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Review Article

The association between Crimean-Congo hemorrhagic fever and COVID-19 outbreaks in Iraq: A review

Yasameen Hasan Jumaah[1], Noorhan Sabih Al-Maliki[1], Ola Emad Khudhair[1]

[1] College of Biotechnology, Al-Nahrain University, Baghdad, Iraq.

*Corresponding author:

Dr. Noorhan Sabih Al-Maliki

College of Biotechnology,Al-Nahrain University, Baghdad, Iraq.

E-mails: noorhan.sabih@nahrainuniv.edu.iq

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Abstract

The 2019 novel coronavirus originated in Wuhan, China, and is rapidly making its way across the rest of the world, causing a worldwide epidemic. The first case of COVID-19 was reported for a traveler entering the city of Najaf and has since spread to all the cities in Iraq. The WHO declared the latest COVID-19 outbreak a worldwide pandemic on March 11, 2020. Crimean-Congo hemorrhagic fever (CCHF) is also one of the issues facing public health that emerged after the COVID-19 outbreak. It has been spread widely in Iraq. Ticks on human or animal tissue or blood are typically the source of infection. The World Health Organization (WHO) has designated CCHFV as a high-priority virus because of its high death rate and lack of viable medical countermeasures. Despite the differences in transmission dynamics and clinical manifestations, there are overlapping epidemiological factors and potential interactions between these two diseases. These two outbreaks cause a serious health issue in Iraq and a high rate of mortality due to the lack of management and control of their spread; furthermore, the absence of health care in hospitals and the lack of medicines and vaccines. Understanding their association is crucial for effective surveillance, diagnosis, and management strategies to mitigate the burden of both diseases in Iraq. This article discusses the two viruses and their emergence in Iraq.

Keywords: COVID-19, Crimean-Congo hemorrhagic fever, pandemic, vaccines.

Introduction

A zoonosis is essentially an infectious disease brought on by pathogens that are spread from animal to human [1,2]. It is currently a public health concern, particularly in the context of the recent pandemic (COVID-19), which has harmed millions of people worldwide and caused economic damage. As a result, there are still worries regarding the start of new, potentially uncontrollable epidemics, particularly viral ones [3,4]. Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic disease that may impact humans. It is caused by a virus that is part of the Nairoviridae family [5]. Symptoms like fever, myalgia, and gastrointestinal issues characterize the disease. It can also lead to hemorrhagic manifestations from different organs and has a 30% mortality rate [6,7]. Normally, ticks or getting in contact with the bodily fluids of infected animals or people spread this hemorrhagic disease to humans. Considering that they can harbour the virus for months or even years, ticks—particularly those belonging to the genus

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Hyalomma—are the virus's natural carriers and reservoirs [8]. Two distinct but important infectious diseases that have an impact on global public health are COVID-19 and CCHF. The main ways that CCHF is spread are either through tick bites or coming into contact with infected animals. Conversely, COVID-19 is predominantly spread by respiratory droplets and close contact with infected persons, and is caused by the new coronavirus SARS-CoV-2. There is rising interest in investigating possible correlations between COVID-19 and CCHF outbreaks, despite their different mechanisms of transmission and clinical manifestations, especially in areas where both diseases coexist, like Iraq. The increase in cases of COVID-19 in Iraq has led to an increase in the number of CCHF cases due to blood exchange procedures performed for COVID-19 patients and a general decrease in public health preventative measures against vectors for CCHF [9,10].

