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23 ABSTRACT

24 The emergence of novel coronavirus (SARS-CoV-2) is marked as the highest
25 pathogenic coronavirus that has crossed from the hosts to the human population in the
26 twenty-first century. The spreading of COVID-19 in different chinese cities and around the
27 world is travel-related viral spread with the unprecedented nosocomial outbreaks. It has
28 also shown with high case-fatality rates, indeed to urgent prophylactic and therapeutic
29 settings. Scientific advancements of the SARS-CoV-2 pandemic allowed for rapid progress
30 to understand the epidemiology and pathogenesis of SARS-CoV-2. This review highlights
31 the the genomic structure of SARS-CoV-2 with the proposed roles of genotype and
32 phenotype of SARS-CoV-2 in pathogenesis and discuss recent results supporting treatment
33 strategies of COVID-19 with a special focus on how these new insights may facilitate
34 rational development of SARS-CoV-2 for targeted therapies in the future.

35 **Keywords:** novel coronavirus, SARS-CoV-2 , COVID-19, pneumonia, *Betacoronavirus*,
36 transmission

37 INTRODUCTION

38 One of the major public health challenges of the 21st Century which cause by
39 coronavirus is outbreaks by the severe acute respiratory syndrome (SARS-CoV), middle
40 east respiratory syndrome (MERS-CoV), and novel coronavirus (severe acute respiratory
41 syndrome-2 (SARS-CoV-2) in Wuhan, China which known as (COVID-19).
42 Coronaviruses (CoVs) have known as the largest positive-sense and single-stranded RNA
43 (+RNA) viruses from coronaviridae family. CoVs have four genera: Alphacoronavirus,
44 Betacoronavirus, Gammacoronavirus, and Deltacoronavirus. Coronaviruses are basically
45 zoonotic that can be transmitted to people from animals. Previously SARS-CoV has been
46 reported to be acivet cats origin and transmitted to humans. MERS-CoV also come from
47 camels to humans and the novel coronavirus (SARS-CoV-2) which discovered in Wuhan,
48 China is coming from bats. Several types of coronaviruses are hosing in animals and cannot
49 transmit to humans [1-5].

50 In late December 2019, series of pneumonia cases with unknown etiology has been
51 reported in Wuhan City, Hubei Province, China. The Chinese government warned the
52 World Health Organization (WHO) about an outbreak of unknown cause. The initial
53 investigation of epidemiological cases has been reported seafood and wet animal wholesale
54 market in Wuhan as the main source of this pneumonia. On 7 Jan 2020, Chinese scientists
55 have successfully isolated a novel coronaviruses which known as (SARS-CoV-2) virus.
56 The SARS-CoV-2 sequencing has been obtainable by WHO on 12 Jan 2020. The genetic
57 sequence collecting of SARS-CoV-2 in a short time is the most important achievement
58 because that is a key role for understanding the COVID-19 properties and doing with other
59 scientists around the world [6-9].

60 Coronaviruses have been genotypically and serologically divided into four genera:
61 alpha and beta coronaviruses. It is hosting by mammals. Gamma coronaviruses are hosting
62 in birds and marine mammals and delta coronaviruses are hosting by birds and swine. The
63 SARS-CoV-2 is a β CoV and has a similar genetic sequence with SARS-CoV that lately
64 named SARS-CoV-2 by the WHO. Since the evolutionary neighbors and outgroups of the
65 novel SARS-CoV-2 have been found in bats, it is speculated that the natural host of the
66 Wuhan novel coronavirus may also be bats and it is likely to have an unknown intermediate
67 host-vector during bat-to-human transmission [3, 10-14]. In this m review, we summarized
68 the recent findings of SARS-CoV-2 and provide a brief introduction of genomic structure
69 SARS-CoV-2 with the proposed roles of genotype and phenotype of SARS-CoV-2 in
70 pathogenesis. These isight may facilitate rational development of SARS-CoV-2 for
71 targeted therapies in the future.

72

73 **Genomic structure and Genomic organization of SARS-CoV-2**

74 Generally, SARS-CoV-2 is like to be similar to some beta coronaviruses (β -CoV)
75 which have been detected in bats. It is different from SARS-CoV and MERS-CoV. The β -
76 CoVs are mainly divided into four lineages. SARS-CoV and SARS-CoV-2 are from
77 lineage B, and it has more than 200 virus sequences. The MERS-CoV is from lineage C
78 that has over 500 viral sequences. All coronaviruses mainly encode a surface glycoprotein
79 and spike that play a key role in binding with the receptor of host cell and mediate viral
80 entry. The receptor-binding domain (RBD) as a single region of the spike protein of the β -
81 CoVs can mediate the interaction between the host cell receptor leading to cleave the spike
82 and release the spike fusion peptide mediating virus entry. SARS-CoV-2 has S protein on

83 surface and forms a club-like structure. Surmizing that the structural properties of SARS-
84 CoV-2 are mainly matching with SARS-CoV and MERS-CoV, and the phylogenetic tree
85 of coronaviruses including the SARS-CoV-2 presented in figure (1-A) [15, 16].

