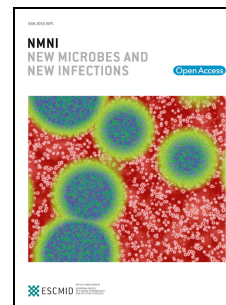


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Epidemiology, genome, and clinical features of the pandemic SARSCoV-2: a recent view

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1 Abstract

2 Since the emergence of the Severe Acute Respiratory Syndrome- Coronavirus-2
3 (SARS-CoV-2) in Chinese Wuhan, the globally confirmed cases according to WHO
4 statistics reached 292,124 in 189 countries by March 22. The deaths cases reached
5 12,784 with estimated case-fatality rate ranges from 0.5 to 5.7%. Children are the
6 least affected population by the disease, while the highest rate of death is among
7 elderly and people with comorbidities. The majority of infected individuals are
8 asymptomatic or only with mild symptoms. After the incubation period, the most
9 common symptoms are fever, cough, and fatigue. Asymptomatic carrier state is of
10 paramount importance due to their ability to spread the infection and shedding the
11 virus into air and surroundings. Although much is still unknown about SARS-CoV-2,
12 the scientific research progresses in an unprecedented pace toward understanding the
13 nature, effective control, prevention, and treatment of SARS-CoV-2. Various reports
14 have suggested an *in vivo* evolution of the virus which may explain the rapid spread
15 and changing epidemiology of SARS-CoV-2 but further evidences are needed.
16 Unfortunately, no effective treatment or therapeutic drug is available for the disease
17 and only supportive treatment and classical intervention measures are the available
18 choices for confronting SARS-CoV-2 pandemic.

19

20 Keywords:

21 CoVid-19, epidemic, *Coronavirus*, transmission, asymptomatic, pneumonia, Europe,
22 2109-noCoV, quarantine.

23 **Abbreviations:**

24 CCDC: Chinese Centre for Disease Control and Prevention, CDC: Centres for
25 Disease Control and Prevention (USA), ECDC: European Centre for Disease
26 Prevention and Control, WHO: World Health Organization, ACE2: Angiotensin-
27 Converting Enzyme 2, SARS: Severe Acute Respiratory Syndrome, UTR:
28 Untranslated region, CT: Computerized Tomography.

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40 **Introduction**

41 Emerging viral diseases are frequent public health threats owing to their potentials to
42 develop from small outbreaks to epidemics and pandemics. On 31 December 2019,
43 Chinese health authorities announced dozens of pneumonia infections in Wuhan city
44 (Hubei province) without a recognized aetiology [1]. The first reported cases of
45 pneumonia in Wuhan had a previous history of visiting or association with a local
46 seafood market where wildlife animals are sold. The infectious agent was
47 subsequently identified on January 12 as a novel coronavirus (2019-nCoV) envisaged
48 to be originated from Huanan seafood market [2]. Due to its high similarity in terms
49 of clinical symptoms and biological nature with the causative agent of severe acute
50 respiratory syndrome (SARS), the novel coronavirus named SARS-CoV-2 by the
51 International Committee on Taxonomy of Viruses. After rapid isolation of the virus
52 on January 7, genome sequence became publically available and submitted on
53 January 12 (GenBank: MN908947.2.
54 <https://www.ncbi.nlm.nih.gov/nuccore/MN908947.2>). Phylogenetic analyses showed
55 that SARS-CoV-2 is closely related to two SARS- coronaviruses of bat origin, bat-
56 SL-CoVZC45 and bat-SL-CoVZXC21, but distant from human SARS-CoV (79%
57 sequence homology) and Middle East respiratory syndrome (MERS) coronavirus
58 (MERS-CoV) (50%) [3,4]. Epidemiological investigations showed that different
59 animals (Bats, pangolins, snakes) could have been intermediate hosts that facilitate
60 the spill-over of SARS-CoV-2 as a distinct human Betacoronavirus from bats to
61 human population [4–6].

