

REVIEW ARTICLE

## Comparative Study on COVID-19 Pandemic in Middle East

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### **ABSTRACT**

The novel coronavirus disease-2019 (COVID-19) has been spreading rapidly around the World and declared as a pandemic by WHO. In December 2019, patients presenting with viral pneumonia due to an unidentified microbial agent were reported in Wuhan city in China.

A novel coronavirus was subsequently identified as the causative pathogen, provisionally named 2019 novel coronavirus (2019-nCoV). The novel coronavirus pneumonia (COVID-19) is an infectious acute respiratory infection caused by the novel coronavirus the virus is a positive-strand RNA virus with high homology to bat coronavirus. As per WHO's situation report of 28 April 2020, Coronavirus is continuing to spread globally with now more than 3000004 cases worldwide. All Arab countries have reported COVID-19 cases.

The confirmed cases of the corona virus 2019 (COVID-19) pandemic were announced in Arab gulf countries, as follows, the first case of the COVID-19 disease caused by the SARS-CoV-2 virus in the United Arab Emirates was confirmed on 29<sup>th</sup> January 2020, the source of the infection was from China. In February 2020, it was first reported that the ongoing global pandemic was transmitted to Iraq, Bahrain, Oman, Qatar and Kuwait and the source of the viral admission were from Iran. On 2<sup>nd</sup> March - 2020, Saudi Arabia confirmed its first case, a Saudi national returning from Iran via Bahrain. The case fatality rate in Gulf Countries, which are less than 1% in Oman, UAE, Kuwait, Bahrain and Saudi Arabia, hitting 7.5% in Iraq.

Scientifically, we compared the ABO blood group distribution in Gulf area patients with COVID-19 confirmed by SARS-CoV-2 test. Blood group O was associated with a lower risk for the infection compared with non-O blood groups whereas blood group A then AB were associated with a higher risk for acquiring compared with non-A and non-AB blood groups. Also, high risk for diabetes, cardiovascular disease, blood clotting and

interleukin secretion was assigned with blood groups in different orders, patients with certain blood group have another disease must be under care and observation when infected with SARS-2 to reduce complication of infection. This is the first study of an association between the ABO blood group and COVID-19 in Arab Gulf area. It should encourage further investigation of the relationship between the ABO blood group and the COVID-19 susceptibility.

## **KEYWORDS**

Blood group; COVID-19; SARS-CoV-2 virus

## **INTRODUCTION**

Persons with pneumonia cases were recognized in December 2019 in Wuhan, China; later the virus responsible for pneumonia was identified as B-coronavirus and initially named by World Health Organization to a 2019-novel coronavirus (2019-nCoV). Officially WHO called the disease as COVID-19 while the new virus named as SARS-CoV-2 by coronavirus study group. Rapid Spreading of COVID-19 across the world led WHO declaring it a pandemic in 11<sup>th</sup> of March 2020. Rapid steps were taken by scientists at China and other countries. Chinese researchers isolated the virus responsible for COVID-19 on 7<sup>th</sup> January 2020 and came out to genome sequence of SARS-CoV-2 [1]; it is enveloped non-segmented positive sense RNA virus with 96.2% identity to a bat CoVRaTG13, whereas it shares 79.5% identity to SARS-CoV. Genome sequence analysis suggests that bat is the natural host of virus origin, and it might transmit to human via unknown hosts. SARS-CoV-2 could use angiotensin-converting enzyme (ACE2) as a receptor just the same for SARS-CoV [2].

