

The Deadly Scourge Call COVID-19: Will Mankind Find a Panacea to this Pandemic?

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Abstract

As human civilization rises, the combat with diseases emerges with it. Beginning with the earliest documented pandemic of 430 BC in Athens during the Peloponnesian war to the ongoing novel coronavirus disease 2019 (nCOVID-19), mankind has been ravaged by different warfares from the microbial populations. As the carnages recorded daily from COVID-19 infection rages unabated, there is an on-going concern that this event with all its dynamics and attendant consequences has in its embryo the potential to triggered the global economy into a quagmire and leave an indelible deleterious impact on mankind. It is against this background that this review discusses succinctly the historical origin of human coronaviruses with the chronology, genome, epidemiology, transmission, pathogenesis and therapeutic options for the nCOVID-19 infection. We highlight that currently over 210 countries around the globe and two international conveyances have been affected by the pandemic. High mortality occurs mostly among senile individuals and patients with multiple comorbidities; however very few pediatric cases have so far been reported. The zoonotic source of SARS-CoV-2 is yet to be affirmed. Nevertheless, the sequence-based analysis suggested bats as the potent reservoir. Several reports have suggested person-to-person contact has the most probable route of transmission. Hitherto, no promising clinical therapies or prevention strategies is in prospect against human coronaviruses. This review opines that more research is expeditiously required to identify novel chemotherapeutic drugs for treating COVID-19 infections. In order to develop pre- and post-exposure prophylaxis against COVID-19, there is an urgent need to establish an animal model to replicate the severe disease currently observed in humans. However, the momentous question still yet to be answered is - will the world find a panacea to this ravaging pandemic?

Keywords: Coronaviruses; COVID-19; Pandemic; Transmission; Pathogenesis; Therapeutic

Introduction

As the carnages arising from coronavirus disease 2019 (COVID-19) in the world rages unabated, there is this on-going tension, that this pandemic with all its dynamics and antecedents has in its embryo the potential to have inimical effect on the well-being of humanity and also plummet the world's economy into another quagmire with all its attending crises. This assertion is by all means valid if circumspect prognoses of current events are made. Thus, the pertinent questions that policy makers, scientists, public health professionals, medical experts and other stakeholders should be asking are: How can the past knowledge help in real-time management of the pandemic? What insights have we gains from this ongoing imbroglio for future disease management and prevention? Hidden in the background of these questions is a more or less direct recrimination: why do we fail to learn from previous events? The remarks of some pundits seem to be: "there is

nothing absolutely amazing about COVID-19 pandemic" [1]; while to the layman, it is just a myth or conspiracy theory. The history-as-lessons school of thought bases its assumption on the fact that epidemics are structurally juxtapositional events, regardless of the place and time they occur. The COVID-19 outbreak "creates a feeling of déjà vu with the severe acute respiratory syndrome (SARS) outbreak of 2003 [2].

Coronaviruses are a large family of viruses that can be transmitted between animal and people, cause illnesses ranging widely in severity from common cold to more severe respiratory syndromes. The first known deleterious ailment caused by a coronavirus emerged with the 2003 SARS epidemic in Guangdong province of China. This virus was affirmed to be a member of the Beta-coronavirus subgroup and was given the nomenclature of SARS-CoV [3,4]. From the wall of Guangdong, China, SARS spreads sporadically like ravaging forest fires to other part of the world infecting

more than 8000 people and leaving more than 776 dead. Another ugly incident associated with severe illness emerged a decade later in 2012 in Saudi Arabia, when a couple of Saudi Arabian nationals were diagnosed to be infected with another coronavirus named as the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The World Health Organization (WHO) reported that MERS-CoV epidemics recorded 2,428 cases with 838 fatalities [5]. This MERS-CoV belongs to the member of the beta-coronavirus subgroup and phylogenetically differ other human-CoV.