62 Since February 26, the reported new cases outside China are surpassing the cases
63 being reported in China mainland [7]. Currently, the numbers are increasing rapidly
64 specially in European region with overwhelming deaths in Italy. Till March 22, the
65 total cases of infections were 292,142 in 189 countries around the globe with
66 approximately 12,784 deaths cases. Reports show that adults and elderly are the most
67 infected by SARS-CoV-2, with slight predominance in men, while only low
68 proportion of paediatrics had contracted the infection [8–10]. Moreover, the presence
69 of previous diseases such as diabetes, cardiovascular or respiratory malfunction
70 significantly affects the outcomes. Indeed, being elderly or delay in diagnosis were
71 found to substantially increase the case-fatality rate [10,11]. The aim of this review is
72 to concisely discuss what is currently known about SARS-CoV-2 and its
73 overwhelming pandemic.

74 **Virology and genome of SARS-CoV-2**

75 SARS-CoV-2 is an enveloped positive-sense unsegmented single-strand RNA virus
76 that belong to the genus *Betacoronavirus* (β CoV) (Figure 1A) [12]. The whole-
77 genome sequences of SARS-CoV-2 isolated from patients in Wuhan or visited
78 Wuhan showed a genome of 29844 - 29891 nucleotides in size, encoding
79 approximately 9860 amino acids and lacks the hemagglutinin-esterase gene [4,12].
80 SARS-CoV-2 genome has great sequence similarity (89% - 96.3%) with two bat
81 coronaviruses; SARS-like-CoVZXC21 and bat-SL-CoVZC45, and 79% - 82% with
82 that of human SARS-CoV [4,12,13]. The genome contains 14 open reading frame
83 (ORF) encoding 27 proteins (Figure 1B). The longest ORF is located at the 5'-

84 terminus encoding for 15 non-structural proteins collectively involved in viral
85 replication and possibly in immune evasion. The 3'-terminus of the genome encodes
86 for structural and accessory proteins [3]. Hypervariable genomic hotspots have been
87 detected in spike gene and in other ORFs for non-structural proteins [14].

88 Interestingly, the unique aspects of SARS-COV-2 were found in genes of spike
89 glycoprotein, orf8, and orf3b. Spike protein is composed of two subunits; S1 domain
90 of a single polypeptide containing the receptor-binding domain and the S2 composed
91 of highly conserved polypeptides associated with the envelope. The external
92 subdomain of SARS-CoV-2 spike globular head S1 has only 40% similarity with its
93 counterparts in bat- and human SARS-CoV virion [12]. The outer portion of the
94 external subdomain responsible for direct contact with the human receptor (ACE2)
95 has the most diversity in amino acids. Such variations are believed to be evolved
96 from homologous recombination between a bat coronavirus and other coronavirus of
97 unknown origin [5]. Orf3b is putative novel protein that seems to play a pivotal role
98 in pathogenesis of SARS-COV-2. The orf8 is an accessory protein shorter than its
99 counterparts found in other *Betacoronavirus* with unknown function.

100 **Epidemiology and transmission of SARS-CoV-2**

101 During the past two decades, China has witnessed the emergence of three respiratory
102 viral outbreaks that turned into epidemics; avian influenza H5N1 in 1997 [15],
103 SARS-CoV in 2003 [16], and the ongoing SARS-CoV-2 (in 2019-2020). Only the
104 first cases of SARS-CoV-2 had associations with Huanan seafood market, while the

105 subsequent sources of infection were infected individuals. Human-to-human
106 transmission is believed to be the major route for disease spreading worldwide [17].
107 The intermediate host in Wuhan was suspected to be snakes and/or pangolins [5] but
108 it still to be confirmed. Travel and importation played a critical role in delivery of
109 SARS-CoV-2 to Korea, Japan, the Middle East, and Europe [18,19]. During the early
110 weeks of the epidemic, the basic reproductive values (R_0) were calculated between 2
111 and 3.5, which is higher than SARS [20,21]. The R_0 is defined as the expected
112 number of secondary cases infected by a single infectious person in a susceptible
113 population.