As an emerging acute respiratory infectious disease, the virus spreads through the respiratory tract, by droplets, respiratory secretions, and direct contact among population for a low infective dose [3,4]. The SARS-CoV-2 isolated from nasal and pharynx swabs as well as from faecal swab and blood, indicating the possibility of multiple routes transmission. The receptor protein ACE2 present in abundance on lung alveolar epithelial cells and enterocytes of small intestine [5,6]. The epidemiological investigation suggest that the incubation period is almost 1 days - 14 days, mostly 3 days - 7 days; virus is contagious during the latency period and high transmissible especially for elderly and people with seriously diseases. Patients with COVID-19 presented common symptoms such as fever, malaise, and dry coughs. However, there was a quirk: Not everyone who was infected shows the symptoms of disease and called as asymptomatic. The mainly defence strategy against COVID-19 is the option of immune system which vital to fight and overcome the viral infection, one of the findings is how blood group and their associated antibodies might associate the immune response against SARSCoV-2 as well as ABO antigens that may be susceptible to viral infection. Blood groups were distributed among human population and vary across population and geographical regions due to natural selection, the environment and disease. The four blood groups were known for their role in blood transfusion. Human received incompatible blood, powerful naturally occurring anti-A or anti-B antibodies could cause a blood transfusion reaction, as well as many other diseases are related with blood group and Rh factor such as diabetes, cardiovascular disease, viral infections, and interleukin production. Many other criteria may influence other than the virus strain itself as season and temperature, sex and age of patients, blood group, sanitation and alienating strategies as well as early discovery of infection by COVID-19. Early diagnosed infected persons limited the rate of virus transmission to others;

controlling the outbreak and decreased the rate fatality of COVID-19 disease (China CDC weekly; WHO25 March 2020).

### **TRADITIONAL FIRST CONFIRMED INFECTION IN GULF COUNTRIES**

The neighbouring countries belong to Gulf take their containment measures after the first confirmed case of infection to lessen and prevent the incidence of infections with COVID-19, the origin of first diagnosed COVID-19 will present in table [1] for Gulf countries. Data presented by WHO for confirmed cases of COVID-19 regarding Arab Gulf countries revealed that Iraq came at the third number of cases at 5-March, keeping forth position till 8 April. While, Iraq had the fifth and sixth position in total confirmed cases at mid of April and 19 April respectively. The infection situation also, revealed that total number of confirmed cases on 19 April was bellow other countries that recorded first case at the end of February 2020 such as Qatar, Kuwait and United Arab Emirate. On 28<sup>th</sup> April- 2020 Iraq became at the last position among Gulf countries (Table 1).

**Table 1:** The origin of first confirmed case of COVID-19 at Arab Gulf region.

<b>Country</b>	<b>Date for 1<sup>st</sup> Case</b>	<b>Origin of 1<sup>st</sup> Case</b>
Iraq	24-2-2020	Iran
Saudi Arabia	2-3-2020	Iran
Qatar	27- 2-2020	Iran
Bahrain	21-2-2020	Iran
United Arab Emirates	23-1-2020	China
Kuwait	24-2-2020	Iran
Oman	24-2-2020	Iran

