University of Thi-Qar Journal of Science (UTsci)
ISSN Onlin:2709-0256, ISSN Print: 1991-8690 Volume (8), No.1

Mini-Review: SARS-CoV-2 and COVID-19

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Dhurgham A .H. Alhasan
Department of Microbiology - College of Veterinary Medicine, University of Thi-Qar
Thi-Qar, Iraq
dhurghamalhasan@gmail.com

Husein A. Husein Al-Saidy
Department of Environment and Polluton-Marshes Research Center- University of Thi-Qar
Thi-Qar, Iraq
husseinali_unix79@yahoo.com

https://doi.org/10.32792/utq/utjsci/v8/1/2

***Abstract*— On 31 December 2019, the cases of pneumonia caused by unknown etiology had emerged. These cases were reported in Wuhan city, Hubei Province of China. Chinese authorities identified the causative agent and announced to be a novel coronavirus. The tentative name of disease is COVID-19, abbreviating of coronavirus disease-19. The incubation period of the disease ranges from 2 to 14 days, however, 80% of the patients have mild or asymptomatic illness while 15 % and 5% of the patients had exhibited sever and critical cases respectively. The etiology of COVID-19 was known as SARS-CoV-2 and belongs to betacoranviruse as reported by the International Committee on Taxonomy of Viruses (ICTV) especially Coronaviridae Study Group (CSG). In addition, this virus is currently believed to be within bat-coronaviruses besides it possesses a close relationship with SARS-CoV more than MERS-CoV. Although, the majority of the diagnosed patients had symptoms, there were asymptomatic persons who can spread the SARS-CoV-2. Upon the emergence of worldwide distribution of this virus, the WHO had declared it as a global outbreak and pandemic. Unfortunately, at present time, there are neither vaccine and nor an approved COVID-19 specific drug against SARS-CoV-2. One of the remarkable pathogenesis mechanistic step of this virus is taking possession of the affinity to angiotensin-converting enzyme 2 (ACE2). This mini-review summarizes the origin and molecular identification of the virus as well as the host immune responses.**

***Keywords*— SARS-CoV-2 , COVID-19, ACE2, origin.**

I. INTRODUCTION

On 31 December 2019, the cases of pneumonia caused by unknown etiology. These cases were reported in Wuhan city, Hubei Province of China. On 7 January 2020, Chinese authorities identified the causative agent to be a novel coronavirus and it has the tentative name which is 2019-nCoV, abbreviating of coronavirus disease-19 (Lu *et al.*, 2020; WHO, 2020).It caused severe acute respiratory disease currently is known as coronavirus disease 19 (COVID-19). The virus belongs to *Coronaviridae* as characterized by the International Committee on Taxonomy of Viruses (ICTV) especially *Coronaviridae* Study Group (CSG).

Depending on the viral phylogeny and taxonomy as well as the expertise, CSG showed the virus belongs to coronaviruses causing severe acute respiratory syndrome (SARS). Therefore, there is a sisterly relationship clade between 2019-nCoV and SARS-CoVs. For this reason, the virus (2019-nCoV) is known as SARS-CoV-2 (Gorbalenya *et al.*, 2020; WHO, 2020). Relatedly, two pandemics outbreaks had globally been reported were SARS-CoV emerged in China which led to be etiology of SARS in 2020. Also, the Middle East region, Saudi Arabia, had emanating MERS-CoV was a noval betacoronavirus species which caused Middle East respiratory syndrome in 2012 (Zhong *et al.*, 2003; Zaki *et al.*, 2012; de Wit *et al.*, 2016; Arabi *et al.*, 2018).