114 WHO declared SARS-CoV-2 as a Public Health Emergency of International Concern
115 on January 30 and as a controllable pandemic in March 11. According to WHO
116 statistics (March 22), the most reported cases were in China (81,498), Italy (53,578),
117 Spain (24,926), Germany (21,463), Iran (20,610), France (14,296) Korea (8,897), and
118 USA (15,219). Populations of about 54.6% of reporting countries are undergoing
119 local transmission of the infection [22]. Shockingly, more than 160 thousands
120 confirmed cases were reported within the last 12 days [7]. Based on reports from the
121 Chinese Centre for Disease Control and Prevention (CCDC), human-to-human
122 transmission via respiratory droplets and contact are the major routes to acquire the
123 infection. So far, no reliable evidence of vertical (intrauterine) transmission has been
124 published. Transmission of infection to healthcare workers resulted in more than
125 2000 cases in China and 1423 in Italy (as of March 17) [23,24].

126 Early March witnessed a rapid increase of cases in Italy, Spain, France, Germany,
127 and Iran. Currently all European countries are affected and thousands of new cases
128 are reported on daily basis without known dynamics. Perhaps no pre-existing
129 immunity in the population and all individuals are considered susceptible. The
130 transmission chain might went unnoticed during the incubation period of infected or
131 asymptomatic individuals who are transferring the infection actively. A mutant yet-
132 unknown new type may be a major factor for the current overwhelming increase in
133 cases despite the pre-emptive implemented precautions and countermeasures taken by
134 at-risk countries. Indeed, genomic analysis of 103 genomes derived from SARS-
135 CoV-2 showed that genomes are diverged into two types; S (the ancestor) and L [25].
136 The L type was prevalent during early January 2020, but decreased in later weeks.
137 Furthermore, recent studies support the evolution of the virus by successive
138 mutations and recombination processes [26,27]. Comparative studies of genomes
139 sequenced from European cases compared to previously sequenced genomes in China
140 are needed to verify the previous findings.

141 By March, the number of new cases in China are getting low with time, while Italy
142 and Iran are the new hotspots from which new infections are disseminated to the
143 nearby countries. In the Middle East and central Europe, the reported cases to WHO
144 are growing with time (Figure 2). In the European continent, the total confirmed
145 cases reach 141,858 and 7,319 deaths until March 22 (10:00 CET) [28]. According to
146 the epidemiological data by Italian Higher Institute of Health (ISS), the mortality rate
147 (5.4%) is higher than of China (2.3%) and total deaths in Italy exceeded the number

148 documented in China. This may be attributed to the fact that most infected individuals
149 are the elderly in addition to the incapacity of healthcare system to cope up with the
150 rapid increase of new cases [23].

151 **Turning into a pandemic**

152 Unlike its precedent SARS outbreak, SARS-CoV-2 had unique characteristics and
153 chances to become a pandemic. First, the initial case definition set by Chinese CDC
154 (CCDC) was narrow and based solely on pneumonia signs. Subsequent analysis of
155 the first cases showed about 81% of cases have mild disease, which undoubtedly
156 increased the transmission within the community by the asymptomatic carrier state
157 [10]. The WHO estimated the mortality rate to be between 3 and 4% with increased
158 value for elderly or individuals with previous comorbidities. Due to the lack of data
159 regarding the true number of infected individuals worldwide, it is still early to
160 calculate the exact value of mortality rate. Second, the current definition (March 22)
161 of suspected case set by WHO is a patient with any acute respiratory illness and
162 having been in contact with a confirmed or probable SARS-COV-2 case in the last 14
163 days prior to onset of symptoms. The above definition is based on reports calculated
164 the incubation period to range from 1 to 14 days [29]. However, recent reports found
165 an incubation period might be as long as 24 days [30,31]. This period is much more
166 than the 14 days used by WHO for guidance the quarantine policies, consequently,
167 truly infected persons may be missed during their long incubation period and
168 contribute to the spread of SARS-CoV-2. Additionally, international surveillance
169 estimated that up to two-thirds of exported case from China went undetected [32].

