

Covid-19 Virus Variants and Gender Distribution over the Common Four Waves of the Outbreak

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Abstract

Background: Coronavirus disease-19 (COVID-19), produced by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic, giving rise to a serious health threat globally.

Aims: The aims of the current study were to investigate the distribution of the viral variants that caused the epidemic and to determine the rate of infection in a gender-based approach.

Methods: The current study is a retrospective cohort study which involved 999 cases of covid-19 infection recovered from passengers crossing Ibrahim Al khalel border, Zakho, Kurdistan region, Iraq. Sample collection started at 15th March until 15th October 2020. All patients admitted in march 2020 were considered to be in the first wave, all those whose admission date started at January 2021 in the second wave. The admission of July 2021 was considered as the third wave of the pandemic in this region, and the patients admitted in February 2022 assigned to the fourth wave of the epidemic. The infection was confirmed by RT-PCR after obtaining swab samples from the upper respiratory tract (nasopharyngeal/oropharyngeal exudate). Multiple virus variants were investigated in the present work by utilizing variant-specific primers and the resultant viral strains were assigned to the waves of infection. During the current study, four waves of COVID-19 were reported.

Results: The minimum percentage (11.01 %) of the participants were affected during the first wave while the higher percentage (47.65 %) was for those who experienced the disease during the fourth wave; moreover, 12.71 % and 28.63 % were reported for the participant who have been through the second and the third waves, respectively. The results also revealed that females were more affected by the disease (52.65 %) compared to the males (47.35 %). The results showed that six virus variants dominated the four

waves of viral spread. The alpha (B.1.1.7) and the alpha (B.1.1.7.2) variants were reported in the four waves of the disease, three more variants namely beta (B.1.351), delta (B.1.617.2), and delta (B.1.617.3) were reported in the second, third, and fourth waves of the pandemic; while omicron BA.2 (B.1.1.529.2) variant was reported in the fourth wave exclusively. There was statistically significant association between gender and the wave of infection ($p < 0.001$).

Conclusions: In conclusion, the infection had differential pattern of distribution by gender and the presence of multiple variants in a single wave referred to the rapidly changing nature of the virus.

Keywords: RT-PCR, Covid-19, Omicron, Variants

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Introduction

Coronavirus disease-19 (COVID-19), happens because of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic, it led to major health threat worldwide. However, Coronaviruses have been also identified in animals and can cause a range of severe diseases such as gastroenteritis and pneumonia (1, 2). Previous coronavirus outbreaks have been reported, including severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV), which is characterized as a significant public health threat (3). In 2002, coronavirus infections (SARS-CoVs) distributed in Guangdong, south China, leading to high fever, breathlessness and pneumonia, and rapidly spread to various areas around the world. The contagion has spread in 26 countries, resulting in about 8096 cases and 774 deaths (4). Whereas MERS-CoV was first detected in Saudi Arabia in 2012. The disease has mild respiratory symptoms that can lead to acute respiratory syndrome and death. 2494 cases were infected by the virus, of which 858 died in more than 25 countries (5,6).

On December 2019, unknown pneumonia was first recorded in Wuhan city, Hubei province. Patients have manifested high fever (more than 38 °C), dry cough, indisposition, and difficulty breathing. The infection has been related to the seafood market of Wuhan, China and named COVID-19 (7,8). It spread rapidly to other Far East Asian nations, then to the Middle East and Europe. In acute cases the disease causes pneumonia, septic shock, metabolic acidosis and bleeding (9). The incubation period has been estimated from 5 - 14 days and may vary from patient to patient according to age and infection history (8). The World Health Organization (WHO) later renamed the illness caused by SARS-CoV-2 as Coronavirus Disease-2019 (COVID-19) (10). Person-to-person transmission by inhalation or contact with droplets emerged as a major source of infection, while more recently aerosols, the stability of SARS-CoV-2 on surfaces, and the potential of fecal-oral infection routes have been discussed (11,12). Many

countries have experienced multiple waves of coronavirus outbreaks. During the 2020 pandemic, empirical data show that characteristics varied between waves (13).