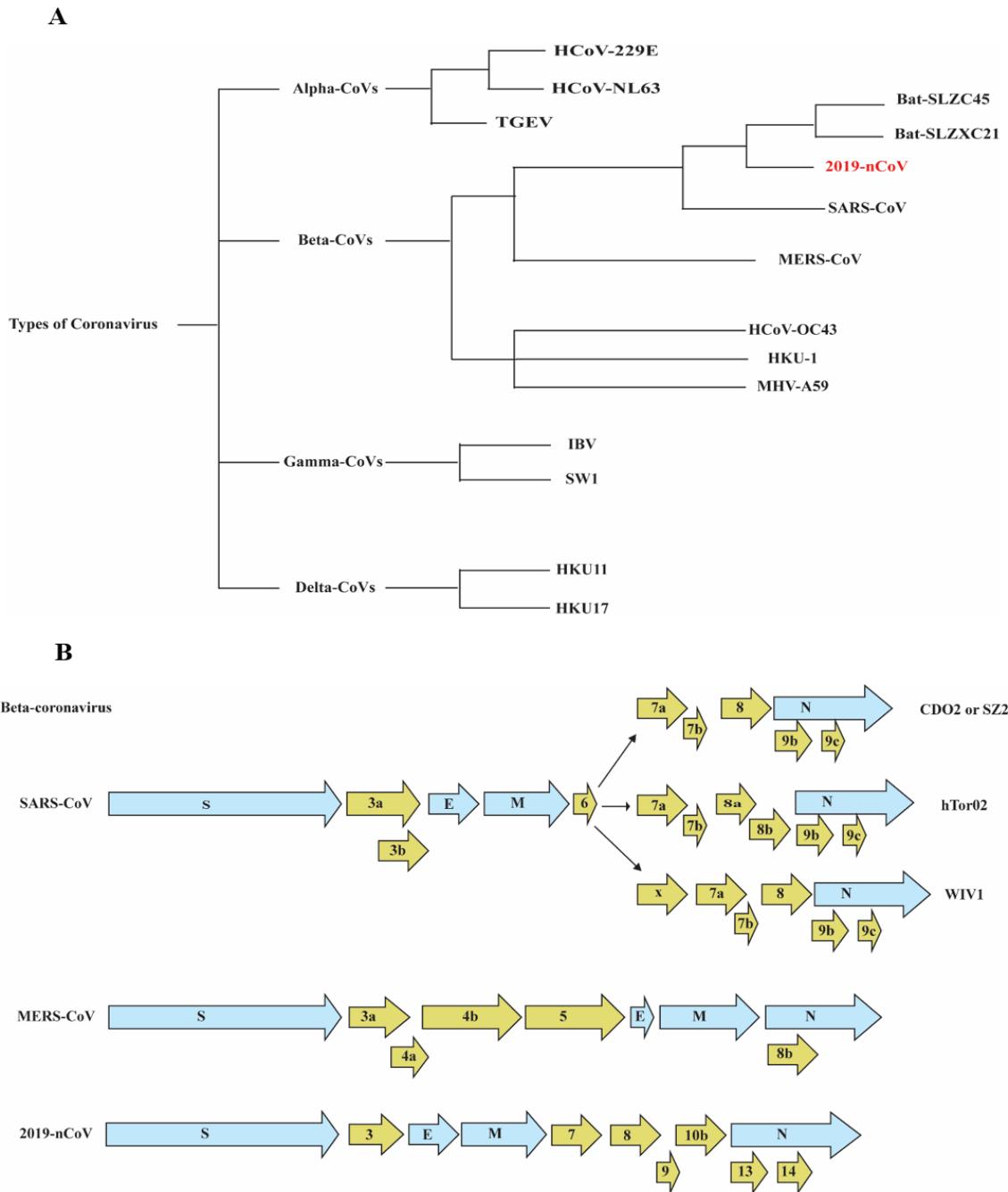
86 Genetically, coronaviruses have been previously described to be the largest genome
87 of RNA viruses with the longest stable RNAs in nature. The basic set of coronaviruses has
88 the relicate (Rep 1a and 1b), the spike, envelope, membrane and nucleoprotein, ordering -
89 Rep1a-1b-S-EM-N-30. The variable number of encoding nonstructural proteins genes have
90 a role for the character of all groups. Many modelsto explore the discontinuous synthesis.
91 Notably, a chinese scientist has successfully isolated the SARS-CoV-2 on 7 January 2020
92 and explored the genome sequencing of the SARS-CoV-2. The genome sequences of
93 SARS-CoV-2 currently known are almost identical and homological sequencing. It is
94 similar to SARS-CoV more than MERS-CoV. Related study has revealed that by reading
95 more than 20.000 viral from specimens the most contigs were matched with the genome of
96 the lineage B from betacoronavirus by more than 85% identity with a bat SARS-like CoV
97 (bat-SL-CoVZC45, MG772933.1). The genome sequences details of the isolated SARS-
98 CoV-2 coronaviruses and coding regions have revealed in tables (1,2) and figure (1-B).
99 The researcher also reported that there is 86.9% nucleotide sequences which identity to a
100 bat SARS-like CoV. The collected genome of three samples with SARS-CoV-2 were
101 clustered together, and formed an independent subclade within the arbovirus subgenus.
102 Related work analyzed nine samples of SARS-CoV-2 and found that the genome of these
103 samples was extremely similar by more than 99.98% sequence analogy. SARS-CoV-2 has
104 88% identity to two bat-derived SARS-like coronaviruses, bat-SL CoVZC45 and bat-SL-
105 CoVZXC21 which collected in Zhoushan, eastern China in 2018. They also shared that