170 Third, the containment measure was challenging in the first phase of the outbreak in
171 Wuhan due to its high population, immense trade and wide travel connections within
172 China and the world. Furthermore, the industry, commerce, and travel of China with
173 the rest of the world has doubled since 2000 which aided SARS-CoV-2 quick spread
174 [33,34]. The Spring Festival and Lunar Year events also believed to played a critical
175 role in SARS-CoV-2 spread within China and the region as millions of Wuhan
176 dwellers travelled out of the city before the lockdown measure implementation and
177 just after the outbreak. The same situation applies for Europe where international
178 travel and business are intense and free travel within the Eurozone is permitted. The
179 exact underlying reason(s) for the ongoing rapid spread of SARS-CoV-2 in Europe is
180 still unknown. The suspected *in vivo* evolution of the virus and transmission by
181 asymptomatic carriers may be major factors. [27,35,36].

182 Fourth, in SARS-CoV-2 infections, shedding of virions starts earlier than clinical
183 manifestations and shedding peak is still unknown [37]. Isolation of individuals after
184 symptoms onset will be too late and transmission to others would already occurred
185 during the incubation period [30,38]. Person-to-person transmission of SARS-CoV-2
186 from asymptomatic cases was documented in first clusters in Germany and Vietnam
187 during early February [39,40]. Dependence on temperature for ruling out
188 asymptomatic carriers as it used during SARS containment deemed inefficient in
189 SARS-CoV-2 [41]. Additionally, the R_0 value of SARS-CoV-2 is higher than of
190 SARS (3.28 vs 2.2) [20,21]. High transmissibility of SARS-CoV-2 is obvious by a

191 global increase of more than 72,000 cases in three days according to WHO reports
192 (from March 18 to 20) [7].

193 **Pathology and clinical features**

194 SARS-CoV-2 exploits the angiotensin-converting enzyme 2 receptor (ACE2), same
195 receptor of SARS, in lower respiratory tract of human for entry into lung cells
196 [42,43]. Cellular surface serine protease TMPRSS2 is also employed by SARS-CoV-
197 2 for priming of spike protein S to facilitate membrane fusion with host cell [42].
198 ACE2 is also prevalent on other cells outside lung [44]. The exact pathophysiology of
199 SARS-CoV-2 and its closely related outbreaks-associated coronaviruses remains
200 elusive. Cytokines storm and viral evasion of cell-mediated immune response play
201 important roles in pathogenesis and disease severity [45]. Higher levels of
202 inflammatory chemokines and cytokines (GCSF, IP10, MCP1, MIP1A, TNF α , and
203 other interleukins) result in lung injury that requires urgent admission to intensive
204 care units [8].

205 Children are the least affected population by the disease, however, this observation
206 might be biased by low number of sampled children in the earlier reports. Moreover,
207 children have less contact with potential sources due to fewer outdoor activities and
208 parental protection. Some scholars believe that immune system of children develops
209 less intense cytokines storm or their respiratory tracts are healthier because they have
210 not been exposed to pollutants as adults, yet supporting evidences are still
211 unavailable.

212 After an incubation period of 5-14 days, SARS-CoV-2 infected people commonly
213 present by features of pneumonia including fever, dry cough, dyspnoea, myalgia, and
214 fatigue. Acute respiratory distress syndrome (ARDS) is a feature in severe cases.
215 Other symptoms include productive cough, headache, haemoptysis, and diarrhoea
216 were also documented [8]. A report from the CCDC estimated that only 5% are
217 critically ill (e.g., with shock, respiratory failure requiring mechanical ventilation, or
218 multiple organ dysfunction), 14% of patients had severe pneumonia (e.g., shortness
219 of breath, low oxygen saturation, or had more than 50% of their lung parenchyma
220 involved on chest imaging within 1-2 days). Meanwhile, most patients (81%) showed
221 no or mild pneumonia [10]. The overall case-fatality rate was 2.3 percent, however,
222 case-fatality rate between 5.8 percent in Wuhan to 0.7 percent in the rest of China
223 were reported. Fortunately, no deaths were reported among noncritical cases [46].