The most recent outbreak associated with the coronavirus family is the coronavirus disease 19 (COVID-19) which begins towards the end of 2019 in Wuhan city, China and after that spread around the globe. COVID-19 is a novel coronavirus that has no previous identification among humans. The first case was identified in the Hubei province of China towards the end of December 2019. The outbreak originated from the Hunan seafood market in Wuhan city of China, where live animals such as bats, snakes, frogs, marmots, birds, rabbits etc. were sold and rapidly infected more than fifty (50) peoples [6]. The coronavirus disease 19 (COVID-19) is a highly transmittable and virulent viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). With each day passing by, more and more cases of COVID-19 are being detected; bring to light the reality of a pandemic. Conscientious efforts are being demonstrated at the individual, national and international level to understand the genomics, modes of transmission, pathogenicity, and management strategies for the novel corona virus 2019 (nCoV-2019) disease. It is against this background that this article gives a succinct and in-depth overview of the historical origin of Coronaviruses with the chronology, epidemiology, transmission, pathogenesis and therapeutic options for the COVID-19 infection. It is the aspiration of the authors that this systematic review will contribute to the knowledge base of the nCoV-2019 disease; and stir up more research interest and political will from various stakeholders that will help to accelerate the conquest of this deadly, unwanted alien that invade the kingdom of humanity.

Historical background of human coronaviruses

The historical origin of the human coronaviruses can be traced to 1965 when Tyrrell and Bynoe discovered that they could passage a virus named B814 [7]. This virus was observed in the human embryonic tracheal organ cultures obtained from adult respiratory tract suffering from common cold. The presence of an infectious agent was demonstrated by inoculating the medium from these cultures intranasally in human volunteers; a significant proportion of the subjects came down with colds, but Tyrrell and Bynoe could not grow the pathogen in tissue culture at that time. Coincidentally, Hamre and Procknow [8] were able to culture a virus with unique features in tissue culture from samples obtained from medical students with colds. Both B814 and Hamre's virus, which she called 229E, were ether-sensitive and therefore presumably required a lipid-containing coat for infectivity. Still, these 2 viruses were not related to any known myxo- or paramyxoviruses. McIntosh, *et al.* [9] while working in the laboratory of Robert Chanock at the National Institutes of Health reported the recovery of multiple strains

of ether-sensitive agents from the human respiratory tract by using a technique similar to that of Tyrrell and Bynoe. These viruses were termed OC, meaning that they were grown in organ cultures.

During the same epoch, Almeida and Tyrrell [10] performed electron microscopy on fluids from organ cultures infected with B814 and discovered particles similar to the infectious bronchitis virus of chickens. The particles were medium sized (80 - 150 nm), pleomorphic, membrane-coated, and covered with widely spaced club-shaped surface projections. The 229E agent identified by Hamre and Procknow [8] and the previous OC viruses identified by McIntosh *et al.* [9] had a similar morphology (Figure 1).

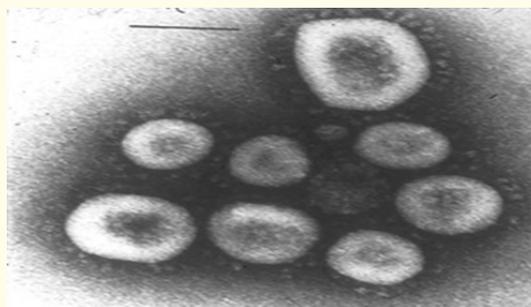


Figure 1: Coronavirus OC16. Reprinted with permission from Proc Natl Acad Sci USA. 1967;57;933-940.

Ongoing research using serologic techniques has generated a substantial quantity of information regarding the epidemiology of the human respiratory coronaviruses. It was discovered that in temperate climates, respiratory coronavirus infections frequently occur in the winter and spring than in the summer and fall. Data showed that coronavirus infections contribute as much as 35% of the total respiratory viral activity during epidemics. Generally, the proportion of adult colds produced by coronaviruses was estimated at 15% [9]. While research was proceeding to explore the pathogenicity and epidemiology of the human coronaviruses, the number and significance of animal coronaviruses were growing tremendously. Coronaviruses were described that caused disease in multiple animal species, including chickens, dogs, rats, pigs, mice, turkeys, calves, rabbits, and cats. Pathogenesis of these disease states differs remarkably and was complex, demonstrating that the genus as a whole has the potential to initiate numerous varieties of disease mechanisms [11]. Human and animal coronaviruses were segregated into 3 broad categories based on their antigenic and genetic makeup. Group I contained virus 229E and other viruses, group II contained virus OC43 and group III is made up of avian infectious bronchitis virus and several related avian viruses [12].