The aims of the current study were to investigate the distribution of the viral variants that caused the epidemic and to determine the rate of infection in a gender-based approach.

Materials and methods

Study design

We conducted a retrospective cohort study (all data were fully anonymized before the researchers accessed) of all cases (999 cases) of SARS-CoV-2 infection in Ibrahim Al khalel border, Zakho, Kurdistan region, Iraq. All patients admitted in march 2020 were considered to be in the first wave and all those admitted from January 2021 in the second wave. During July 2021 considered as the third wave of the epidemic in this region, and the patients admitted in February 2022 assigned to the fourth wave of the epidemic.

Data collection and study population

SARS-CoV-2 infection was confirmed by RT-PCR using swab samples from the upper respiratory tract (nasopharyngeal/ oropharyngeal exudate). RNA was extracted by a special kit (Zebio) then reverse-transcribed to cDNA and subsequently amplified by the Rotor-Gene Q, Real-Time PCR Instrument with rotor-gene-6000 software.

Study Population. COVID-19 infection database was queried to identify all recorded, gender, the distribution of viral variants according to the wave of infection, the cases in which such information was missing were excluded.

Statistical analysis

Data analysis was performed using SPSS-26 software package. Chi-square of independence test was used for data analysis. A $p \leq 0.05$ was considered as statistically significant.

Results

The results of the present work showed that the area of interest had recorded four waves of COVID-19 pandemics. Figure 1 revealed that the minimum percentage (11.01 %) of the participants were affected during the first wave while the higher percentage (47.65 %) was for those who experienced the disease during the fourth wave; moreover, 12.71 % and 28.63 % were reported for the participant who have been through the second and the third waves, respectively.

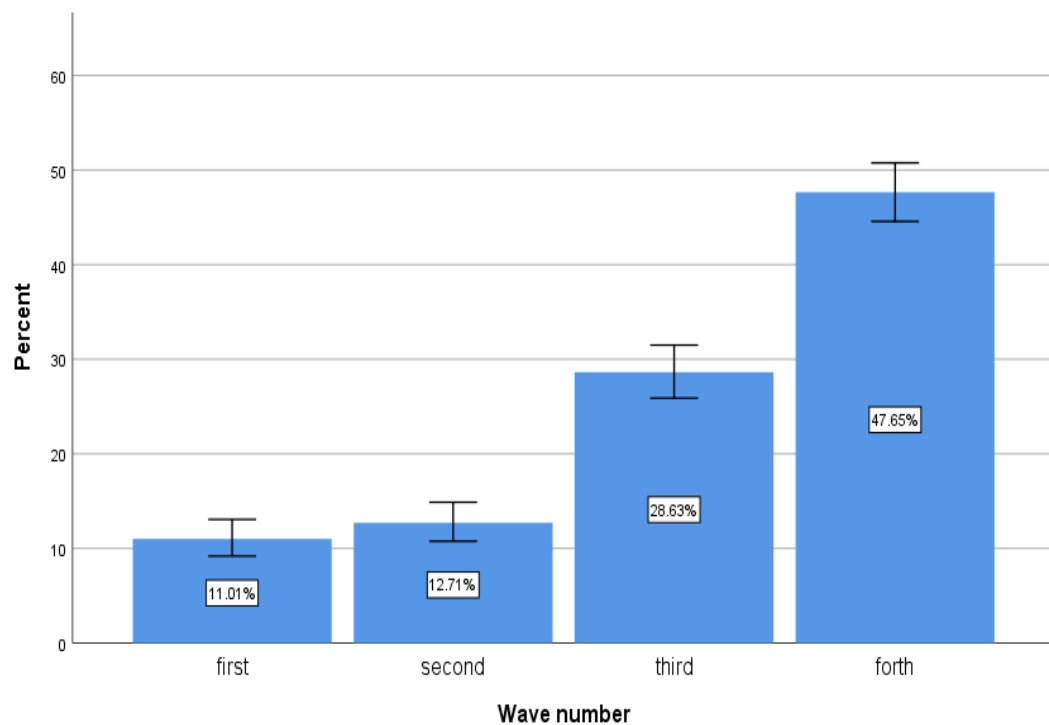


Figure 1: The frequency of the participants classified according to the wave of the pandemic