224 Leukocyte count in most cases shows lymphopenia, nonetheless, total white cell
225 count may be low or higher than normal. D-dimer, prothrombin time, hepatic
226 transaminases and procalcitonin are high among critically ill patients. Abnormal chest
227 radiographic features were seen in almost all patients [8]. Bilateral patchy shadows
228 are frequently seen on chest X-ray, while ground glass opacifications (GGO) are
229 found in cases with ARDS. Typical CT findings include; multiple GGO with or
230 without reticular pattern, and parenchymal consolidations involving both lungs
231 [47,48]. Other common CT features include; microvascular dilatation, thick interlobar
232 septa and air bronchogram [48]. Interestingly, CT changes have also been seen in
233 patients before the onset of clinical symptoms and before viral RNA detection from

234 upper respiratory specimens [49]. Time required for recovery ranges from 2 weeks in
235 mild infections to 3-6 weeks in severe disease. Extrapulmonary complications include
236 acute injuries in heart, liver, and kidneys are known [9,50].

237 **Diagnosis**

238 Travel history is no longer valid as a criterion to build the diagnosis on since local
239 transmission account for the majority of infection acquisition expected in locations
240 where no cases have been identified previously. The clinical manifestations
241 accompanied by radiographic evaluation and laboratory diagnosis (detection of viral
242 RNA) are the only possible approach for definitive diagnosis [51]. Generalizations
243 regarding symptoms and laboratory indices still cannot be drawn because SARS-
244 CoV-2 pathology and its reflections are still not completely understood. Due to
245 variations in epidemiology and clinical features of SARS-CoV-2 infections,
246 physicians and specialists are highly recommended to continually update their
247 management strategies based on WHO interim guidelines for diagnosis and cases
248 definitions (suspected, probable, and confirmed).

249 The most convenient laboratory tests for SARS-CoV-2 diagnosis is the real-time
250 reverse transcriptase-PCR (rRT-PCR) of nasopharyngeal specimens. A regularly
251 updated source for various protocols based on rRT-PCR assay is available at WHO
252 website [52]. As in any diagnostic test, false positive and false negative results have
253 been reported but at very low frequency [30]. According to CDC recommendations,
254 the accepted clinical specimens are bronchoalveolar lavage fluid, nasopharyngeal

255 swabs (but not throat swabs), and blood [53]. Bronchoalveolar lavage fluid were
256 found superior to other respiratory specimens (positive rate 93%) followed by sputum
257 (72%), nasal swab (63%), fibrobronchoscope brush biopsy (46%), pharyngeal swab
258 (32%), and faeces (29%) [54]. Due to the increasing number of healthcare-associated
259 infections, strict adherence to usage of personal protective equipment (PPE) and
260 airborne precautions is highly recommended. A concise guide for healthcare staff,
261 researcher, and public health workers has been published [55].

262 **Confronting the pandemic**

263 In the absence of specific therapy and anti-SARS-CoV-2 drugs, the urgent
264 implementation of classical public health measures are the only reliable actions to
265 mitigate the pandemic and gradual control of infection spread. A very recent small-
266 sized clinical trial has found promising results for treatment of SARS-CoV-2 in
267 France. The administration of 600 mg of hydroxychloroquine plus azithromycin on
268 daily basis resulted in effective clearance of the virus from the nasopharynx within
269 six days [56]. The mechanism of action is the alkalisation of epithelial
270 phagolysosome containing the virus. These results are founding the current
271 therapeutic protocol in IHU Méditerranée Infection, France. Further large-sized
272 ongoing clinical trials (including hydroxychloroquine among other drugs) will
273 provide further pieces of evidence for treatment options.