Coronavirus genome and structure

Coronaviruses are medium-sized (65 - 125 nm in diameter) RNA viruses with a very characteristic appearance in electron micrographs of negatively stained preparations. Corona represents crown-like spikes on the outer surface of the virus; thus, the named

“Coronavirus” (Figure 2). The nucleic acid is about 30 kb long, positive in a sense, single stranded, and polyadenylated. The RNA is the largest known viral RNA and codes for a large polyprotein. This polyprotein is cleaved by viral-encoded proteases to form the following: an RNA-dependent RNA polymerase and an ATPase helicase; a surface hemagglutinin-esterase protein present on OC43 and several other group II coronaviruses; the large surface glycoprotein (S protein) that forms the petal-shaped surface projections; a small envelope protein (E protein); a membrane glycoprotein (M protein); and a nucleocapsid protein (N protein) that forms a complex with the RNA. The coding functions of several other ORFs are vague. Coronaviruses’ replication strategy involves a nested set of messenger RNAs with common polyadenylated 3-ends. Only the unique part of the 5-end is translated [12]. Mutations are common in nature. Also, coronaviruses are capable of genetic recombination if 2 viruses infect the same cell at the same time.

Figure 2: Structure of respiratory syndrome causing human coronavirus.

All coronaviruses develop in the cytoplasm of infected cells, budding into cytoplasmic vesicles from the endoplasmic reticulum. These vesicles are either extruded or released from the cell within the same time frame, which result in the annihilation of the cell. All group I coronaviruses, including 229E, use human aminopeptidase N as their cellular receptor [13]. Mouse hepatitis virus, a group II coronavirus, uses a member of the carcinoembryonic antigen family as its receptor [14]. The receptor for OC43 is not known, but it may be one of the several cell surface molecules, including 9-*O*-acetylated neuraminic acid and the HLA-I molecule [15]. The SARS coronavirus uses angiotensin-converting enzyme II as its cellular receptor [16,17].

Origin and chronology of COVID-19 infections

A group of patients toward late December 2019 were on hospitals admission with an initial diagnosis of pneumonia of an unidentified etiology. Epidemiologically, these patients were linked to a seafood and wet animal wholesale market in Wuhan, Hubei Province, China [18,19]. Early reports forecasted the onset of a potential Coronavirus outbreak given the estimate of a reproduction number for the 2019 Novel (New) Coronavirus (COVID-19, named by WHO on February 11, 2020) which was deemed to be significantly more than 1 (ranges from 2.24 to 3.58) [20]. Within next 2 - 3 months, it has spread worldwide to the extent that it was

declared a global pandemic on March 11, 2020, by World Health Organization (WHO) [21].

In December 2019, the first cases of COVID-19 were reported [22]. From December 18, 2019 to December 29, 2019, five patients were hospitalized with acute respiratory distress syndrome resulting in the mortality of these patients [23]. By January 2, 2020, 41 admitted hospital patients had been identified as having laboratory-confirmed COVID-19 infection, less than 50% of these patients had underlying ailments, including diabetes, hypertension, and cardiovascular disease [24]. The assumption as at then was that these patients got the infection in that hospital, most probably due to nosocomial infection. Hence, concluding that COVID-19 does not have high infectivity, but rather spread due to numerous patients getting infected at different locations within the hospital by nebulous mechanisms. Moreover, only patients that got clinically sick were tested, thus implying that a greater number of patients were presumably infected than was reported [25]. As of January 22, 2020, the total cases of the 2019-new coronavirus (COVID-19) reported in 25 provinces (districts and cities) in China were 571 [26]. The China National Health Commission reported the details of the first 17 deaths up to January 22, 2020. On January 25, 2020, a total of 1975 cases were confirmed to be infected with the COVID-19 in mainland China with a total of 56 resulting deaths [6]. Another report on January 24, 2020, estimated the cumulative incidence in China to be 5502 cases [27]. As of March 14, 2020, there are 155,854 confirmed COVID-19 cases and 5,814 deaths globally have been reported in China and across over 150 countries of the world; with a high predominant disease load in Italy, United States, Spain, South Korea, Iran, Hong Kong, Macau, and Vietnam [21].