106 there are distant 79% from SARS-CoV and 50% MERS-CoV. Chinese national institute
107 for viral disease control and prevention has recommended using an open reading frame for
108 the novel coronavirus 1AB (Open Reading Frame, ORF1ab), nucleocapsid protein
109 (Nucleoprotein, N) primers and probes gene regions [8, 11-13, 17-19].

110 **Table 1: Summary of Genes Target [20, 21]**

Genes Target	Sequence (5' to 3')
ORF1ab	Forward primer (F) CCCTGTGGGTTTACACTTAA
	Reverse primer (R) ACGATTGTGCATCAGCTGA
	Fluorescent Probe (P) FAM-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1
N	Forward primer (F) GGGGAACCTCTCCTGCTAGAAT
	Reverse primer (R) CAGACATTTGCTCTCAAGCTG
	Fluorescent Probe (P) FAM-TTGCTGCTGCTTGACAGATT-TAMRA

111



112

113 Figure 1: The phylogenetic tree of coronaviruses and genomic structure of coding regions;

114 (A) The phylogenetic tree of Coronaviruses includes SARS-CoV-2 (B) Coding regions of

115 COVID-19, SARS-CoV, and MERS-CoV SARS-CoV-2. SARS-CoV; severe acute

116 respiratory syndrome coronavirus. MERS-CoV; the Middle East respiratory syndrome

117 coronavirus

118

119 **Table 2: Describing the early samples collecting from patients of COVID-19 in**
120 **Wuhan with detailed information [21].**

Numbering	Species name	Isolate	Length (bp)	Serial submission date
MN908947	Wuhan seafood market pneumonia virus	Wuhan-Hu-1	29875	2020
NC_045512	Wuhan seafood market pneumonia virus	Wuhan-Hu-1	30473	2020
MN975262	Wuhan seafood market pneumonia virus	COVID-19_HKU-S Z-005b_2020	29891	2020
MN938384	Wuhan seafood market pneumonia virus	COVID-19_HKU-S Z-002a_2020	29838	2020
GWHABKG 00000000	Wuhan seafood market pneumonia virus	IPBCAMS-WH-02	29889	2020
GWHABKH 00000000	Wuhan seafood market pneumonia virus	IPBCAMS-WH-03	29899	2020
GWHABKI0 00000000	Wuhan seafood market pneumonia virus	IPBCAMS-WH-04	29890	2020
GWHABKF 00000000	Wuhan seafood market pneumonia virus	IPBCAMS-WH-01	29899	2020
GWHABKJ0 00000000	Wuhan seafood market pneumonia virus	IPBCAMS-WH-05	29883	2020
MK539948	Porcine epidemic diarrhea virus	CT	4161	2019

121

122 **The role of genotype and phenotype of SARS-CoV-2 in pathogenesis**

123 In international gene banks such as GenBank have several Sars-CoV-2 gene
 124 sequences that achieve by scientists. These findings are very important for allowing
 125 researchers to trace the phylogenetic tree of the virus. All the recognized strains are
 126 different according to the mutations. [22]. Pathophysiology and virulence mechanisms of

127 CoVs and SARS-CoV-2 can use links for the nsps function and their structural proteins.
128 Together, nsp may has ability to block the innate immune response in the host [23]. The
129 envelope as structural functional msy play a key role of the virus pathogenicity by
130 promoting the viral assembly and release. There are some features like nsp 2, and 11 still
131 not clearly prescribed. The matter of viral mutations is key for explaining potential disease
132 relapses. Research required to deeply focus on the structural characteristics of SARS-COV-
133 2, it will increase the cahns to understand pathogenetic mechanisms. The clinical data has
134 shown less extra respiratory involvement with SARS-COV-2 compare with SARS-COV,
135 it may due to the lack of extensive data.

136 On SARS-CoV-2 surface there is a spike glycoproteins and homotrimers which
137 may link to host receptors and paly a key role in viruse entery. It mainly has two subunits
138 (S1 and S2). S proteins are homotrimers of compose the spikes on the viral surface, guiding
139 the [24]. Notably, S2 subunit of SARS-CoV-2 contain a fusion peptide, a transmembrane
140 domain and cytoplasmic domain which are very conserved. These characersits may
141 provide a potential targeting drug.

