group. COVID-19 infection is more common in Rh-D positive people than in Rh-D negative groups. The phenotypic blood groups A and O seems to become a potential risk for SARS-CoV-2, according to the majority of findings. Individuals with A blood group phenotype are often more vulnerable to infection in both Asia and Europe continents, whereas those that have the O blood group phenotypes are more exposed in Africa, South America, and North America. Individuals with blood groups AB and B phenotypes were appeared the least affected by COVID-19 infection. To strengthen this link, more trustworthy quality and rigorous study evidence is required. In addition, further genetic research is needed to understand the link between blood types and infection.

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