Global statistics on COVID-19

From December 2019 to date, COVID-19 pandemic is affecting a total of 212 countries and territories around the world and two (2) international conveyances. There are currently 4,256,583 confirmed cases, 287,354 deaths, and 1,529,535 recovered from the coronavirus COVID-19 outbreak as of May 12, 2020, 07:07 GMT. The statistics available on the number of active cases and closed cases presently is depicted in table 1. The breakdown of the current total number of confirmed cases and deaths country by country is depicted in table 2. At the moment, the number of cases is growing up even due to the 3rd and 4th generation transmission which signifies that the disease burden is likely going to increase further in coming few weeks.

Transmission

Based on the enormous number of infected people that were exposed to the wet animal market in Wuhan City of China where live animals are routinely sold, it is surmised that this is the most probable zoonotic origin of the COVID-19. All efforts made to establish a reservoir host or intermediate carriers from which the infection may have spread to humans end in futility. Initially, two species of snakes were identified to be a possible reservoir of the COVID-19. However, hitherto, there has been no sustainable proof of coronavirus reservoirs other than mammals and birds [28,29].

| Active Cases | | Closed Cases | |
|---------------------------------------|---------------------------------|---------------------------------------|----------------------|
| 2,439,694 Currently infected patients | | 1,816,889 Cases which had an outcome | |
| 2,392,749 (98%) in Mild Condition | 46,945 (2%) Serious or Critical | 1,529,535 (84%) Recovered/ Discharged | 287,354 (16%) Deaths |

Table 1: Number of active and closed cases of COVID-19 infection updated to May 12, 2020 (07:07 GMT). Source: <https://www.worldometers.info/coronavirus/#countries>. (click source for current update).

Genomic sequence analysis of COVID-19 indicated 88% identity with two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses [30,31], suggesting that mammals are the most likely link between COVID-19 and humans. Numerous reports have opined that person-to-person transmission is the most probable route of transmitting COVID-19 infection. This hypothesis is corroborated by cases reported within families and among people who did not visit the wet animal market in Wuhan [32,33]. Person-to-person transmission occurs primarily via direct contact or