Background

Both COVID-19 and Crimean-Congo hemorrhagic fever (CCHF) are zoonotic illnesses that have the ability to spread from person to person and cause significant outbreaks or epidemics. In comparison with COVID-19, which is caused by the SARS-CoV-2 virus, not much is known about CCHF, which is caused by the CCHF virus (CCHFV). A nairovirus belonging to the Bunyaviridae family, CCHFV is mainly transmitted by ticks or animals to animal workers. Cattle are the main hosts of CCHFV; during their asymptomatic viremic stage, the tick becomes infected. There have been cases of CCHFV being brought to countries outside of these endemic zones, such as India and some eastern European nations, as a result of returning tourists incubating the virus. This virus is endemic in regions of Africa, the Balkans, the Middle East, and parts of Asia. While CCHF outbreaks are recurrent, increasing in the spring and summer, the number of cases in Iraq has been rising since 1999, with over 300 cases reported in 2019. Multiple outbreaks have occurred in different regions. According to epidemiological studies, CCHF mostly affects farmers and those working in the livestock industry and is found in parts of Iraq. The disease is severe because it can cause epidemics, like the one that occurred in Dohuk in 2007 and resulted in 221 confirmed cases of CCHF. Environmental factors leading to higher tick on livestock and increased human-tick contact as a result of farm displacement as a result of conflict and financial challenges have been responsible for the rise in CCHF cases in Iraq. These recently resettled communities have poor herd immunity, which leaves them vulnerable to CCHFV. Cases in these locations have the potential to spread to other parts of Iraq as well as Iran [11,12].

Taxonomy and structure

Coronaviruses are encased, icosahedral symmetric particles with a diameter of around 80–220 nm. Their single-strand, non-segmented, positive-sense RNA genome is roughly 26–32 kb in size. One of the major groupings of viruses that are members of the family Coronaviridae, suborder Cornidovirineae, and order Nidovirales is the coronavirus (CoV). Nairoviridae is a family of the Bunyavirales order that comprises three primary genera, one of which is Orthonairovirus, which contains the CCHF virus along with fourteen other viral species.

This virus resembles a spherical particle with a diameter that ranges from 80 to 120 nm. Its single-stranded RNA genome has a segmented negative-sense. Three distinct segments comprise it: small, medium, and large (abbreviated S, M, and L, respectively) [13,14].

Figures 1 and 2 show the difference in taxonomy and structure between (CoV) and (CCHFV)