142

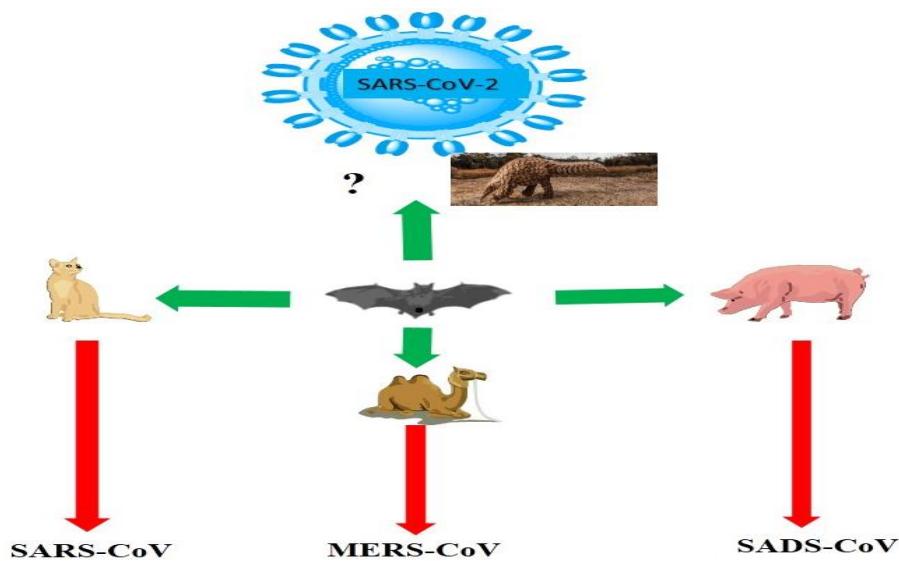
143 **Origin and transmission of COVID-19**

144 Coronaviruses have known as largest group of viruses that can cause many diseases.
145 The patients have been shown with different clinical symptoms compared with the
146 common cold of lung infections with MERS and SARS. The novel coronavirus
147 COVID-19 discovered for the first time in December 2019 in Wuhan, China. The
148 transmission of SARS-CoV-2 has been previously described which can be transmitted

149 from person to person. Most cases that transmitted from humans to humans have
150 occurred by the environment with absence of appropriate infection control precautions.
151 Many wild animals can carry pathogens and act as vectors for certain infectious diseases.
152 Civets, bats, bamboo mice and badgers are common hosts of coronaviruses. The
153 outbreak of viral pneumonia in Wuhan has a lot in common with the outbreak of SARS
154 in Guangdong in 2002, and both have occurred in the winter. The outbreak originated
155 from the contact between live animals traded in human and animal markets, where
156 seafood, poultry, snake, bats, and farm animals were sold and was caused by unknown
157 corona. Since the evolutionary neighbors and outgroups of the Wuhan novel
158 coronavirus have been found in bats, it is speculated that the natural host of the Wuhan
159 novel coronavirus may also be bats. Like the SARS coronavirus that caused it in 2002,
160 the new coronavirus is likely to have an exact intermediate host-vector during bat-to-
161 human transmission and related studies suggesting pangolin [25-28]

162 The novel coronavirus SARS-CoV-2 and SARS-CoV viruses are all coronavirus
163 from the bats origin, and many coronaviruses associated with coronaviruses in humans
164 are associated with bats, and many coronaviruses have natural hosts in bats. It is likely
165 that bats are the primary host of the new Wuhan coronavirus, which has completed bat-
166 intermediate host-human transmission through evolutionary mutation. However, there
167 may be more intermediate hosts, from bats to humans, that have not yet been cleared.
168 Coronavirus pathways from animal to human and person to person: contact transmission
169 and droplet transmission, the general differentiations of COVID-19 with the previous
170 reported coronaviruses SARS and MERS has reported in the table (3). Many of COVID-
171 19 patients reportedly to have some link with large seafood and animal market proving

172 that the transmission is animal-to-person. Furthermore, the outbreak is still spreading
173 and the number of patients in different cities and moving to other countries are
174 increasing indicating that SARS-CoV-2 can be easily transmitted from person to person
175 [7, 17, 29-34].