274 The rigorous and gigantic efforts of China in implementing public measures are
275 obviously effective as new cases are declining steeply. Indeed, China have applied

276 the largest quarantine in history to contain the disease, hence, cut of person-to-person
277 transmission chain, isolation, quarantine, social distancing, and community
278 containment are the only promising measures to fight SARS-CoV-2. As a respiratory
279 virus with substantial transmissibility, applying of social distancing to reduce
280 interactions between people in a mass scale is beneficial especially when detection of
281 cases is swift [57]. If the community transmission continued in expansion, social
282 distancing would be insufficient and community containment would be needed. The
283 efficiency of community containment is apparent in China where normal daily life is
284 gradually being sustained recently in Wuhan after a significant decline of cases.
285 Nonetheless, such measure is challenging and requires a partnership with local and
286 state officials of different fields. Media should also tap their abilities to communicate
287 with trusted information about containment benefits and pre-empt false rumours and
288 panic.

289 As the world witnessing a significant decline in new cases in China, the will of
290 political and healthcare authorities should push forward to implement a lockdown of
291 hotspot zones and a comprehensive tracing of contacts associated with confirmed
292 cases. The cost of wide tracking and community containment would not be
293 outweighed by the long-term economic losses and disease burden if the transmission
294 continued. Additionally, rapid responses and decision making alongside free or at
295 least affordable laboratory testing will facilitate the delineation of hotspot zones.
296 Certain community containment procedures such as cancellation of public events and
297 closure of institutions are seen in numerous countries. These precautions will not be

298 fruitful unless parallel thorough surveillance accompanied by medical observation
299 and legal actions are taken if quarantine violations occurred. Recently, Italy, France,
300 and Spain, and Philippines started the implementation of lockdown measures, with
301 law enforcement in some cases, to control the overwhelming increase in cases. In
302 third-world countries, lockdown measure is extremely challenging owing to the high
303 proportion of low-wage jobs where workers seek opportunities at daily basis. Finally,
304 efficient deactivation of different coronaviruses (SARS-CoV-2 was not evaluated)
305 was reported with disinfectants such as 62 - 71% ethanol, 0.5% hydrogen peroxide or
306 0.1% sodium hypochlorite within 1 minute and this efficacy is highly expected to
307 apply for SARS-CoV-2 [58].

308 **Issues to be investigated**

309 Despite the intense research and clinical investigations, certain issues of SARS-CoV-
310 2 pandemic await exploration. First, the origin of the virus and the nature of spill-over
311 from its natural reservoir to human is still unanswered. It is known that bats and
312 Pangolins are hunted for food in China but this has not been confirmed so far to be the
313 cause [6]. Moreover, viral replication and human immune response to SARS-CoV-2
314 are still largely unknown. Second, the virus was detected in faecal samples from
315 infected patients and its potentials for oral-faecal transmissibility is still unaddressed
316 by researchers [54,59,60]. Third, the phylogenetic analyses have shown genomic
317 variations in SARS-CoV-2 genomes sequenced in different countries through
318 different periods. Whether the in vivo evolution occurs in human or other
319 intermediate animal host is still unproven. Indeed, the existence and identity of an

320 intermediate host is highly expected with few evidences but not experimentally
321 proven. Fourth, the period for which SARS-CoV-2 virion retains its infectivity when
322 shed and deposited on surfaces and environment is also unclear. Indeed, the efficacy
323 of hand washing in deactivating SARS-CoV-2 virion has not been tested. Fifth, the
324 reason of predominance of SARS-CoV-2 infections in men is also not known.
325 Smoking habit in Asian men populations was expected to be the underlying cause,
326 but no solid evidence is yet available [61]. Sixth, the initial administration of
327 corticosteroids during early stage of SARS epidemic was justified by their mitigation
328 of inflammatory response but subsequently halted due to delay in viral clearance [62].
329 Lately, a small-sized (n=201) observational study reported that methylprednisolone
330 treatment was associated with decrease in death risk of patients with ARDS [63].
331 Whether the same effects of corticosteroids happen in SARS-CoV-2 infection are still
332 unclear.