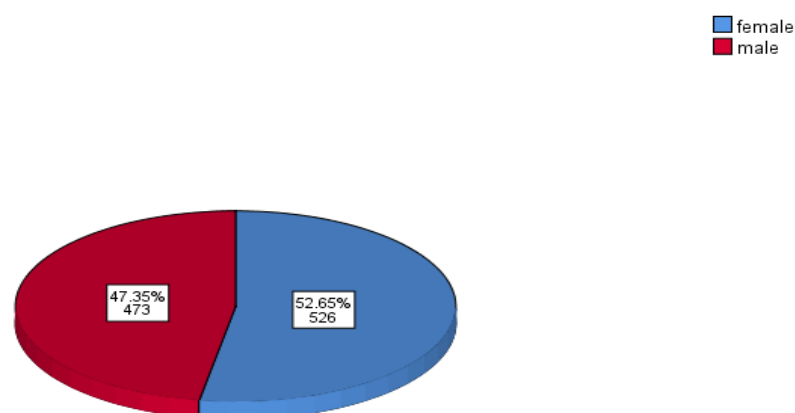


Figure 2: A pie chart showing the distribution of gender in the present work.

The results of the current study showed that female participants (52.65 %) were higher than the males (47.35 %) (Figure 2). The results showed that the six variants of the virus were unevenly distributed across the waves of the pandemic. The alpha (B1.1.7) and the alpha (B1.1.7.2) variants were reported in the four waves of the disease with percentages of 13.1 % and 15.4 %, respectively, three more variants namely beta (B.1.351), delta (B.1.617.2), and delta (B.1.617.3) were reported in the second, third, and fourth waves of the pandemic; they constituted 17.0 %, 19.8 %, and 20.0 % of the total patients, respectively. Finally, omicron BA.2 (B.1.1.529.2)

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variant was reported in the fourth wave only with a percentage of 14.6 % of the total cases (Figure 3).