The ongoing reported common symptoms of COVID-19 are fever, dry cough, throat sore, dyspnea, and fatigue (Cheng *et al.*, 2020; Huang *et al.*, 2020; Wang *et al.*, 2020). The incubation period of the disease ranges from 2 to 14 days, however, 80% of the patients had mild or asymptomatic illness while 15 % and 5% of the patients had exhibited sever and critical cases respectively (Prompetchara *et al.*, 2020; Rokni *et al.*,2020). Asymptomatic persons have a role in spreading SARS-CoV-2, yet they suffer from the symptoms 14 days after the viral infection (Al-Tawfiq, 2020; Rothe *et al.*, 2020). Reports about the increasing the prevalence of asymptomatic viral infections have inclined including rhinovirus influenza virus and coronavirus infections (Camargo *et al.*, 2012; Granados *et al.*, 2015; Al-Tawfiq and Gautret 2019). Concerning coronavirus asymptomatic MERS-CoV infections average of the various reports was about 9.8% where it was inclined within the last few years from 0% to 28.6% while the serological studies revealed that asymptomatic SARS-CoV infection were up to 13% (Wilder-Smith *et al.*, 2005).Both in Germany and China reported cases of adults and children of asymptomatic SARS-CoV-2 infections have been issued (Chan *et al.*, 2020; Rothe *et al.*, 2020). This may bring about the assumption of the contribution of these asymptomatic cases in the transmission and wide distribution of the infection.

A. Origin of SARS-CoV-2 and its genetic features:

The first-ever reported in the modern medical history coronavirus infection was on 1962 in the United States and Britain at the same time where the virus is isolated from patients of natural respiratory tract infection. (Kendall *et al.*,1962; Monto, 1974). Remarkably, coronaviruses are enveloped and characterized by unusual, large and positive-sense RNA genome as well as a unique strategy of the replication as well as the projected spikes on their surfaces (Drexler *et al.*,2010; Fehr and Perlman, 2015; de Wit *et al.*, 2016; Coutard *et al.*, 2020).The *Coronaviridae* family belongs to the *Nidovirales* order. This family embraces *Coronavirinae* subfamily which has four groups of coronaviruses are *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronaviruses*. The *Coronaviridae* classification is based on the morphology of the viral particles, genome organization, unique strategy of RNA replication, and nucleotide sequence homology (Fehr and Perlman, 2015; Carroll *et al.*, 2016). SARS-CoV-2 belongs to *Betacoronavirus* group (Lu *et al.*, 2020; Wu *et al.*, 2020; Zhu *et al.*, 2020).

Some members of coronaviruses cause mild respiratory illnesses such as 229E and OC43, HKU1 and NL63 (Corman *et al.*,2018; Sahin *et al.*, 2020; Zhu *et al.*, 2020). Other coronaviruses are causative agents of severe acute reparatory syndromes like SARS-CoV and MERS-CoV which were emerged in China (2002) and Saudi Arabia (2012) respectively (Ge *et al.*, 2013; Arabi *et al.*, 2018;Sahin *et al.*, 2020). In December 2019, the cases of severe acute respiratory syndrome caused by unknown etiology began to be reported in China and was initially known as a 2019-nCoV (novel coronavirus) (Shereen *et al.*, 2020; Zhou, F *et al.*, 2020; Zhu *et al.*, 2020). This virus had a relating clade within subgenus *sarbecovirus* belonging to genus *Betacoronavirus*. This virus is currently considered as the seventh emerging member of human pathogenic coronaviruses (Lu *et al.*,2020; Wu *et al.*, 2020; Zhu *et al.*,2020).

Genetically, coronaviruse genome size is extraordinarily large which has the 26.4–31.7 kb (Woo *et al.*, 2014; Luk *et al.*, 2019). However, the complete genomes of SARS-CoV-2, SARS-CoV, and MERS-CoV were already measured to be 29.9 kb, 27.9 kb, and 30.1 kb respectively (Guo *et al.*, 2020). This genetic closeness was confirmed by sequence analysis which showed that SARS-CoV-2 has 77.5% and 50% similarities to SARS-CoV and MERS-CoV respectively (Kim *et al.*, 2020). Moreover, uncovering of the complete genome of SARS-CoV-2 which is built up of (29,903 nucleotides) had revealed that this novel virus is mostly associated (89.1% nucleotide identical) with a cluster of the SARS-like CoVs especially *Betacoronavirus* and *sarbecovirus* which were formerly identified in the bats of China. This indicates the ability of this virus (SARS-CoV-2) to spread from animals into humans as an emerging zoonotic disease (Wu *et al.*, 2020). The genetic material analysis of SARS-CoV-2 has revealed that there is 89.1% genetic homology with that of bat CoV (bat-SL-CoVZC45) and (99.94%-99.99%) of other countries including that of Wuhan outbreak of this novel corona virus (Kim *et al.*, 2020).