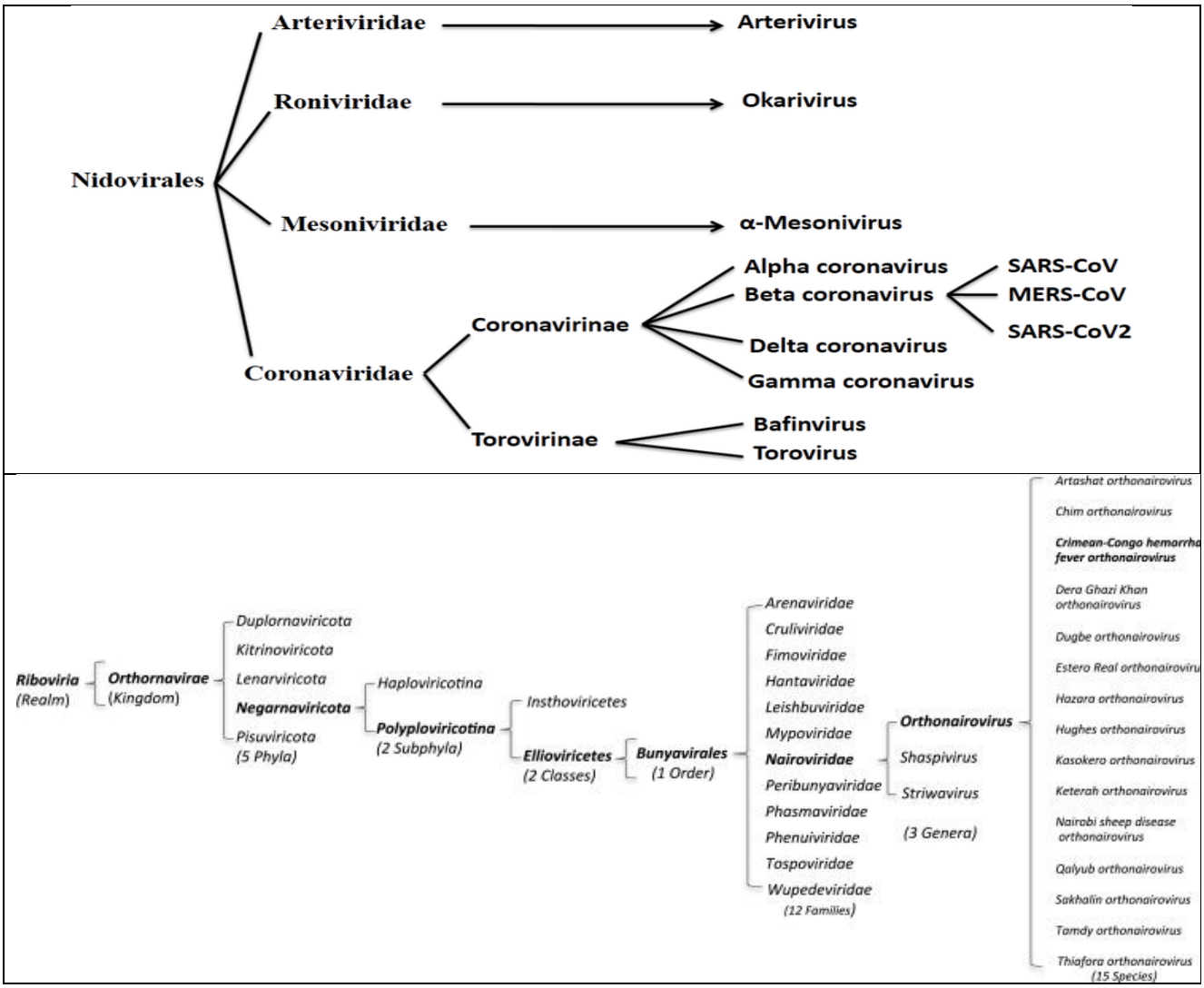

Figure (1): taxonomy of (CoV) and (CCHFV)

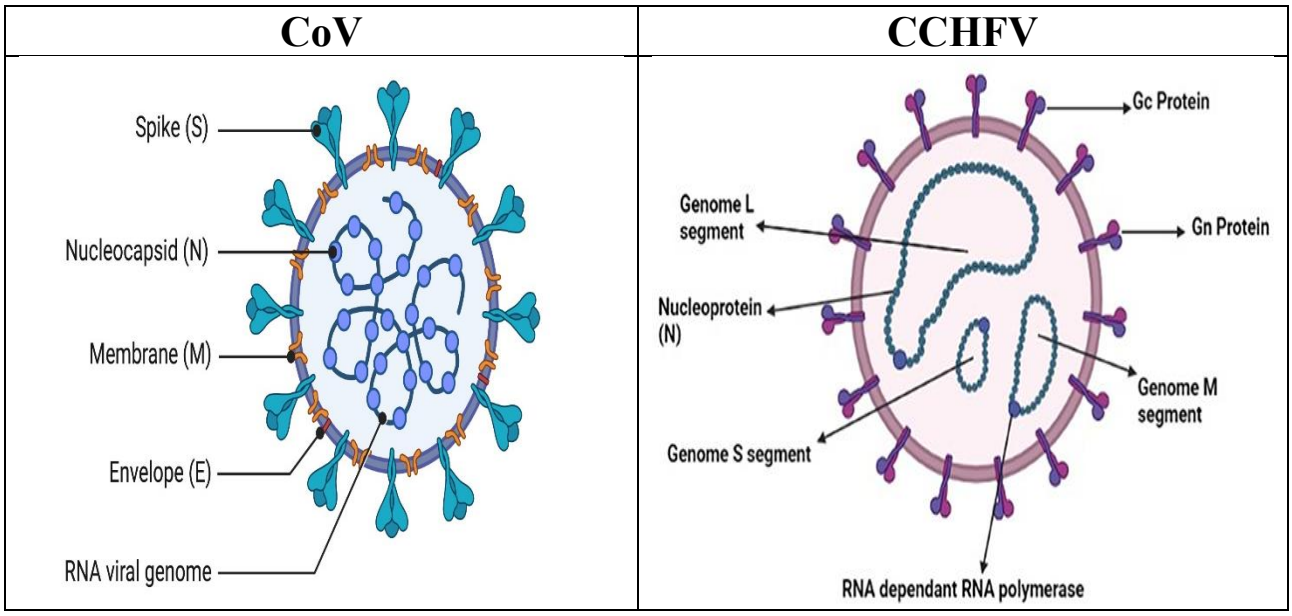

Figure (2): structure of (CoV) and (CCHFV)