333 **Conclusion**

334 The epicentres of SARS-CoV-2 globally is expected to multiply especially in poor
335 nations. Genomic, virological, and medical analyses are progressing in unprecedented
336 strides. Such analyses are expected to contribute to understanding of epidemiology,
337 pathogenesis, treatment, and prevention. Suspected case definition is expected to get
338 revised at any moment, hence, medical staff and epidemiologists should be keep
339 updated for better control of the pandemic. Moreover, they are also highly advised to
340 employ protective measures since they are at-risk populations due to exposure to
341 infection nosocomially. The clinical manifestations varied widely and mild or

342 asymptomatic cases may not seek a medical care and go undetected and exacerbate
343 transmission scenario. The exact routes of pathogenesis, transmission and pandemic
344 dynamics of the SARS-CoV-2 are under intense investigation. Till now, classical
345 public health measures and control intervention are the only way to fight SARS-CoV-
346 2 pandemic.

347 **Conflicts of interest**

348 The authors declare no conflicts of interest.

349

350

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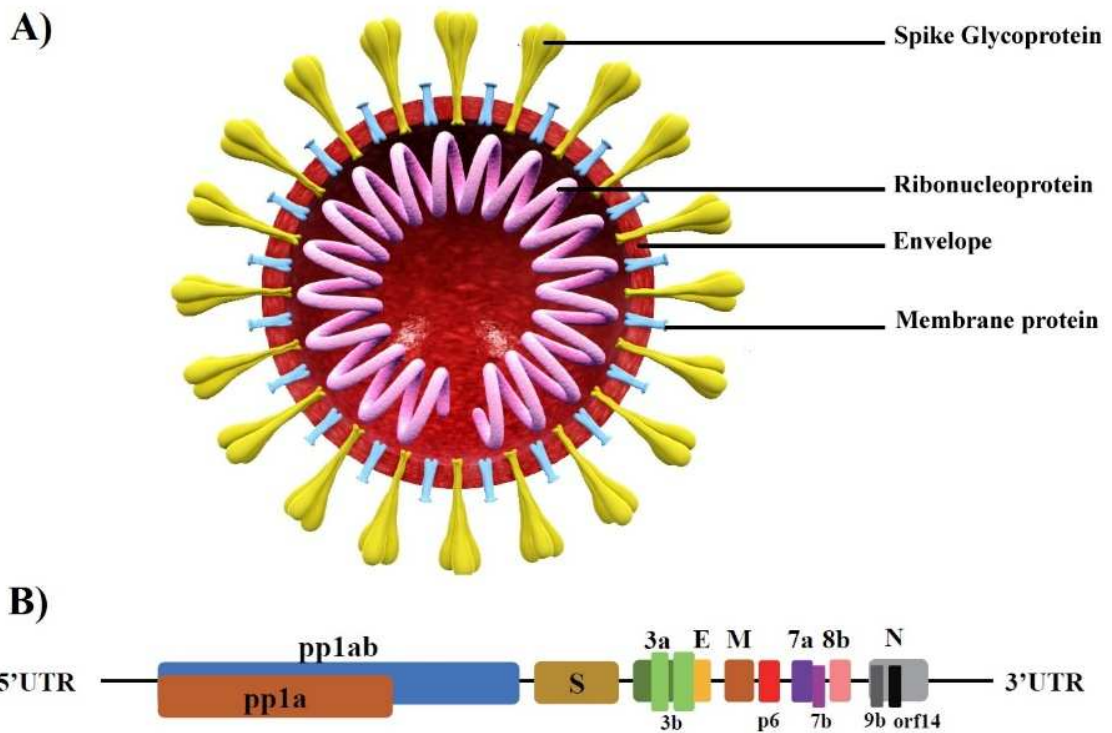
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553 **Figures**