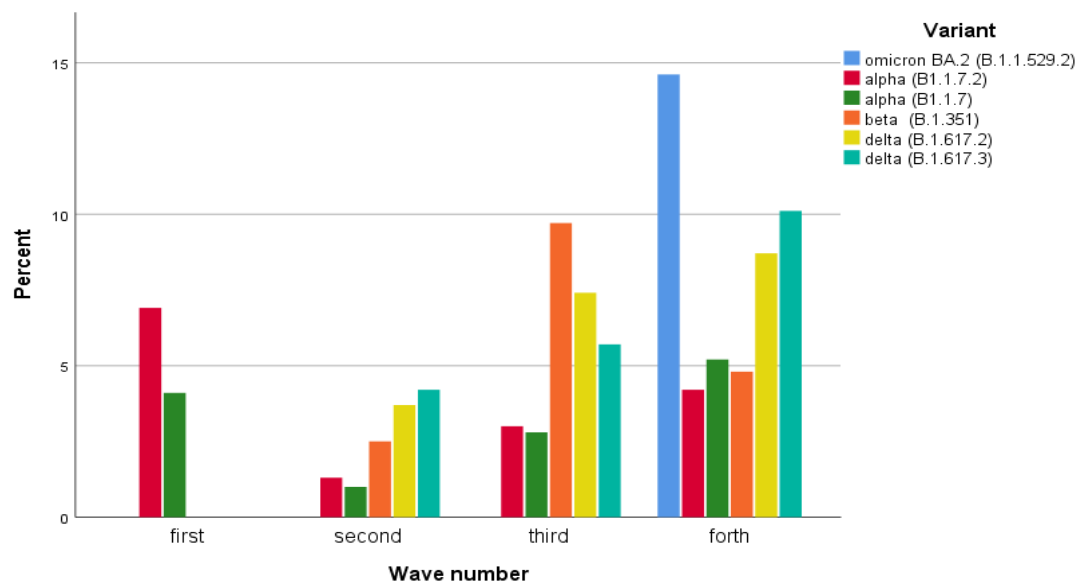


Figure 3: The distribution of viral variants according to the wave of infection

In the current study, the association between gender and the wave of infection was investigated. There was statistically significant association between gender and the wave ($p < 0.001$) with a higher percentage of females (52.65 %) having the infection compared to males (47.35 %) (Table 1).

Table 1: The frequency of participants' gender according to the wave

Gender		First wave	Second wave	Third wave	Fourth wave	Total	P value
Female	Count	38	53	168	267	526	<0.001*
	% within gender	7.2%	10.1%	31.9%	50.8%	100.0%	
Male	Count	72	74	118	209	473	
	% within gender	15.2%	15.6%	24.9%	44.2%	100.0%	

*Significant at $p \leq 0.05$

Discussion

Iraq reported its first COVID-19 case on 24 February 2020. The patient was an Iranian student who has been studying in the Najaf governorate and had entered the country before the implementation of banning Iranian nationals from entering Iraq. Only two days later, a family of four from Kirkuk governorate was diagnosed with the disease; the family had just returned from Iran. On the third of March 2020, the Sulaymaniyah governorate reported the death of 69-years

old COVID-19 patient (14), this was the first death due to the disease, after which the number of cases and deaths started to escalate.

In the first wave (March/2020), most reported cases occurred among people of Kurdistan region. In addition, severe illness was characterized by continuous cough, exhaustion, tasteless tongue, difficulty breathing, loss of smell, and fever greater than 37°C (15). Main risk sources were close contact with a previously confirmed patient and community risk. From that time, the number of cases of COVID-19 in Kurdistan region increased slowly but steadily due to both imported cases and local transmission. Since the first wave, clusters of outbreaks have been traced to super spreading events in sports venues or indoor entertainment establishments (16). By the end of February 2021, there was a sharp rise in the number of daily reported cases, which culminated in the second wave of the pandemic. Relaxation of interventions, negligence in public behavior, waning immunity, some superspreader religious and political events, and the emergence of more transmissible variants (B.1.617 lineage) are the various reasons that led to the onset of the second wave (14). The main risk sources were cluster communities and close contact with earlier positive cases of the disease. One of the factors behind the outbreak was the dense living conditions of the population in the surrounding community and the lack of personal precautions to prevent infection spread (16). During the third and fourth waves, super spreading events were recognized at the entertainment establishments, shopping, bars, and various types of touristic places in different Kurdistan regions. Number of cases increased more than the first and second waves combined. The result of the present work was compatible with many studies in Iraq, the neighboring countries, and the all the countries, that showed a direct increase in number of infected people during the four wave (17,18). The fourth wave differed from the previous ones by the emergence of omicron variant which has led to extraordinary rates of COVID-19 worldwide. Omicron hosts a striking number of mutations in its spike gene. Early reports have provided evidence for extensive immune escape and reduced vaccine effectiveness, leading to a higher transmission rate (19). The results were also in line with Lami and coworkers who clarified that during weeks 9 to 14 of the outbreaks, the cases were steadily increasing, almost doubling weekly. After a slight decrease in weeks 15 and 16, the number of cases started to rise again in week 17. However, the major surge in the number of cases occurred in week 23 (the first week of June). Since then, cases continued to increase dramatically until weeks 41 and 42 when a significant decrease happened (17). Current study findings harmonized with the results of another group of investigators (20) who found that the infection rate was higher in females (57.5%) as compared to males (42.5%) in the inhabitants of Basrah city and Hartha district; the results were also compatible with results of Musa and Ateya (21) who had described a nearly similar findings, another group of researchers reported contradictory finding in Iraq/ Najaf where they revealed that males (57%) were found to be more infected than females (43%) (22). Our results were in line with results of De Francia and coworkers (23) who found the number of women who had the infection was higher than the number of men in each period-related percentage. The higher infection rate in females than males reported in this study could be