Finally, the genetic similarity between SARS-CoV-2 and SARS-CoV is (79.6%) of their full-length genome sequences as well as the similar pairwise protein sequence of them. They share same host cell entrance receptor /mechanism. ACE2 is the same entranceway receptor when they infect the host cells of the respiratory passages of patients. Consequently, as the protein receptor binding domain (RBD) of SARS-spikes provides the affinity and regulation of species interaction and transmission among humans. RBD analysis had led to the assumption that SARS-CoV-2 and SARS-CoV are related in their receptors, natural host (bat) and cell infection. Furthermore, SARS-CoV-2 RBD gives the consistent and compatible interaction between the virus and its host (Shereen *et al.*, 2020; Ren *et al.*, 2020; Wan, *et al.*, 2020; Wu *et al.*, 2020; Zhou, P *et al.*, 2020).

In contrast, dipeptidyl peptidase (DPP)-4 and aminopeptidase N (APN) receptors of other CoVs are not used by SARS-CoV-2 (Zhou, P *et al.*, 2020). DPP-4 is a particular receptor for MERS-CoV (Prompetchara *et al.*, 2020; Wan *et al.*, 2020) while SARS-CoV-2 and SARS-CoV recognize ACE2. In addition, the spikes, RBDs, and RBM (receptor binding motif) of human MERS-CoV and bat MERS-like Covs have a lower similarity in their sequencing proteins (Wan *et al.*, 2020). Additionally, SARS-CoV-2 and SARS-CoV share similar tissue preference mainly through spreading to the respiratory tract of their victims and a bat is natural host for both (Li *et al.*, 2005; Drexler *et al.*, 2010; Ithete *et al.*, 2013; Guo *et al.*, 2020). SARS-CoV-2 shares the similarity which observed were 79.0% and 51.8% of the nucleotide sequence with SARS-CoV and MERS-CoV respectively (Ren *et al.*, 2020).

Regarding bat coronaviruses, researchers had tested 315 bats belonging to seven different species of the bats distributed in the north of Germany. They found that four lineages of their group1 coronaviruses associated with the four verspertilionid bats species including *Myotis dasycneme*, *M. daubentonii*, *Pipistrellus nathusii*, and *P. pygmaeus*. Also, they showed that German bat coronaviruses have sister pedigree with group (clade) Chinese type I coronaviruses which possessed the relationship with *M. ricketti* (bat) in China. (Gloza-Rausch *et al.*, 2008). This may encourage the hypothesis which emphasizes that 229E and SARS-CoV are ancestors of MERS-CoV through the studied phylogenic relationship between the bat and the mentioned viruses (Becker *et al.*, 2008; Ithete *et al.*, 2013). Furthermore, bat may probably be a reservoir for 229E and NL63 while OC43 and KU1 were thought to be originated from the rodent viruses. Also, ancestors of the OC43 may be transmitted from the camel and swine (Corman *et al.*, 2018).

Previously (2005), SARS-like CoVs had identified within *Rhinolophus sinicus* , wild horseshoe bats in Chinese Yunnan Province. Later on, in China on 2013, a live isolate of SARS-like CoVs was obtained from the incubated cells of Vero E6 in the bat feces. This isolate (SARS-like CoVs) was found to have the affinity to ACE2 by its S protein as well as it holds the notable similarity (95%) between its genome and that with SARS-CoVs including human and civet infecting ones (Sun *et al.*,2020).Interestingly, beside the close linkage to bat CoVs, amino acids of NSP7 and E proteins identity of SARS-CoV-2 was found to be 100% identical that of bat SL-CoVZC45. This relationship may support the claim that bats were probably be the host for SARS-CoV-2. In the markets of China, as the bats are considered a commercially selling by which it may lead to getting contact to diverse animal species. Therefore, further indicators and studies are extremely needed to confirm the bat is a reservoir for SARS-CoV-2 (Wu *et al.*, 2020). At this paradox, SARS-CoV-2 is

similar to the human, bat, and civet isolates of SARS-CoV. The relating link revealed 76%-78% of whole protein as well as 73%-76%, and 50%-53% of similarity for their RBD, and RBM respectively. The only exception is the insertion of one amino acid residue however, it occurs in a loop part from the binding piece of ACE2. There is no deleting or inserting changes in the RBM of both viruses including isolates of SARS-CoV collected from human, bat, and civet. In addition, RBM contains 14-ACE2 residues. Among these residues, 9 are completely conservative while 4 are incompletely conservative (Wan *et al.*, 2020).