176

177 Figure 2: Animal origins of human CoVs including novel COVID-19.

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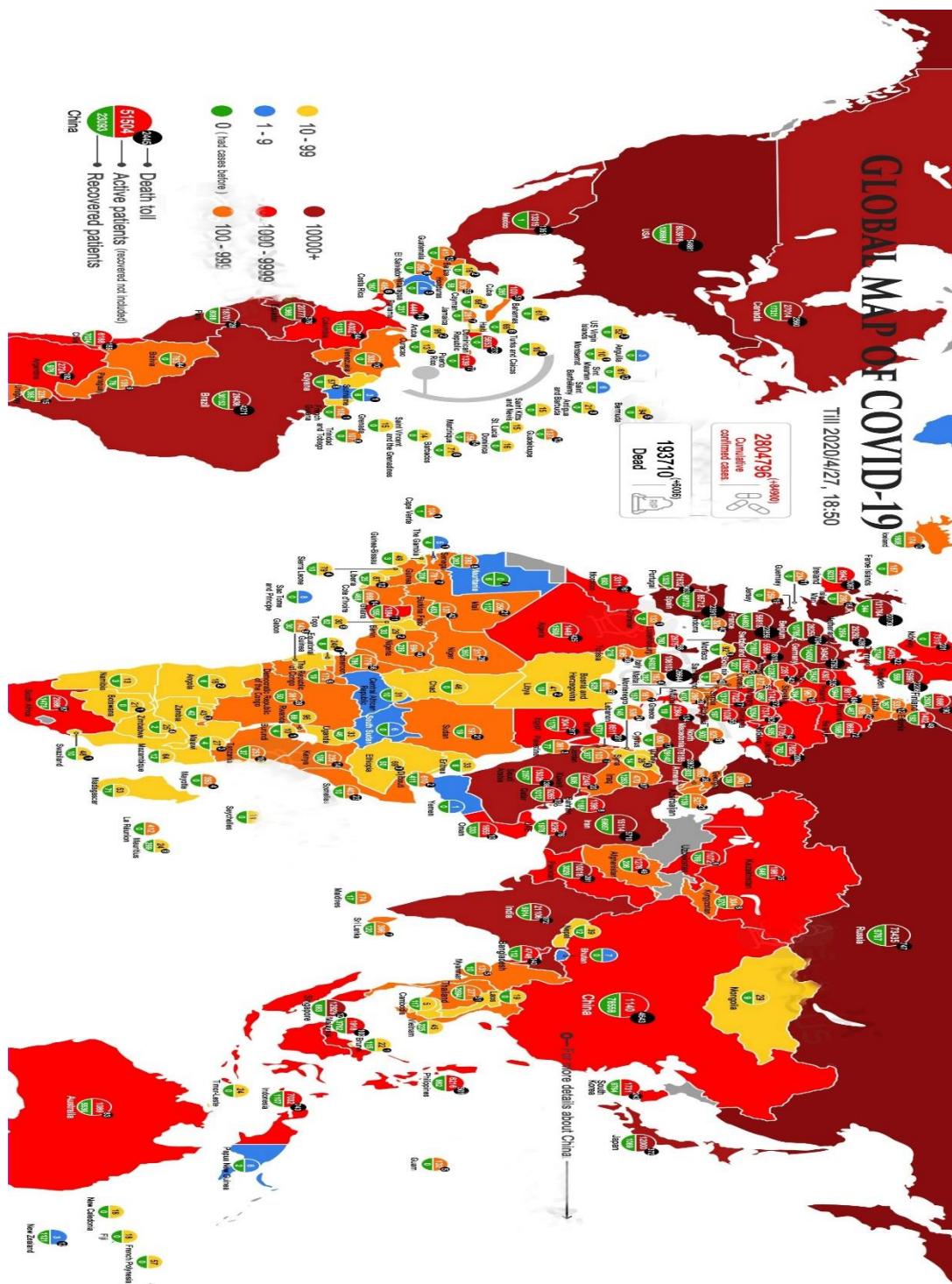
Table 3: General differentiation of COVID-19, SARS and MERS

Name	SARS-CoV	MERS-CoV	COVID-19*	References
Up to April 27, 2020				
Year	2002	2012	2019	
confirmed cases	8,422	2,494	> 3 milion	[35-37]
Incubation period	2-7 days	5.5-14 days	2-14 days	[38-40]
Outbreaks	large	large	large	[35, 36, 41]
Clinical features	fever, cough, malaise, headache, headache, muscle pain, and respiratory infection	fever, cough, headache, muscle pain, and respiratory infection	multiple system infections and mainly respiratory tract infections, such as pulmonary edema, ARDS, or multiple organ failure and have died	[7, 42, 43]
Mortality	10%	35%	≥6% even now	[7, 30, 44]
Transmission, person to person	quickly	moderate	quickly	[42]
Location	Starting from Guangzhou, Guangdong, China, Spread 37 countries	Starting from Middle Eastern Countries, spread 27 countries	Starting from Wuhan, Hubei, China, Spread 21 countries	[35, 36, 41]
Main host	batas	batas	batas	[30]
Intermediate host	civets	camels	?	[30]
			may pangolin	
Severity	Sever	Sever	Sever	[42, 43]