| S/N | Country, Other | Total Cases | Total Deaths | S/N | Country | Total Cases | Total Deaths |
|-----|----------------|-------------|--------------|-----|-----------------------|-------------|--------------|
| 1 | USA | 1,385,834 | 81,795 | 108 | Burkina Faso | 760 | 50 |
| 2 | Spain | 268,143 | 26,744 | 109 | Andorra | 755 | 48 |
| 3 | UK | 223,060 | 32,065 | 110 | Paraguay | 724 | 10 |
| 4 | Russia | 221,344 | 2,009 | 111 | Mali | 712 | 39 |
| 5 | Italy | 219,814 | 30,739 | 112 | Diamond Princess | 712 | 13 |
| 6 | France | 177,423 | 26,643 | 113 | Uruguay | 711 | 19 |
| 7 | Germany | 172,576 | 7,661 | 114 | Kenya | 700 | 33 |
| 8 | Brazil | 169,594 | 11,653 | 115 | Tajikistan | 661 | 21 |
| 9 | Turkey | 139,771 | 3,841 | 116 | Georgia | 639 | 11 |
| 10 | Iran | 109,286 | 6,685 | 117 | San Marino | 628 | 41 |
| 11 | China | 82,919 | 4,633 | 118 | Jordan | 562 | 9 |
| 12 | India | 70,827 | 2,294 | 119 | Channel Islands | 546 | 41 |
| 13 | Canada | 69,981 | 4,993 | 120 | Tanzania | 509 | 21 |
| 14 | Peru | 68,822 | 1,961 | 121 | Jamaica | 505 | 9 |
| 15 | Belgium | 53,449 | 8,707 | 122 | Malta | 503 | 5 |
| 16 | Netherlands | 42,788 | 5,456 | 123 | Taiwan | 440 | 7 |
| 17 | Saudi Arabia | 41,014 | 255 | 124 | Equatorial Guinea | 439 | 4 |
| 18 | Mexico | 36,327 | 3,573 | 125 | Réunion | 436 | - |
| 19 | Pakistan | 32,081 | 706 | 126 | Venezuela | 422 | 10 |
| 20 | Switzerland | 30,344 | 1,845 | 127 | Palestine | 375 | 2 |
| 21 | Chile | 30,063 | 323 | 128 | Sierra Leone | 338 | 19 |
| 22 | Ecuador | 29,509 | 2,145 | 129 | Congo | 333 | 11 |
| 23 | Portugal | 27,679 | 1,144 | 130 | Mauritius | 332 | 10 |
| 24 | Sweden | 26,670 | 3,256 | 131 | Isle of Man | 330 | 23 |
| 25 | Belarus | 23,906 | 135 | 132 | Montenegro | 324 | 9 |
| 26 | Singapore | 23,822 | 21 | 133 | Chad | 322 | 31 |
| 27 | Qatar | 23,623 | 14 | 134 | Benin | 319 | 2 |
| 28 | Ireland | 23,135 | 1,467 | 135 | Vietnam | 288 | - |
| 29 | UAE | 18,878 | 201 | 136 | Rwanda | 285 | - |
| 30 | Israel | 16,506 | 258 | 137 | Zambia | 267 | 7 |
| 31 | Poland | 16,326 | 811 | 138 | Cabo Verde | 260 | 2 |
| 32 | Ukraine | 16,023 | 425 | 139 | Ethiopia | 250 | 5 |
| 33 | Austria | 15,882 | 620 | 140 | Liberia | 211 | 20 |
| 34 | Japan | 15,847 | 633 | 141 | Haiti | 209 | 16 |
| 35 | Bangladesh | 15,691 | 239 | 142 | Sao Tome and Principe | 208 | 5 |
| 36 | Romania | 15,588 | 982 | 143 | Martinique | 187 | 14 |
| 37 | Indonesia | 14,265 | 991 | 144 | Faeroe Islands | 187 | - |
| 38 | Colombia | 11,613 | 479 | 145 | Madagascar | 186 | - |
| 39 | Philippines | 11,086 | 726 | 146 | Togo | 181 | 11 |