The genome of SARS-CoV-2 and SARS-CoV besides MERS-CoV has still 50-untranslated region (5'UTR), and open reading frame (ORF)including 1a and 1b (Shereen *et al.*, 2020). RNA 5'two-thirds of coronaviruses contain ORF1ab is encoding to form the replicase polyproteins. RNA 3' third one is encoding to produce forms of the proteins which are nucleocapsid (N), matrix (M), envelope (E) and spike (S) glycoprotein (Luk *et al.*, 2019) as well as producing accessory types of proteins that have interaction with innate immune responses of the host (Perlman and Netland, 2009; Woo *et al.*, 2014; Guo *et al.*,2020). CoV encoded proteases split the ORF1ab translated product into an enzyme set of the 16 non-structural proteins (NSP), e.g. RNA-dependent RNA polymerase (RdRp), papain-like proteases (PLpro), helicase (Hel), chymotrypsin-like protease (3CLpro) and two methyltransferases (Perlman and Netland, 2009; Luk *et al.*, 2019). Interestingly, the RNA of alpha and betacoronaviruses contains UUUAAAC, conserved sequence, that maintain the distinctive movement (slippage) of the ribosome to obtain ORF1ab transcription (Drexler *et al.*, 2014).

Additionally, there is a strange location in the spike protein of SARS-CoV-2 has been identified which is not present in the SARS-like coronaviruses. This location is a furin-like cleavage position (Coutard *et al.*, 2020). Moreover, SARS-CoV-2 shares the RBD amino acid sequence with SARS-CoV. Furthermore, SARS-CoV-2 genome contains ORF8 is also most related to the bat SARS-like CoVs (Ren *et al.*, 2020). After the MERS- CoV outbreak, a previous study concluded why the coronaviruses can emerge new species and not only strains or genotypes. There are three reasons for getting this phenomenon. First, unfaithfulness of CoVs –RdRp which leads to occur the mutation (one position per 1000-10000 nucleotides) through their replication. Second, these viruses are characterized by a unique RNA replicating strategy and the randomly transform of the template. Third, genome of coronaviruses is the largest compared with RNA-genome viruses. As a result of these factors, CoVs have further flexibility by which they can modify their genes (Woo *et al.*, 2014).

Evidence of closely related coronavirus strains between distantly related animals supports the hypotheses of interspecies jumping and development of seriously risky epidemic or even pandemic outbreaks. In the wet markets of China where contacting humans with animal food, it is probably to getting viral mutation, recombination, and modification due to mutated genes that may be given. In these markets (Woo *et al.* ,2006). Regarding MERS-CoV and 229E; dromedary camels represent reservoir host of them, however, MERS-CoV had found the way to infect the human population, then it spread by travelling to be worldwide viral infection (de Wit *et al.*, 2016: Corman *et al.*,2018).

B. Identification

COVID19 infection diagnosis is currently performed through using computed tomography (CT) of the chest and symptoms in addition to the case history help in the identification of SARS-CoV-2. Notably, the patients who have mild or no symptoms, their CT scan reflected normal images (Cheng *et al.*, 2020). However, it is still necessary that all suspected patients should be isolated even when they have no SARS-CoV-2 infection evidences. In addition, some patients who had exhibited positive results of the viral RNA test but they did not give rise to an indicative SARS-CoV-2 pneumonia representative images on one hand. Electron micrographs revealed that after three days of virus incubation in the host cell (Vero cells) it spreads in wide range in its organelles particularly in the vesicles. The observed virus size is 70-90 nm in diameter, however, four days are enough to infect 80% of the affected tissue (Kim *et al.*, 2020).