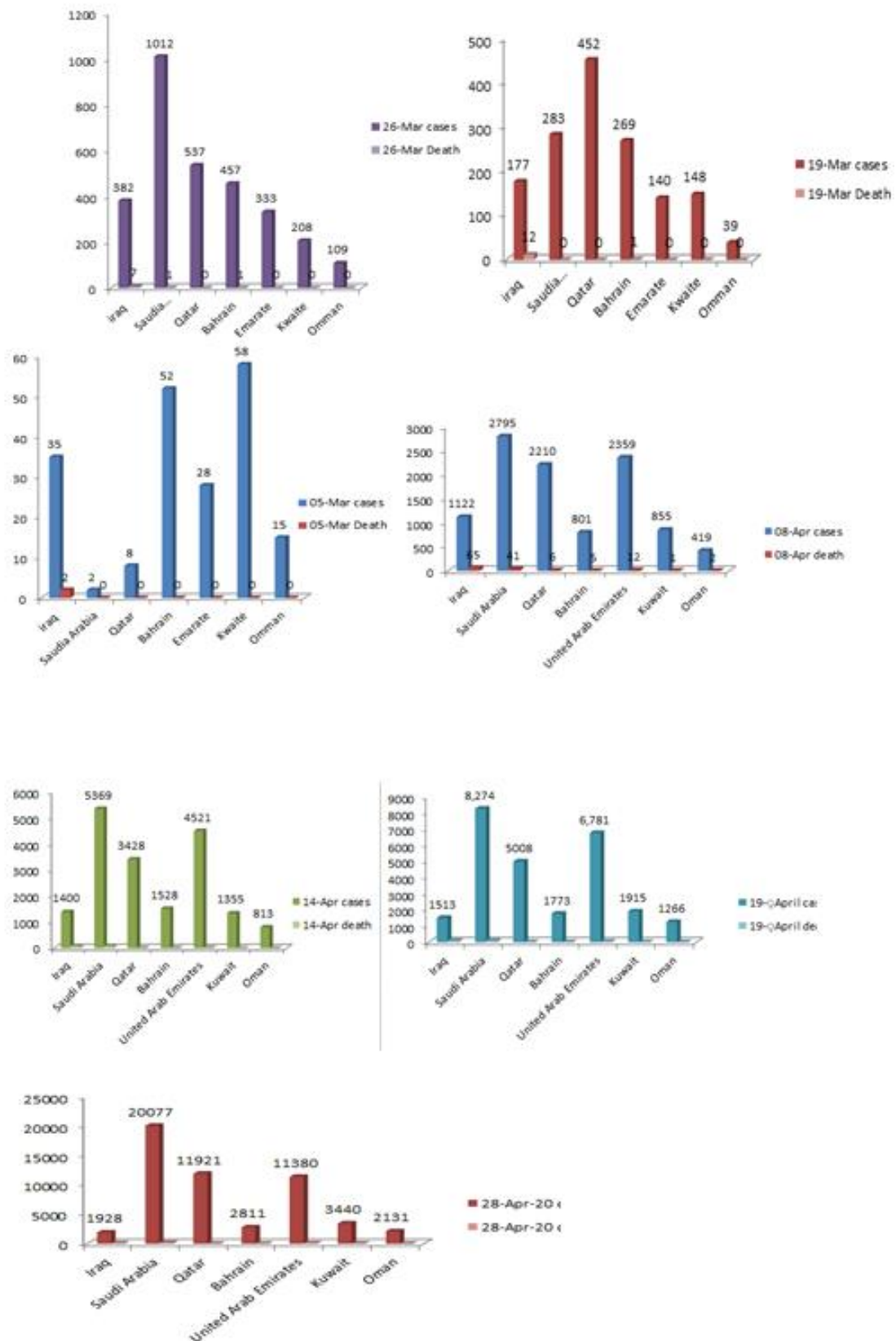
### **CONFIRMED CASES OF COVID-19**

COVID-2019 regular prevalence data were obtained from the official website between March till 19- April 2020. The charts have been designed to describe the infections in Gulf area; total cases were analysed for confirmed infection and deaths in Iraq, Kuwait, Saudi Arabia, UAE, Qatar and Oman with the first case of infection and its origin. On the other hand, early confirmed first case in Saudi Arabia began may be the reason for its higher count of cases as illustrated in figure [1]. Many reasons may contribute to relatively low incidence of confirmed COVID-19 in Iraqi population, high temperature (reached to 30-32 at April), prevention of socials aggregation such as Fridays prey, religions occasions, closed schools and Universities. Iraqi hygiene's practices were very good in street and houses; they almost wear clothes and masks, wash their hands with soap, shopping with care avoiding aggregation. Other factors may influence infection such blood group in which blood group O is more abundant in Iraqi population; researchers found that individuals with blood group O are more resistant to infections including SARS and COVID-19. Also, vaccination strategies for Iraqi population that taken on during past decades; vaccination of BCG and Measles may induce immune responses against COVID-19 infection (Figure 1).

### **RELATIONSHIP BETWEEN ABO BLOOD GROUP AND COVID-19**

When comparing total cases of COVID - 19 in Gulf countries with the origin of their first case as Iran which reached to 92542 at 28-April 2020, this may contribute to other factors such blood group and their associated diseases such as diabetes, hypertension and cardiovascular diseases. Blood group O is more abundant in Iraqi, Kuwait, Oman, Saudi Arabia and UAE population; researchers found that individuals with blood group O are more resistant to infections including SARS and COVID-19 while, blood group A may need more attention to prevent infection [7].The classification of human blood based on the inherited properties of red blood cells

(erythrocytes) as determined by the presence or absence of the antigens A and B, which are carried on the surface of the red cells. Persons may thus have type A, type B, type O, or type AB blood (Table 2).