179

180 **The epidemiological and risk factors of COVID-19**

181 In December 2019, several patients with pneumonia were observed in Wuhan,
182 China. The epidemiological evidence was mainly associated with Huanan seafood. The
183 number of people was growing up the rapidly unknown cause. The clinical futures were
184 like coronavirus infection which was lately named COVID-19 by WHO. As of April 27,
185 2020, there were more than 3 milion confirmed cases and the suspected cases more 203.332
186 fatalities. Up to now, there are around 33 Chinese provinces and more than 183 countries
187 have been reported with COVID-19, the geographical distrubion of the confirmed cases of
188 COVID-19 has explored in figure (3). The infections in family clusters and medical stuff
189 have been proved to be human-to-human transmission. The COVID-19 cases are still
190 growing rapidly from diffrent international locations, and it become the highst public
191 concern leading to a wide range of outcomes like economic impacts and some cases loss
192 the lives. Perouse epidemic of different coronavirus infections such as SARS in Guangdong,
193 China has affected around 37 countries and the confirmed cases were more than 8000 cases
194 in 2003. So far, some of cases have occurred to the laboratory stuff accidents or via animal
195 to human transmission. In the seven years between the first case of MERS in April 2012
196 and November 2019, there were around 2494 confirmed cases [8, 29, 30, 36, 45]



197

198 Figure 3: The geographical distribution of the confirmed cases of COVID-19, April 27, 2020 [46].

199

2020 [46].

200 **The severity of COVID-19 in immunocompromised patients**

201 The number of infected people with COVID-19 is rapidly increasing around the
202 worlds. The majority of severe COVID-19 have been reported in immunocompromised
203 patients and adults more than 80> years old. Most of reported cases were with cardiac
204 disease, cancer, hypertension, and in patients treated with immunosuppressive targeted
205 therapies. Chinese report of 72 314 cases record with COVID-19 showed that the Case-
206 fatality rate in adults more than 80> years was 14.8%. Related work revealed that the older
207 patients were with sever systemic symptoms, extensive radiological ground-glass lung
208 changes, lymphopenia, thrombocytopenia, and increased C-reactive protein and lactate
209 dehydrogenase levels [47, 48].

210 Pregnancy is known as mmunocompromised state that demands some
211 pathophysiological disorders such as cardiovascular and other abnormalities. COVID-19
212 as pandemic can infect all human including pregnant patients. Viral myocarditis and
213 cardiomyopathy were showed in non-pregnant COVID-19 patients. It also recently
214 reported in pregnant COVID-19 patients. Recent works have reported that confirmed
215 COVID-19 cases in pregnancy were severe infection with cardiac dysfunction and
216 moderately reduced left ventricular ejection fractions (LVEF) of 40%-45% and
217 hypokinesis. From seven cases, five of them showed with symptoms of COVID-19 such
218 as cough, fevers, chest pain, myalgias and headache [49, 50] .

219

220 **Clinical features and inflammatory indications of COVID-19**

221 Coronaviruses have been know as the largest group of viruses that cause many
222 diseases. Patients present some futures like common cold and also presnted different

223 clinical symptoms ranging from the common cold to that cause by MERS and SARS [51-
224 53]. Common signs usually include respiratory symptoms, fever, cough, shortness of
225 breath and breathing difficulties [7, 54]. The acute infection can cause pneumonia, severe
226 acute respiratory syndrome, kidney failure, and even death. The data of the first 41
227 confirmed cases with COVID-19 in a related study have been explored a wide range of
228 symptoms, most of these futures are similar to previous cases of SARS. Some patients had
229 fatigue with rarer symptoms such as headache and diarrhea [7]. They also reported the
230 infection with SARS was more frequently runny noses, diarrhea and sore throats than those
231 with COVID-19. They also have shown that some of the deadly cases occurred as a result
232 of SARS-CoV-2 infection were among old people or with underlying diseases such as
233 diabetes, hypertension and liver disease [7, 55]. They have noted that SARS infections also
234 did not only influence people with other conditions.

235 From 99 patients Chen et al have described the clinical manifestations with patients
236 average 55.5 years old that were fever 83%, cough 82%, shortness of breath 31%, muscle
237 ache 11%, confusion 9%, headache 8%, sore throat 5% patients, rhinorrhoea 4%, chest
238 pain 2%, diarrhea 2%, and nausea and vomiting 1%. The imaging examination explored
239 that 75% showed bilateral pneumonia, 14% of patients showed multiple mottling and
240 ground-glass opacity, and one (1%) patient had a pneumothorax. 17% of patients
241 developed acute respiratory distress syndrome. 11% of patients studied had worsened
242 during a short period and died of multiple organ failure [30].

243

244

245

246 Treatment and control management strategies of novel COVID-19

247 The health authorities and WHO consider the novel SARS-CoV-2 as a serious public
248 health concern “Pandemic” and the immediate health risk of COVID-19 to the community
249 is high. Initially, the prevention and treatment of major infectious diseases such as AIDS
250 and other infections have been suggested for this infection and the Chinese medical
251 insurance companies have covered the cost of COVID-19 treatment. The genome
252 identification of the novel SARS-CoV-2 has a key role for treatment. The people health
253 care currently is being in treatment for the complications. Up to now, there are therapeutic
254 strategies of COVID-19 or other coronaviruses and many vaccines are under clinical trials
255 [56].