On other hand, other patients possess the representative imaging results of SARS-CoV-2 pneumonia but with a negative observation of the viral RNA test. Remarkably, it was observed that the second viral RNA test was done for negative ones, in the first examination may exhibit a positive manifestation during the isolation of the patients. Hence considering of the imaging finding must not be neglected (Zhang *et al.*, 2020). Laboratory investigation for identification of SARS-CoV-2 infection is currently depends on RT-PCR for viral RNA detection where specimens collected from the respiratory tract were used. Two priMERS-CoV and probe were used to detect the gene of E protein. These priMERS-CoVwere forward primer: 5′-ACTTCTTTTTCTTGCTTTCGTGGT-3′ and reverse primer 5′-GCAGCAGTACGCACACAATC-3′ while 5′CY5-CTAGTTACACTAGCCATCCTTACTGC-3′BHQ1 represented the probe. For amplification, the steps were performed by 50°C / 15 min. , 95°C / 3 min. and then 45 cycles / 95°C during 15 s and 60°C / 30 s (Huang *et al.*, 2020).

Moreover, two genes were also detected (genes of *ORF1ab* and N genes). Forward primer: CCCTGTGGGTTTTACACTTAA and reverse primer was ACGATTGTGCATCAGCTGA whilst the probe: 5′-VIC-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3′ have interested to detect and amplify the *ORF1ab*. Simultaneously, detection of N gen has done through using forward primer: GGGGAACTTCTCCTGCTAGAAT; reverse primer: CAGACATTTTGCTCTCAAGCTG, and the probe 5′-FAM- TTGCTGCTGCTTGACAGATT-TAMRA-3′. *ORF1ab* and N genes were amplified together by RT-PCR. The conditions were 50 °C / 15 min., 95 °C / 5 min. for incubation aspect, 40 denaturing cycles at 94°C during 15 s, and 55 °C / 45 seconds to obtain the fluorescence hint (Wang *et al.*, 2020).Then, Ct-value, cycle threshold value was estimated according to National Institute For Viral Diseases Control and Prevention, China . If Ct-value has less than 37 indicates to the positive test and 40 of the value or more denotes to the negative test (http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.Html). When Ct-value is 37-39, this indicates to retesting (Wang *et al.*, 2020).

To amplify a gene of *RdRp*, the used molecular set was forward primer: 5′-GTGARATGGTCATGTGTGGCGG-3’; reverse primer: 5’-CARATGTTAAASACACTATTAGCATA-‘3; and probe: 5’-CAGGTGGAACCTCATCAGGAGATGC-3’ (in 5-FAM/3’- BHQ format). Also, the E protein gene was detected by using forward primer: 5’-ACAGGTACGTTAATAGTTAATAGCGT-3’;

reverse primer: 5’-ATATTGCAGCAGTACGCACACA-3’ and probe: 5’-ACACTAGCCATCCTTACTGCGCTTCG-3’ (5-FAM/3’-BHQ format). The process was performed by conditions of RT-PCR were 50°C /30 min. to get the reverse transcription, and 95 °C /10 min. for the inactivating the reverse transcriptase , then amplifying process was run by 40 cycles of 95°C /15 s and 60°C / 1 min. (Kim *et al.*,2020).However, another work was done to identify the *orf1a* by which as forward primer: 5′-AGAAGATTGGTTAGATGATGATAGT-3′; reverse primer: 5′-TTCCATCTCTAATTGAGGTTGAACC-3′; and probe: 5′-FAM-TCCTCACTGCCGTCTTGTTGACCA-BHQ1-3′. In this molecular target, the style of the internal control was performed by using the genes of human *GAPDH* that forward primer was 5′-TCAAGAAGGTGGTGAAGCAGG-3′; and 5′-CAGCGTCAAAGGTGGAGGAGT-3′ as reverse primer while probe was 5′-VIC-CCTCAAGGGCATCCTGGGCTACACTBHQ1-3′. Sequentially, the RT-PCR cycling conditions were 42°C /30 min., followed by 95°C / 10 min., and 40 amplifying cycles including 95°C/ 15 s and 58°C / 45 s .The fluorescence was given by the 58°C phase (Lu *et al.*, 2020).