attributed to their role in caregiving within the family or prolonged period of exposure to index cases within the family (24). Women have less access to information than men, Consistent with global trends, the COVID-19 pandemic has catalyzed a dualistic public health crisis in the Kurdistan Region of Iraq (KRI). The KRI has also seen a surge of gender-based violence (GBV) throughout COVID-19 (25). All viruses change over time, and SARS-CoV-2 is no exception, a change in the genetic sequence is called a mutation (26). Genomes that differ from each other in genetic sequence are called variants. Variants can differ from each other by one or more mutations. When a phenotypic difference is demonstrated among the variants, they are called strains (27). Both Beta-B.1.351 (severe illness and death; current data do not indicate more severe illness or death than other variants) and delta-B.1.617.2 (severe illness and death, may cause more severe cases than the other variants) strains were found during third wave of the outbreak (16). Main risk sources were close contact with a previously confirmed patient, active and community surveillance, and cluster communities. Due to the highly transmissible nature of COVID-19, delayed intervention may have led to rapid spread. Hence, this study found considerable differences between the three waves of the COVID-19 pandemic in Kurdistan region. Our results indicate that the third wave is more serious than previous waves, which may be due to a lack of strong social distancing policies and public health interventions. Our findings differ from other studies showing that the first wave of COVID-19 pandemic had the most negative impact on public health. In contrast, the second wave evidenced more stable evolutionary dynamics (16). In addition, sufficient epidemiologic investigations and contact tracing could not be performed during the third wave, and there was a marked increase in the proportion of unknown routes of transmission. Reason for the obvious differences across phases and waves is not yet known, although it has been suggested that a new variant of COVID-19 emerged in Kurdistan region in the middle of 2021, and transmission to the general population was replicated across the country. The globalisation, settlement, and population characteristics related to high human mobility and interaction predict disease diffusion (28). However, in this study, the most striking difference between the first, second, and third waves in Kurdistan region was implementing public health interventions. Health vulnerabilities are especially related to disease exposure in the short-term. There is a larger share of women in the health sector, and as home and family caregivers, which makes them more exposed to contagion. Occupational sex-segregation might also bring different levels of exposure. As an example, women are more present in client-facing roles while men concentrate in logistics or security. Providing protective equipment and materials and COVID-19 testing to higher-risk populations will be key to prevent their contagion (29). Evidence from infectious disease outbreaks similar to COVID-19 indicates that women and girls can be affected in particular ways, and in some areas, face more negative impacts than men. Gender gaps in outcomes across endowments, agency and economic opportunity persist across countries. The impact of the COVID-19 pandemic will be amplified by those pre-existing gender differences. For the most part, the negative impacts can be expected to exacerbate (i.e. more individuals are affected) and deepen (i.e. the conditions/disadvantages of

some individuals worsen) (30). In conclusion: In conclusion, the infection had differential pattern of distribution by gender and the presence of multiple variants in a single wave referred to the rapidly changing nature of the virus.

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Author contributions

Marwan Khalil Qader was responsible for laboratory work.

Fatima Nawaf Abdulkareem and Haveen Khalid Hasan were responsible for sample collection. Amir Hani Raziq and Rana Adil Hanoon were responsible for writing the manuscript and data analysis

A distinction is made between five types of contributions: Conceived and designed the analysis; Collected the data; Contributed data or analysis tools; Performed the analysis; Wrote the paper.

Conflict of interest

We are the authors declare that we do not have a conflict of interest to disclose.

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