256 Basically, the characterization of the novel COVID-19 is closely related to SARS-
257 CoV and the efficacy of different treatments of SARS-CoV and MERS-CoV remains
258 unclear. Notably, Ribavirin and other types of IFN have been used with MERS infections
259 as monotherapy or combined with broad-spectrum antibiotics and oxygen. The treatment
260 of MERS has started only on the late-stage infection when the immunological system
261 predominates, and antiviral drugs have a little benefit. Ribavirin has used frequently during
262 the SARS infections which usually used as a combination with corticosteroids leading to
263 an anti-inflammatory effect. IFN α has used as a combination with thymosins or
264 immunoglobulins resulting to stimulate T cells [57-62]. Recent research has used antiviral
265 treatment for COVID-19 patients. Many drugs have been used as potential therapeutics
266 against COVID-19 such as remdesivir, chloroquine, hydroxychloroquine,
267 lopinavir/ritonavir, umifenovir, antipyretics, IFN- α , ACE Inhibitor (ACEi) and
268 Angiotensin Receptor-1 Blocker (ARBs). There also some specific drugs are currently

269 undergoing the clinical studies to evaluate the efficacy and safety profiles such as SARS-
270 Cov-2 specific antibodies and SARS-CoV-2 specific protease drug candidate. Notably,
271 there wide range of natural products and traditional medicines have been to be one of
272 potential strategies against COVID-19. The medicines used for the complications included
273 carbapenems, cephalosporins, quinolones and tigecycline targeting *Staphylococcus aureus*
274 as a methicillin-resistant, linezolid, and antifungal drugs also have been used. Hence, we
275 summarized the potential drugs in table no (..). [30]. Altogether, Ribavirin, IFN α and
276 various types of IFN may have potential efficacy for treatment strategies of COVID-19.

277 Standard recommendations to prevent infection by CDC and WHO including
278 continuously hand washing, covering mouth and nose when coughing and sneezing. Avoid
279 close contact with anyone showing symptoms of respiratory illness such as coughing and
280 sneezing. Travelers from or to most infected area are advised to obey the standard infection
281 control precautions such we mentioned above.

Table 4: Potential therapeutic strategies of COVID-19

No	Treatment	Molecular pathway/ Mechanism	Type of drug	Reference
	Remdesivir	Nucleoside inhibitor Adenosine analogue incorporates into nascent viral RNA chains	Ebola virus infection Developed for the SARS-CoV-2 treatment	[63, 64]
	Chloroquine	It may be effective by two mechanisms: pH-dependent stages of replication through Glycosylation process and inhibit	Antimalaria	[65-67]
	Hydroxychloroquine	inhibit pH-dependent stages of replication	Antimalaria	[64, 66]
	Lopinavir/ritonavir	protease inhibitors and doing as a part of HAART regimen of HIV	HIV	
	Umifenovir	Non-nucleoside broad-spectrum antiviral licensed for influenza treatment and prophylaxis	Broad-spectrum antiviral licensed for influenza treatment and prophylaxis	[68]
	Antipyretics	upregulate ACE2 receptors	antipyretic agent.	[69]
	Systemic Corticosteroids	Viral shedding time and maintain a systemic anti-inflammatory state that will minimize the precipitation of ARDS, dyspnea, and severe pneumonia.	the management of ARDS	[70, 71]
	ACE Inhibitor (ACEi) and Angiotensin Receptor-1 Blocker (ARBs) (Captopril) Enalapril	Block the SARS-CoV-2's binding with human ACE-2 And reduces symptoms of severe pneumonia	Hypertension	[72-74]
	Cyclosporin A	Interferes with functional interactions between viral proteins and one or multiple members of the large cyclophilin family	Immunosuppressant	[75]
	Teicoplanin	Block the SARS-CoV-2's to cross cells.	Bacterial infection	[76, 77]
	SARS-CoV-2 specific antibodies	Inhibits SARS-CoV-2 entry into cells	SARS-CoV-2	[78]
	SARS-CoV-2 specific protease drug candidate	Blocks viral infectivity and no more details about its mechanism	SARS-CoV-2	[78]
	IFN- α		antiviral activity, clinical trial to treat MERS-CoV hepatitis	[79]