C. Immune responses:

Prevailingly, the SARS-CoV-2 and SARS-CoV adhere to the lower parts of the respiratory tract. Then, they infect the ACE2 of the alveolar epithelial cells. Both viruses induce extremely host releasing cytokines which gives rise to a tissue destructive cytokine storm, a mechanism that ends with the failure of organ function. In this context, the viral entrance (respiratory cells entry) provokes the local immune cells for producing cytokines and chemokines to reach pulmonary endothelium (Jiang *et al.*, 2020). However, the cytokine releasing syndrome (CRS) was noticed in severe patients who infected with SARS-CoV-2. Also, lymphocytopenia was investigated in those patients (Shi *et al.*, 2020).

Large amounts of plasma cytokines such as IL1B, IFNγ and MCP1 were observed in the critical cases of patients infected with SARS-CoV-2. Those patients have acute respiratory distress syndrome (ARDS) (Huang *et al.*,2020). The CRS is a one way by which SARS-CoV patients had developed ARDS that may led to their death because of releasing elevated cytokine products such as IFN-a, IL-1b, TNF-a, etc. as well as large concentrations of chemokines e.g., CCL2- CCL5, CXCL8- CXCL10,etc. In a similar way, severe MERS-CoV patients had reported to develop high levels of IL-6 and IFN-a in addition to CCL5,CXCL8 and CXCL-10 in their serum (Li *et al.*,2020). Totally, the neutrophils, serum IL-6 and c-reactive protein were reported to be increased while lymphocytes decreased.

Additionally, the severity of COVID-19 and patient death associated with those changing levels of the neutrophils and lymphocytes (Prompetchara *et al.*, 2020). Titers of IgG and IgM have recorded an elevated level in the serum of SARS-CoV-2 patients (Zhou,P *et al.*, 2020). Some patients suffer from below normal ratio of leukocytes and other infected persons increased in the leukocyte and neutrophil ratios. Clinically, lymphocytes took a decreasing level in numerous patients. If lymphocyte level became completely decreasing, it can propose to be a factor for diagnosis a new coronavirus. Finally, it was concluded that the SARS-CoV-2 depletes many immune cells leading to inhibit the cellular immunity. Intravenously given immunoglobulines activate anti-infection of severe cases (Chen *et al.*,2020).

Unfortunately, white blood cell account appeared to be of different ranges among SARS-CoV-2 patients. However, most patients kept normal or decreased value of the account as well as lymphocytopenia. Severe cases had recorded significant elevated ratios of neutrophils while lymphocytes continuously decreased. Besides, the interleukins (IL-6, IL-10) and TNF-α had the excess (Guo *et al.*,2020). In this context; the majority of patients possessed noteworthy lymphopenia. Also, the neutrophil range and account of WBCs were elevated (Wang *et al.*, 2020) whilst, the laboratory investigation of the Taiwanese first COVID-19 case infected with SARS-CoV-2 had the lymphopenia (Cheng *et al.*, 2020).

The serological outcome of the disease involves detection of immunoglobulin G (IgG) in the patient majority specimens which were found to be induced by the N protein of SARS-CoV-2 during the early first four days from the development of the disease. Additionally, S and N proteins of this virus represent major detected immunogens in the patients infected with this virus (Rokni *et al.*, 2020). Therefore, serological investigations including ELISA and complete blood picture as well as cytokines blood levels. In this context, ELISA test for the detecting IgG and IgM were obtained from the patients infected with SARS-CoV-2.The samples were tested with nucleocapsid protein of the bat SARSr-CoV Rp3 where the results had showed that there is a more than 90% identical amino acids in the of N protein for both viruses. Moreover, no results of the cross reaction with other human CoVs (Wu *et al.*, 2020; Zhou, P *et al.*, 2020). The majority of patients possessed noteworthy lymphopenia. Also, the neutrophil range and account of WBCs were elevated (Wang *et al.*, 2020). WBC account appeared the different ranges in the SARS-CoV-2 patients. Most patients kept normal or decreased value of the account as well as lymphocytopenia. Severe cases had recorded significant elevated ratios of neutrophils while lymphocytes continuously decreased . Besides, the interleukins (IL-6, IL-10) and TNF-α had the excess (Guo *et al.*, 2020).