| | | | | | | | |
|----|-----------------------------|--------|-----|-----|------------------------|-----|----|
| 40 | S. Korea | 10,936 | 258 | 147 | Myanmar | 180 | 6 |
| 41 | South Africa | 10,652 | 206 | 148 | Eswatini | 175 | 2 |
| 42 | Dominican Republic | 10,634 | 393 | 149 | South Sudan | 156 | - |
| 43 | Denmark | 10,513 | 533 | 150 | Guadeloupe | 154 | 13 |
| 44 | Serbia | 10,176 | 218 | 151 | Gibraltar | 147 | - |
| 45 | Egypt | 9,746 | 533 | 152 | French Guiana | 144 | 1 |
| 46 | Kuwait | 9,286 | 65 | 153 | CAR | 143 | - |
| 47 | Panama | 8,616 | 249 | 154 | Brunei | 141 | 1 |
| 48 | Czechia | 8,177 | 283 | 155 | Nepal | 134 | - |
| 49 | Norway | 8,132 | 224 | 156 | Cambodia | 122 | - |
| 50 | Australia | 6,970 | 97 | 157 | Uganda | 121 | - |
| 51 | Malaysia | 6,726 | 109 | 158 | Bermuda | 119 | 8 |
| 52 | Morocco | 6,281 | 188 | 159 | Trinidad and Tobago | 116 | 8 |
| 53 | Argentina | 6,278 | 314 | 160 | Guyana | 109 | 10 |
| 54 | Finland | 5,984 | 271 | 161 | Mozambique | 103 | - |
| 55 | Algeria | 5,891 | 507 | 162 | Aruba | 101 | 3 |
| 56 | Kazakhstan | 5,279 | 32 | 163 | Monaco | 96 | 4 |
| 57 | Bahrain | 5,236 | 8 | 164 | Bahamas | 93 | 11 |
| 58 | Moldova | 4,995 | 175 | 165 | Barbados | 84 | 7 |
| 59 | Ghana | 4,700 | 22 | 166 | Cayman Islands | 84 | 1 |
| 60 | Afghanistan | 4,687 | 122 | 167 | Liechtenstein | 82 | 1 |
| 61 | Nigeria | 4,641 | 150 | 168 | Sint Maarten | 76 | 15 |
| 62 | Luxembourg | 3,888 | 101 | 169 | Libya | 64 | 3 |
| 63 | Oman | 3,573 | 17 | 170 | French Polynesia | 60 | - |
| 64 | Armenia | 3,392 | 46 | 171 | Malawi | 57 | 3 |
| 65 | Hungary | 3,313 | 425 | 172 | Yemen | 56 | 9 |
| 66 | Thailand | 3,017 | 56 | 173 | Syria | 47 | 3 |
| 67 | Bolivia | 2,831 | 122 | 174 | Syria | 45 | 2 |
| 68 | Iraq | 2,818 | 110 | 175 | Macao | 45 | - |
| 69 | Greece | 2,726 | 151 | 176 | Mongolia | 42 | - |
| 70 | Cameroon | 2,689 | 125 | 177 | Saint Martin | 39 | 3 |
| 71 | Azerbaijan | 2,589 | 32 | 178 | Eritrea | 39 | - |
| 72 | Uzbekistan | 2,509 | 10 | 179 | Zimbabwe | 36 | 4 |
| 73 | Croatia | 2,196 | 91 | 180 | Antigua and Barbuda | 25 | 3 |
| 74 | Guinea | 2,146 | 11 | 181 | Botswana | 24 | 1 |
| 75 | Bosnia and Herze- govina | 2,141 | 113 | 182 | Timor-Leste | 24 | - |
| 76 | Honduras | 2,100 | 116 | 183 | Gambia | 22 | 1 |
| 77 | Bulgaria | 2,004 | 93 | 184 | Grenada | 21 | - |
| 78 | Senegal | 1,886 | 19 | 185 | Laos | 19 | - |
| 79 | Iceland | 1,801 | 10 | 186 | Belize | 18 | 2 |
| 80 | Cuba | 1,783 | 77 | 187 | Fiji | 18 | - |
| 81 | Estonia | 1,741 | 61 | 188 | New Caledonia | 18 | - |
| 82 | Ivory Coast | 1,730 | 21 | 189 | Saint Lucia | 18 | - |
| 83 | North Macedonia | 1,664 | 91 | 190 | St. Vincent Grenadines | 17 | - |
| 84 | Sudan | 1,526 | 74 | 191 | Nicaragua | 16 | 5 |
| 85 | New Zealand | 1,497 | 21 | 192 | Curaçao | 16 | 1 |
| 86 | Lithuania | 1,485 | 50 | 193 | Dominica | 16 | - |
| 87 | Slovenia | 1,460 | 102 | 194 | Namibia | 16 | - |
| 88 | Slovakia | 1,457 | 26 | 195 | Burundi | 15 | 1 |
| 89 | Djibouti | 1,227 | 3 | 196 | Saint Kitts and Nevis | 15 | - |