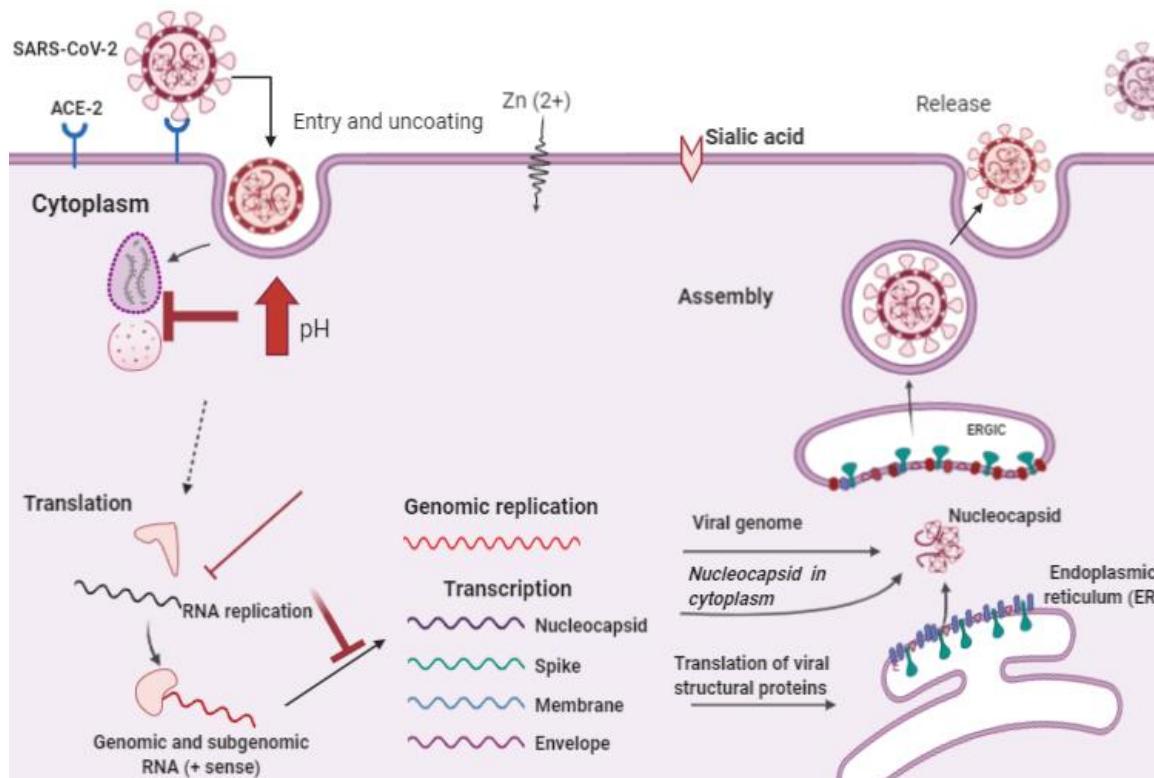
284 **The role of chloroquine and remdesivir as most potential therapeutics against SARS-**
285 **CoV-2**

286 Chloroquine as an amine acidotropic form quinine has been synthesised in 1934 by
287 Bayer in Germany. It was long known as antimalarial medication and became one of the
288 best options for COVID-19 medications. The mechanism of Chloroquine can summarize
289 by three factors; as alkaline vascular and lysosomal pH, immunomodulatory effects and
290 zinc ionophore. The ability of Chloroquine to increase the cell pH play a key role to inhibit
291 Glycosylation leading to prolong the incubation time of SARS-CoV-2 that may will
292 provide a chance for immunological system to detect and dealing with this pathogen. It
293 also can inhibit endocytosis, lysosomal fusion and function [65, 66].

294 Chloroquine as a zinc ionophore can allow the influx of zinc into cells and into
295 lysosomes by its ability to form stable complexes by bonds which supporting the free
296 electronics pairs for functional groups. Hence, chloroquine may inhibit RNA polymerase
297 which depends on RNA RDRP leads to inhibit SARS-CoV-2 RNA. The main usage of
298 Chloroquine as one of the most potential therapy for targeting COVID-19 as Chloroquine
299 phosphate, with dosage 500 mg BID for 5 days for respiratory tract infection and 500 mg
300 BID for 10 days for upper respiratory tract infection. Hydroxychloroquine can used with
301 400 mg BID day 1 as loading dose, then 200 mg BID for 5e10 days as maintenance dose
302 [66].

303 Remdesivir has been described as nucleoside inhibitor and broad-spectrum antiviral
304 drug. It is a monophosphoramidate prodrug and its mechanism of action can summarizing
305 as premature termination of viral RNA replication. It has been developed against Ebola
306 and used with previous coronaviruses MERS-CoV and SARS-CoV. Currently,

307 Remdesivir become the strongest candidate for COVID-19 [63]. The mechanism of
 308 remdesivir and chloroquine against SARS-CoV-2 desecrpded in figure 4.



309 Figure 4. Represent the mechanism of remdesivir and chloroquine against SARS-CoV-2

311 CONCLUSIONS & FUTURE PERSPECTIVES

312 The emergence of COVID-19 basically illustrates and the recent studies have been
 313 described virulence of the new Coronavirus that suddenly appeared and rapidly spread
 314 resulting in widespread health, economic and social consequences. The COVID-19
 315 epidemics can occur anywhere and the evidence indicated that this
 316 novel Coronavirus has an etiologic role in severe acute respiratory syndrome. Effective
 317 preparedness plans and more advanced studies are required to predict and control outbreaks.
 318 The standard recommendations are also required to improve patient management and

319 ensure global health security. Now the question arises, “**Is there any possibility of**
320 **COVID-19 to be seasonally infection?**”

321

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325 **CONFLICT OF INTERESTS**

326 All authors declare no conflict of interest in the current study.

327

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