Epidemiological

Since it is spread by ticks, CCHF is usually linked to the countryside; nevertheless, outbreaks have also occurred in cities, particularly in places with inadequate healthcare facilities and poor sanitation. Conversely, COVID-19 has impacted Iraqi residents in towns as well as villages. People may be more exposed to ticks, the CCHF vector, and come into close contact with others in areas where both diseases are prevalent, such as those with livestock raising and agriculture, which raises the likelihood of COVID-19 transmission. The possibility of co-infection rises due to this overlap in exposure, which also poses difficulties for attempts to control the disease [15].

Turkey and Iran are the main pandemic locations, with over 10,000 cases documented in Turkey since 2002 [16]. CCHF is regarded as endemic in a few countries in the eastern Mediterranean, including Iraq [17]. In 2010, there were 28 suspected cases and 11 confirmed cases. The percentage of instances that ended in death varied from 4% in suspected cases to 36% in confirmed cases [18]. In 2018, three fatal cases were documented; more recently, in 2021, 33 verified cases, including 13 deaths, were reported [17]. Iraq reported 212 instances between January 1, 2022, and May 22, 2022, of which 115 were suspected and 97 were confirmed. Of the 27 fatalities, 14 were linked to suspected cases and 13 to cases with laboratory confirmation. A significant number of cases have been reported compared to 2021 [17]. In addition to all of the above, COVID-19 has further reduced access to alternative healthcare options and become the global centre of attention for the medical community. Since 1979, CCHF has been endemic in Iraq, and the number of patients has risen yearly. However, as with many other diseases, CCHF has faded from the attention of healthcare administrators, leading to increasing of cases in 2018 to 33 cases in 2021 to 212 cases in just 5 months of 2022 [18]

Between January 1, 2022, and May 29, 2022, Iraq recorded 212 instances of CCF. Compared to 2021, when there were only 33 cases reported for the entire year, this is already six times more. Of these 212 instances, 97 (46%) have laboratory confirmation, and 115 (54%) are suspected cases. There have been 27 CCHF-related deaths; of those, 14 were suspected, and 13 were confirmed by a lab. Tick infestations in livestock animals can endanger those who are related to the animals [19].

In Iraq, where raising cattle is a common routine, it is especially concerning. A large number of the deceased were either butchers or shepherds or had some connection to them. With more than 2 million COVID-19 cases since the pandemic's beginning, Iraq's healthcare system is working under immense pressure. Further outbreaks will put the Iraqi people under extreme financial and psychological strain in addition to taking lives [15].

Mode of Transmission

Family members who have had direct contact with incubation carriers or patients, such as friends and relatives, are the main conduits for the spread of SARS-CoV-2 [20]. The nosocomial transition is the main method of transmission for SARS-CoV. The primary method of transmission was thought to be eating wild animals or having direct contact with intermediate host animals; nevertheless, the source(s) and method(s) of SARS-CoV-2 transmission are still unknown [21-22]. The virus is transmitted by coughing or sneezing among close contacts, just like the influenza virus and other respiratory diseases. COVID-19 is more prevalent in older adults, newborns, those with compromised immune systems, and those with heart or lung conditions [23].

All potential SARS-CoV-2 infection pathways, such as droplet transmission (family members, family visitors), intimate contact, and all hospital infections, are instances of the virus spreading vertically from the mother to the fetus [24]. When droplets from respiratory sources—like those released when an infected person coughs or sneezes—are inhaled or consumed by individuals in contact with the transmission, this phenomenon is known as droplet transference. When someone contacts a surface or object contaminated with a virus and then touches

their mouth, nose, or eyes, this is referred to as close proximity. Droplet transmission has also been linked to this type of interaction. Infection can occur when respiratory droplets combine with the air to generate aerosols. when a significant quantity of aerosols is breathed into the lungs in a small area [25].