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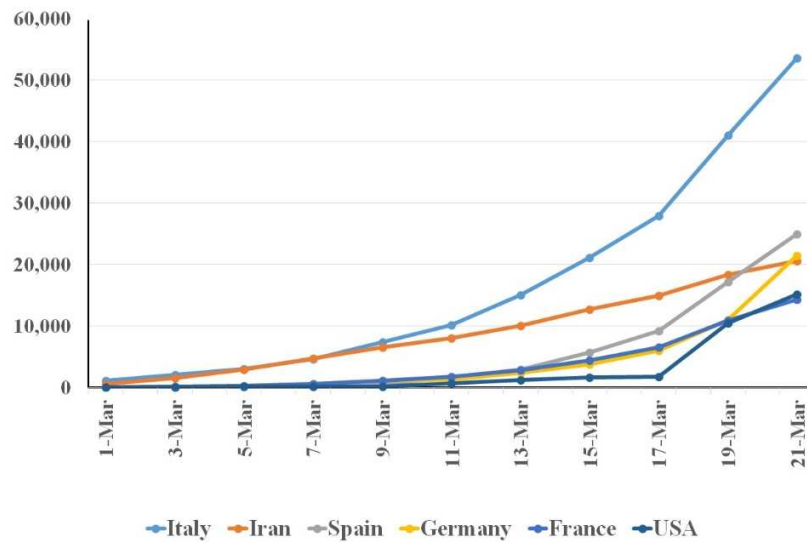
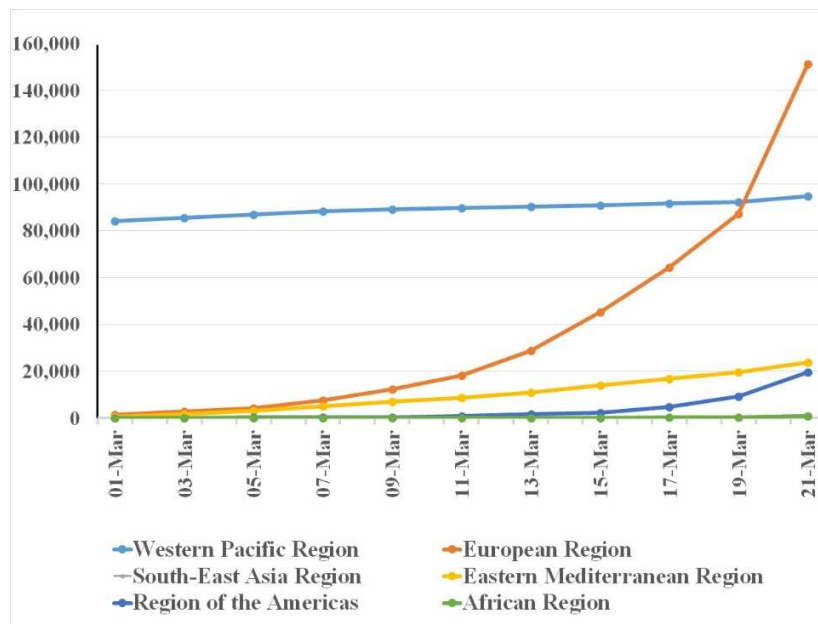
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557 **Figure 1. Structure and genome organization of SARS-CoV-2.** (A) General
 558 structure of SARS-CoV-2 virion. (B) Genome composition of SARS-CoV-2 showing
 559 fourteen open reading frames exist in SARS-CoV-2 genome. The first two ORFs at
 560 the 5'- UTR are coding for polyprotein (pp1a/ab) required for viral replication

561 followed by structural proteins for Spike (S), membrane (M), Nucleoprotein (N). At
 562 the 3'-terminus accessory genes (3a, 3b, p6, 7a, 7b, 8b, 9b, and orf14) are located
 563 with flanking ORFs. Accessory proteins not required for viral replication or other
 564 known functions (adopted from reference [3] with permission).



565

566 **Figure 2. Reported cases of SARS-CoV-2 from March 1 -21.** (A) Total confirmed
567 cases in all regions of the world. (B) Newly reported cases of SARS-CoV-2 in most
568 affected countries (with cases > 8,000). (The numbers are retrieved from WHO
569 situation reports).

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