| | | | | | | | |
|-----|---------------|-------|----|-----|------------------------|----|---|
| 90 | Guatemala | 1,114 | 26 | 197 | Falkland Islands | 13 | - |
| 91 | Somalia | 1,089 | 52 | 198 | Turks and Caicos | 12 | 1 |
| 92 | Hong Kong | 1,048 | 4 | 199 | Vatican City | 12 | - |
| 93 | Kyrgyzstan | 1,037 | 12 | 200 | Comoros | 11 | 1 |
| 94 | Tunisia | 1,032 | 45 | 201 | Montserrat | 11 | 1 |
| 95 | DRC | 1,024 | 41 | 202 | Bhutan | 11 | - |
| 96 | Mayotte | 1,023 | 11 | 203 | Greenland | 11 | - |
| 97 | El Salvador | 998 | 18 | 204 | Seychelles | 11 | - |
| 98 | Latvia | 950 | 18 | 205 | Suriname | 10 | 1 |
| 99 | Cyprus | 901 | 16 | 206 | MS Zaandam | 9 | 2 |
| 100 | Maldives | 897 | 3 | 207 | Mauritania | 8 | 1 |
| 101 | Albania | 872 | 31 | 208 | Papua New Guinea | 8 | - |
| 102 | Sri Lanka | 869 | 9 | 209 | British Virgin Islands | 7 | 1 |
| 103 | Lebanon | 859 | 26 | 210 | Caribbean Netherlands | 6 | - |
| 104 | Niger | 832 | 46 | 211 | St. Barth | 6 | - |
| 105 | Gabon | 802 | 9 | 212 | Western Sahara | 6 | - |
| 106 | Costa Rica | 801 | 7 | 213 | Anguilla | 3 | - |
| 107 | Guinea-Bissau | 761 | 3 | 214 | Saint Pierre Miquelon | 1 | - |

Table 2: Total number of cases and deaths country by country updated to May 12, 2020 (07:07 GMT).
Source: <https://www.worldometers.info/coronavirus/#countries>. (click source for current update)

Figure 3: Possible modes of transmission of COVID-19.

through droplets spread by coughing or sneezing from an infected individual.

Pathogenesis of COVID-19

Based on the likely cells infected, COVID-19 can be sub-divided into three phases that correspond to the diverse clinical stages of the disease [34].

Stage 1: Asymptomatic state (Initial 1 - 2 days of infection)

The inhaled virus SARS-CoV-2 begins to multiply on binding to the epithelial cells in the nasal cavity. Both SARS-CoV2 and SARS-CoV uses ACE2 their primary receptor [31,35]. *In vitro* studies with SARS-CoV suggested that the primary cells infected in the conducting airways are the ciliated cells [36]. However, there is need to revise this conception since single-cell RNA demonstrates a low level of ACE2 expression in conducting airway cells and no clear cell type preference [37]. Local propagation of the virus takes place but with restrict innate immune response. At this stage, the virus can be de-

tected by nasal swabs. Albeit the viral burden may be low, these does not rule out that the individuals are infectious. The RT-PCR value for the viral RNA might be helpful to surmise the viral load and the subsequent infectivity, and clinical course. Perhaps super spreaders could be detected by these studies. The sample collection procedure would have to be standardized, for the RT-PCR cycle number to be helpful. Nasal swabs are usually more sensitive compare to throat swabs [38].

Stage 2: Upper airway and conducting airway response (Next few days)

The virus replicates and moves down the respiratory tract along the conducting airways; and a stronger innate immune response are set-up. Nasal swabs or sputum should yield the virus (SARS-CoV-2) as well as early markers of the innate immune response. The COVID-19 disease is clinically conspicuous at this time. The level of CXCL10 (or some other innate response cytokine) may be predictive of the subsequent clinical course [39]. The primary sources of beta and lambda interferons are the viral infected epithelial cells [40]. An interferon responsive gene is CXCL10 which has an excellent signal to noise ratio in the alveolar type II cell response to both SARS-CoV and influenza [41,42]. CXCL10 has also been reported to be helpful as disease marker in SARS [39,43]. The host innate immune response determination might improve predictions on the subsequent course of the disease and the need for more aggressive monitoring. The disease is usually mild and mostly limited to the upper and conduction airway in nearly 80% of the infected patients [34]. Monitoring of these individuals may be done at home with conservative symptomatic therapy.