Particularly those belonging to the Hyalomma genus, ticks are effective carriers and the main source of CCHFV. Humans typically contract the virus by biting or crushing infected ticks with their bare hands, coming into contact with the tissues or blood of infected animals, or even individuals [26], as depicted in Figure 3. In order for those who come into contact with animal blood, medical employees in laboratories and personnel are more susceptible to infection. It is possible to spread this illness. from one individual to another via contacts or diseases picked up in hospitals. Additionally, Fetal and newborn mortality may result from significant maternal–fetal transmission of CCHF [27]. Tick proliferation occurs in the spring and summer, when the infection rate is highest. The environment in which ticks grow and their capacity to spread this virus are significantly correlated. It should be mentioned that the causal virus is highly transmissible in environments with mammals, including sheep, rabbits, and cattle, regardless of size [28]. By causing the spread of infection, the virus penetrates the tick's intestinal walls and salivary glands, maximizing the insect vector's effectiveness. relies on preventing the tick's natural immunological reaction. Tick survival, behavior, and gene expression can all be impacted by viral infection, which is not always quiet [29-30]. Figure 3 shows the difference in the mode of transmission between CoV and CCHFV.

Symptoms

It's concerning that COVID-19 may share the signs of CCHF. It might be fatal if CCHF is misdiagnosed as COVID-19. Therefore, it is essential to properly exclude suspected CCHF cases [31]. This acute viral infection usually comes with headache, fever, tiredness, inflammation, petechial haemorrhages, headaches, and broad body pain. There have also been reports of photophobia, dizziness, myalgia, malaise, abdominal discomfort, and other gastrointestinal (GI) symptoms [32]. In extreme cases of hemorrhagic fever, oral ribavirin can be administered, yet no antiviral medication is effective against CCHF [33]. There have been several difficulties since CCHF first appeared in Turkey during the COVID-19 pandemic. According to recent reports, computed tomography (CT) findings and clinical symptoms of COVID-19 and CCHF are similar. Therefore, extra caution should be used while interacting with suspects who exhibit these clinical signs. A common symptom of COVID-19 includes fever, dyspnea, weakness, dry cough, and loss of taste and smell. Therefore, in endemic places, CCHF should be considered as part of the differential diagnosis, especially for patients with ground-glass opacities on chest CT scans [33,34].

The diagnosis of co-infections between COVID-19 and CCHF raises notable difficulties because of the overlap in clinical symptoms and the restricted availability of diagnostic testing in resource-constrained environments. Since fever, malaise, and respiratory symptoms are shared by both illnesses, it is challenging to distinguish between them just on the basis of clinical presentation. Accurate diagnosis depends on laboratory confirmation via serological and molecular testing, which may not be easily accessible in all healthcare facilities, especially in rural areas. It is essential for prompt intervention and patient care to increase access to diagnostic technologies and educate medical personnel on how to identify and treat co-infections.

It has been shown that both CCHFV and SARS-CoV-2 are capable of viral evolution and adaptation, which may result in the formation of new strains with changed virulence or transmission dynamics. Viral genome alterations can alter host range, immune evasion, and viral replication, which can impact disease severity and transmissibility. For the purpose of detecting and responding to possible outbreaks as soon as possible, tracking the genetic diversity of viruses and keeping an eye out for new variations are crucial [33].