**Figure 1:** Confirmed cases and deaths of COVID-19 in Gulf countries for March- April.

**Table 2:** The ABO blood groups involve two antigen and two antibodies found in human blood.

<b>System</b>	<b>Recipient Type</b>	<b>Donor Red Cell Type</b>	<b>Donor Plasma Type</b>
<b>ABO</b>	A	A or O	A or AB
<b>ABO</b>	B	B or O	B or AB
<b>ABO</b>	O	O only	O, A, B, or AB
<b>ABO</b>	AB	AB, A, B, or O	AB
<b>Rh</b>	+	+ or -	+ or -
<b>Rh</b>	+	+ or -	+ or -

The four ABO blood groups consist of two antigens (A and B antigens), they are produced by ABO gene and are autosomal codominant. The group O phenotype is an autosomal - recessive phenotype due to the homozygous inheritance of two null ABO alleles; group O also express the H antigen, the biosynthetic precursor to A and B antigens. In addition to red blood cells, ABH antigens are widely expressed in many other tissues and secretions, such as intestinal mucosa, kidney, heart endothelium and other organs and for such reason the virus which display many glycosylated regions could adhere to other organ such as intestinal mucosa. One of the most attractive areas of research is to find whether blood type and their natural antibodies could reduce the spread or severity of infection. On the other hand, many research were focused on the role of blood group in infection incidence of many pathogenic bacterial species as Enterotoxigenic *Escherichia coli*, *Vibrio cholerae*, *Pseudomonas aeruginosa*, as well as many viruses as norovirus. The most acceptable theory is that antigens of blood group on different cells can act as binding receptors which allow bacteria and viruses to attach and enter the cells [8]. On the other hand, anti-A and anti-B antibodies may be part of the body's natural defence that take place in prevent infection or limit it.

The original severe acute respiratory syndrome outbreak caused by SARS-CoV in winter of 2002 to 2003 which infected 8000 persons worldwide, with fatality rate of 10% [9]; SARS-CoV is an enveloped RNA virus which adheres to host cells via viral adhesion glycoprotein the spike protein 210 kDa - 230 kDa with 23 potential N-glycosylation sites [10]. The analysis of glycan structure showed a wide range of structures, including complex N- glycans with 2 to 4 antennae capable of supporting ABH epitopes. The main host target cells of SARS-CoV are respiratory and gastrointestinal mucosa, so its likely most human isolates express ABH antigens on the S protein and host envelope GSLs; expressing A antigen can blocked by monoclonal anti-A and human anti-A [11]. Recent pandemic SARS-CoV-2 is similar in structure to SARS-CoV regarding its spike protein which is called NSP15; scientists from US found 89% identity to NSP15 for both viruses. However, spike protein for SARS-CoV-2 is 10 times - 20 times more likely to attach to human cells which explain its rapid spread though the world.

According to epidemiological study as well as in vitro study, Guillon et al. [9] hypothesized that group O persons are more resistant to SARS-CoV due to ABO antibodies and could decreased the rate of infection throughout the population. The same pattern of distribution of blood group [12] O, A, B, AB occurring in the order O > A > B > AB were reported in the studies from neighbour countries; Saudi Arabia [13], Kuwait [14], Iran [15]. Although, protection from infection may be influenced by the ABO antibodies titer, secretor status and the incidence of group O in population. High titer of anti-A (1:256) gave effective blocking to infection while lower titer was ineffective [16]. Other factors may affect such as the environment of population as industrialized countries tend to be less in ABO- antibodies titer. A non-secretor phenotype would also nullify viral neutralization, since viral transmitted from a non-secretor lacks ABH expression. The result of Zhao and others [7] a significantly increased risk of blood group A for SARS-CoV-2 in comparing to group O. The clinically significant of ABO blood group

have more importance than being responsible of blood transfusion and immunohematology. The differences in major antigens present on the surface of red blood cells and other epithelial cells, have proved association between ABO blood group and number of diseases [8], beside infections, the most important are, cardiovascular disorders, diabetes and interleukin-6 and IL-10, IL-18 which may affects the infection with recent pandemic SARS-CoV-2 (table 3).

**Table 3:** Relationship between ABO group risk factor and diseases.

Disease	Low Risk	High Risk	Order of Risk	Reference
COVID-19	O	A	A-B-AB-O	
Diabetes	O	B	B-A-AB-O	
Hypertension	AB	O	O-A-B-AB	Iraq
	AB	O		Iran
	-	-	AB=B=A=O	Saudi Arabia
Hypertension	B	AB	B-O-A-AB	
Cardiovascular	O	B	B-A-AB-O	
	AB	O	O-A-B-AB	
IL-10	AB	O	O-A-B-AB	
IL-6	AB	O	O-A-B-AB	

The involvement of ABO blood group and diabetes was ensured by many researchers, it was found that blood type O had a lower risk of type 2 diabetes mellitus [17]. Another work found that B group was more prevalent in diabetic patients [18,19].