D. Trial drugs against SARS-CoV-2

At present time, there are neither vaccine and nor an approved COVID-19 specific drug against SARS-CoV-2. However, the combination of the two protease enzyme inhibitors ,lopinavir and ritonavir, had been given for patients who were infected with SARS-CoV-2 in the Chinese hospitals (Huang *et al.*, 2015; Huang *et al.*,

2020).Researchers showed that there were severe side effects observed when lopinavir and ritonavir were used (Cao *et al.*, 2020). Furthermore, oseltamivir and ganciclovir were also used. However, in order to prevent the secondary infection, the patients were treated by antibiotics such as cephalosporins and quinolones. Additionally and antifungal agents had been used. In emergency, methylprednisolone, and dexamethasone were given to the patients (Chen *et al.*, 2020; Rokni *et al.*, 2020). Concerning the SARS-CoV-2 laboratory investigations, specimens from the respiratory tract were taken to be tested by using RT-PCR for detection of coronavirus genes. Examples of these specimens are throat, nasal and pharyngeal swabs (Huang *et al.*, 2020).

As there are no specific anti-coronavirus drugs; inspired by the studies that recommended lopinavir–ritonavir combination as a promising therapy for both MERS-CoV and SARS-CoV infections (Chu *et al.*,2004; Spanakis *et al.*, 2014; Kim *et al.*,2016; Min *et al.*,2016). Chinese medical specialist decided to try this combination for management of patients with SARS-CoV-2 infection. In a randomized trial a heterogeneous group of 199 Chinese hospitalized adult patients of median age 58 years and 60.3% them were male with a conformed sever SARS-CoV-2 infection; the two antiretroviral and a protease inhibitors lopinavir–ritonavir combination given in doses of (400 mg and 100 mg, respectively) twice a day for 14 days in a clinical trial study continued for 28 days. This combination had showed no effect on one half of the patients treated with it over the other half managed with standard care. There was no significant difference in the time of clinical improvement for mild to moderate case, mortality rate for severe cases, viral load and different time intervals of positive viral RNA results between the two halves of the patients. The median time of clinical improvement for hospital discharge between the two groups was only one day, however, the residence time in the intensive care unit was significantly shorter 6 days for those on the antiviral drug combination vs. eleven days for those on standard care. In addition, acute kidney damage, secondary infections and demands for invasive/non invasive mechanical ventilation for cases of respiratory failure were lower in patient receiving lopinavir–ritonavir combination. In contrast, more common observed GI side effects were associated with the use of this combination beside the more serious side effects. The two antiviral drug therapy were stopped for 13.8% of the patients due to adverse effects (Cao *et al.*, 2020).

This may bring about to the assumption that there is no cross receptor binding site equivalency between the old and the SARS-CoV-2 of coronaviruses at least for protease enzyme. However, some of the concerned scientific communities still support the allegation that the effectiveness of this combination of therapy has time-to treatment effects as observed in previous antiviral studies in SARS (Chan *et al.*, 2003). The result of this clinical study of the ineffectiveness of the lopinavir–ritonavir combination was in coincidence of other up-to-date study done in Wuhan of China (Zhou, F *et al.*,2020) as previously reported for ineffectiveness of lopinavir for treatment of SARS-CoV (Yamamoto *et al.*,2004). However, it is essential to denote that a previous study proposed a third drug combination treatment like interferon-β1b is required for enhancing the antiviral activity of this combination in SARS-CoV and MERS-CoV infections **(**Chan *et al.*,2003; Arabi *et al.*,2018)as used for the treatment of the first Taiwan sever SARS-CoV-2 case in a 55 years old female patient (Cheng *et al.*,2020)**.**

II. Conclusions

Up-to-date data emphasize that SARA-CoV-2 is mostly related to SARS-CoV than MERS-CoV. Also, bats may be the animal host reservoir of this virus. Asymptomatically infected persons have a role in the spreading of COVID-19 in the world in different regions. At present, no vaccine and effective drugs against that virus, however, it might be recommended to apply the electricity to kill SARS-CoV-2 as a method to produce a vaccine against COVID-19. Biopsy and post-mortem manifestations are extremely required to provide further information about the virus SARA-CoV-2 pathogenesis and targeted body tissues.

Acknowledgment

We are grateful for all scientists and researchers especially those who have an interest related to SARS-CoV-2. This mini-review represents a simple work to participate in giving knowledge about this virus.

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