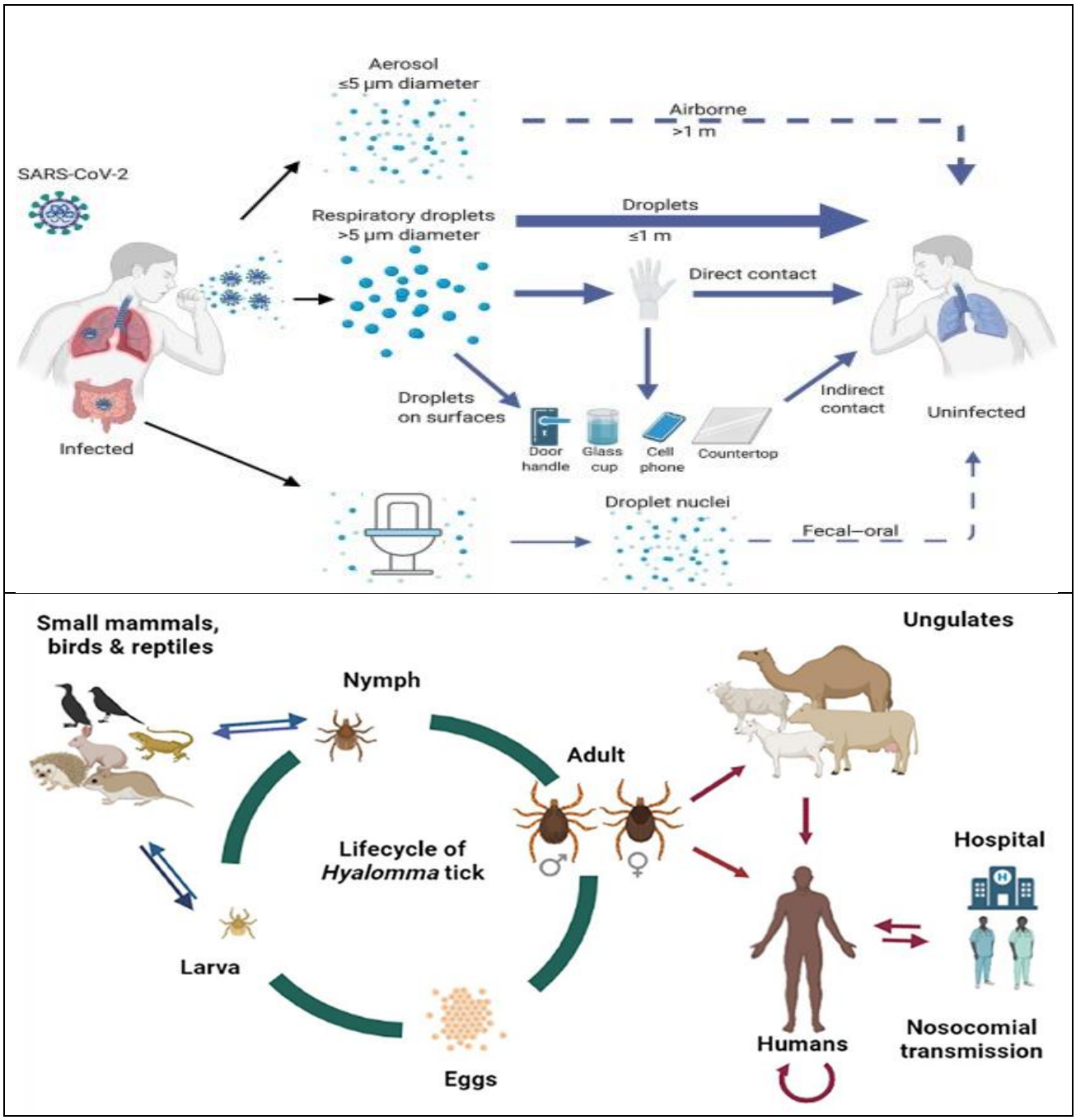

Figure (3): mode of transmission between (CoV) and (CCHFV)

Vaccination and treatment

When the first instance of COVID-19 was recorded for a tourist entering the city of Najaf, it triggered many studies and has since spread to every city in Iraq. On March 11, 2020, the WHO pronounced the most recent COVID-19 outbreak a global pandemic [35,36]. Five COVID-19 strains have surfaced in the UK, South Africa, Brazil, India, and other countries since December 2020. These strains are Alpha, Beta, Gamma, Delta, and Omicron. [37]. To protect people from COVID-19, different companies have created vaccinations using a variety of technologies. In Iraq, three different vaccine kinds were used: Pfizer, AstraZeneca-Oxford, and Sinopharm vaccines [38].