Hypertension has a huge impact on the health of communities at whole world, it suspected to link to ABO blood group via genetic determine at conception and remain fixed for life. Hence, its frequency distribution follows a known pattern governed by gene transmission from generation to generation and varies with the race and geographical distribution of the human being [20]. There are reports of increased cardiovascular (CV) risks in different blood groups (non-O group) and increase in BP is considered as a common CV risk.

A study came from Iraq suggested that blood group O is at risk of hypertension and total cholesterol followed by group A, B then AB [21]. Coronary Artery Diseases in Iranian Patients is more prevalence in blood group O comparing with other group [22]. Other estimation of hypertension gave the percentage as follow B (8.7%) followed by group O (7.6%) group A (3.7%) and group AB (1.9%). Inflammation interleukins are also associated with ABO blood group; ABO antigens O and A2 are associated with increased IL-10 levels and decreased VWF level, and that the ABO antigens also influence the levels of sTF in patients have Artery coronal syndrome which are associated with disease outcomes in ACS patients [23].

Since the emergences of COVID-19 much research were conducted to determine specific comorbidities associated with increased risk of infection and worse outcomes with development of increased severity of lung injury and mortality. The most common comorbidities in one report were hypertension (30%), diabetes (19%), and coronary heart disease (8%). Diabetes has emerged as an important risk factor for severe illness and death from COVID-19 [24]. Diabetes was present in 19% of COVID-19 cases in Wuhan, China, and non-survivors were significantly more likely to have diabetes than survivors (31% vs. 14%, P = 0.0051). While another study found that 27% of patients achieving the primary endpoint of intensive care unit (ICU) admission, mechanical ventilation, or death, compared with 6.1% if none of these complications occurred. Also, Bruce Bode et al. [25] in USA diagnosed that

diabetes and/or uncontrolled hyperglycaemia occurred frequently among COVID-19 patients who had a particularly high mortality rate reached to 28.8% in diabetes patients who infected with COVID-19.

A Chinese study dealing with COVID-19 markers determine that baseline of IL-6 was significantly increased in patients with severe type which is closely related to the maximal body temperature during hospitalization and CT findings. Baseline IL-6 was also significantly related to the increase of baseline level of CRP, LDH, ferritin and D-dimer [26]. The increase of baseline IL-6 level suggests that it may positively correlate with the cytokine storm syndrome of COVID-19. Early study by Jaques [27] demonstrated that a surface viral protein from the SARS virus directly stimulated the production of tumour necrosis factor (TNF)- and interleukin.

Recent pandemic SARS-CoV-2 is similar in structure to SARS-CoV regarding its spike protein which is called NSP15; scientists from US found 89% identity to NSP15 for both viruses. However, spike protein for SARS-CoV-2 is 10 times - 20 times more likely to attach to human cells which explain its rapid spread though the world. Proteome analysis derived from online NCBI databases showed existing the following:

- A polyprotein orf1a 7096 amino acid long (QHD43415.1)
- A surface glycoprotein “Spike” (1273 aa - QHD43416.1)
- ORF3a or structural protein E (273 aa - QHD43417.1)
- An envelope protein (ep – 75 aa - QHD43418.1)
- A membrane glycoprotein (MGP – 222 aa - D43419.1)
- ORF6 (61 aa - QHD43420.1)
- ORF7a (121 aa - QHD43421.1)
- ORF8 (121 aa - QHD43422.1)
- A Nucleocapsid phosphor protein (419 aa - QHD43423.2)
- ORF10 (38 aa - QHI42199.1)

## **CONCLUSION**

Vaccines for BCG and Measles that are causing COVID 19 immune reactions over the last decades; Gulf countries sanitation and immunization approaches; Although there were a thousand of cases in eight countries in April, the amount of coronavirus has been increasing every day, the Gulf countries could have shut their borders down fast enough to avoid the pandemic. However, the pandemic will continue to obscure the culture of these countries, especially during religious visits to Hajj and Umrah.

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