Stage 3: Hypoxia, ground glass infiltrates and progression to ARDS

Unfortunately, about 20% of the infected patients will progress to stage 3 disease and will develop pulmonary infiltrates while some will manifest very severe disease. The fatality rate of this disease at the onset is usually approximately 2%, but this differs remarkably with age [34]. The mortality and disability rates may be revised once the prevalence of mild and asymptomatic cases is succulently explained. At this stage, the virus now reaches the gas exchange units of the lung and infects alveolar type II cells. Both SARS-CoV and influenza preferentially infect type II cells compared to type I cells [44]. SARS-CoV propagates within type II cells, huge numbers of viral particles are emitted, and the cells undergo apoptosis and die [41]. The result is likely a self-replicating pulmonary toxin as the released viral particles infect type II cells in neighbouring compartments. The aberrant wound healing may result into more deleterious scarring and fibrosis compare to other types of ARDS. Recovery will require a vigorous innate and acquired immune response and epithelial regeneration. The most susceptible populations are the senile ones due to their compromise immunity and decreased capability to repair worn out epithelium. The older people also have declined mucociliary clearance and this may permit the pathogen to spread to the gas exchange units of the pulmonary more easily [45].

Potential therapeutic options against COVID-19

Presently, there are no approved specific antiviral drugs or vaccine for COVID-19. Thus, palliative care to help attenuate symptoms is the best current approach being followed by all clinicians globally. This supportive care includes patient isolation to a negative pressure isolation room and providing sufficient rest, hydration, electrolyte balance and nutritional support. Advanced cases involving pulmonary failure, ARDS, cardiac failure and septic shock also need a sophisticated level of care and other life support vis renal replacement therapy, extracorporeal membrane oxygenation (ECMO), invasive ventilation and so on.

At the onset, interferons- α nebulization, broad-spectrum antibiotics, and anti-viral drugs were employed to attenuate the viral load [46,47]. Nevertheless, only remdesivir has demonstrated promising effect against the virus [48]. Using Remdesivir singly or in combination with chloroquine or interferon beta significantly blocked the SARS-CoV-2 replication and led to clinical recovery of patients [49,50]. Currently, numerous other anti-virals are being evaluated against the infection. Nafamostat, Nitazoxanide, Ribavirin, Penciclovir, Favipiravir, Ritonavir, AAK1, Baricitinib, and Arbidol demonstrated moderate results when tested against infection in patients and *in-vitro* clinical isolates [49,51,52]. Diverse numbers of conglomerations, vis combination of antiviral or antibiotics drugs with traditional Chinese medicines, were also evaluated against SARS-CoV-2 induced infection in humans and mice [49].

Conclusion and Perspective

The novel coronavirus emanated from the Hunan seafood market at Wuhan, China and has since spread sporadically to nearly

210 countries and territories around the globe and two international conveyances. Its attendant consequences have led to a significant number of mortalities both in senile individuals and in patients with multiple comorbidities; however, the numbers of pediatric cases so far reported are insignificant. The zoonotic source of SARS-CoV-2 is yet to be affirmed. Nevertheless, sequence-based analysis postulated bats as a likely major reservoir. Several reports have suggested person-to-person contact has the most probable route of transmission. Hitherto, there are no promising clinical therapies or prevention strategies in prospect against human coronaviruses.

Public health measures such as the provision of decontaminating reagents for hands cleansing regularly by public services and facilities, and far-reaching measures to mitigate person-to-person transmission of COVID-19 are necessary to check current outbreak. Adequate efforts and priority should be concentrated on the protection and curbing of transmission amidst vulnerable people vis children, health workers, and aged ones. Also, epidemiological changes in COVID-19 infection should be follow-up, taking into cognizance potential transmission routes and subclinical infections, couple with the evolution, adaptation, and transmission of the virus among humans and likely intermediate animals and reservoirs.

With so much concern and attention surrounding SARS-CoV-2, knowledge of key clinical information and recent developments is of extreme importance both as a patient and as a health care provider. It is luculent however, that intensive research is expeditiously required to identify novel chemotherapeutic drugs for treatment of COVID-19 infections. To develop pre-and post-exposure prophylaxis against COVID-19, there is an urgent need to establish an animal model to replicate the severe disease currently observed in humans. Presently laboriously researches are on-going to develop a nonhuman primate model to study COVID-19 infection by numerous groups of scientists, with the aim to establish fast track novel therapeutics and for the testing of potential vaccines in addition to providing a better understanding of virus-host interactions.

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Conflict of Interest

The authors declare no conflict of interest.

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