Any foreign object that enters the human body causes the body to mount an immunological reaction against it. This immune response includes the development of antibodies and anti-inflammatory substances like cytokines, which are essential for

controlling the immune response in both healthy and diseased conditions. APRs, one type of inflammation biomarker, exhibit significant changes in blood levels during inflammation. The liver creates these vital mediators in both acute and chronic inflammatory diseases [39,40]. Interleukin-6 is the main cytokine that stimulates the synthesis of liver (IL-6). APRs can also be brought on by a variety of research projects [40,41]. Every age group, gender, and race has been impacted by COVID-19, with varying rates of infection. It affects not only the respiratory system but also the gastrointestinal tract, liver, kidneys, and testicles, so the care of this unique group of patients needs extra focus. The biochemical indicators of liver disease include bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) [42].

The three negative-sense RNA segments that make up the CCHFV virus genome are small (S), medium (M), and large (L). The S segment encodes the nucleoprotein (NP) and the glycoprotein precursor (GPC), which subsequently generates mature Gn, Gc, and other nonstructural proteins, and is encoded by the M segment [43]. The L protein, responsible for viral RNA production, is encoded by the L segment. Although CCHFV has been identified from several tick species, Hyolamma ticks are the CCHFV's wide geographic spread makes it a host and biological vector, which strongly corresponds to the distribution of instances of CCHF [44]. After a brief incubation period of about one week, CCHFV infection in humans can cause mild to severe symptoms, including high fever, malaise, myalgia, and gastrointestinal distress. Hemorrhagic illness, which has a fatality rate of 5 to 30% in severe cases, is frequently brought on by disseminated shock, multi-organ failure, and/or intravascular coagulopathy [45]. The WHO has classified CCHFV as a high-priority virus because of its high death rate, broad vector, and lack of effective medical countermeasures for treatment and prevention [46].

While many CCHFV vaccines are offered, the Glycoproteins vaccine (GP) and the Nucleoproteins vaccine (NP) are the most successful. Because of its high immunogenicity and availability, the NP is a suitable target for CCHF vaccinations. Because the NP has B and T cell epitopes, it can stimulate the humoral and cellular immune systems. Immunological reactions [47,48]. The genetic diversity and several diverse lineages of CCHFV that are seen in various parts of the world are important considerations for the development of vaccines. The exceptional degree of conservation of CCHFV's NP across different virus strains indicates that NP may offer protection against several virus strains [49]. Using the glycoproteins Gn and Gc as antigens is one of the most promising methods for creating a CCHFV vaccine. These glycoproteins are found on the virus's surface and are in charge of making it easier for the virus to enter host cells. They are excellent candidates for vaccine development because they are also the main targets of the immune response during infection [50].

Conclusion

The correlation between COVID-19 outbreaks in Iraq and Crimean-Congo hemorrhagic fever demands additional research to clarify any possible connections between these illnesses. To reduce the burden of both diseases and protect public health in Iraq, integrated surveillance, improved diagnostic skills, and focused public health interventions are crucial. Effective collaboration among healthcare providers, academics, and policymakers is imperative in addressing the multifaceted problems presented by the simultaneous outbreaks of COVID-19 and CCHF. Note that the distribution of vectors is altered by global warming, which could raise the likelihood that this virus would spread to previously unexplored areas. Two of Iraq's neighbors, Turkey and Iran, are endemic for CCHF and have corroborated reports of recent outbreaks and an increase in cases. The number of cases has increased during the last two years, according to statements

made by the Iraqi Ministry of Health. More research is required to break the cycle of transmission, particularly in rural regions where raising livestock is popular. Therefore, an attempt ought to be made to widen the gap between the two. Moreover, the danger of transmission is increased by the slaughter of animals. Due to increased killing during holidays like Eid, as well as increased population migration, resulting in cross-border transmission.

Conflict of interest: NIL

Funding: NIL

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