

COVID-19: Anatomy of a Pandemic

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ABSTRACT

SARS-CoV-2, the virus that causes COVID-19, has more than 82% genome similarity with SARS-CoV and more than 89% similarity with two bat coronaviruses, bat-SL-CoVZXC21 and bat-SL-CoVZC45. The virus went and caused the most recent pandemic in human history with fatality totaling more than 3 million deaths, and cases rising up to 176 million worldwide according to the World Health Organization (WHO). In this paper, a retrospective analysis of the emergence and spread of SARS-CoV-2 around the world are presented.

Keywords: COVID-19, coronavirus, SARS-CoV, SARS-CoV-2, MERS-CoV, Orthocoronavirine, severe acute respiratory infection, acute respiratory failure, acute respiratory distress syndrome (ARDS), pulmonary edema, cardiovascular diseases, multiple organ failure, COVID-19 China, COVID-19 United States, COVID-19 Canada, COVID-19 Europe, COVID-19 Russia, COVID-19 Asia, COVID-19 India, COVID-19 Africa.

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I. INTRODUCTION

Coronaviruses (CoVs) have the largest non-segmented RNA genome of ~30 kb in length, that enables these viruses to continuously modify by recombination and mutations creating genetic diversity. This increases the chances of transmission of these viruses among different species and causing various diseases. During the past 20 years, the emergence of SARS-CoV (severe acute respiratory syndrome-coronavirus) and MERS-CoV (Middle East respiratory syndrome-coronavirus) resulted in two pandemics in 2002-03 and in 2012, respectively. Another outbreak of swine acute diarrhea syndrome (SADS) in 2018 was linked to coronaviruses evolving from bats [1]. Currently, the world is in a pandemic of SARS-CoV-2 from the beginning of January 2020. According to the World Health Organization (WHO), as of June 17, 2021, the confirmed cases of SARS-CoV-2 infection are reported to be 176,693,988 with 3,830,304 deaths, worldwide (WHO, 2021).

The clinical picture of COVID-19 patients resembles that of SARS-CoV and MERS-CoV infected patients. Most common symptoms of COVID-19 are cough, fever, myalgia, fatigue, and less common symptoms include headache, diarrhea, sputum production and hemoptysis [2]. SARS-CoV-2 has 82% similarity with SARS-CoV and more than 89% similarity with two bat coronaviruses which include bat-SL-CoVZXC21 and bat-SL-CoVZC45. The transmission pattern of SARS-CoV-2 is similar to that of previous coronaviruses outbreaks involving aerosol or bodily contact with infected persons. The spike protein (S protein) of SARS-CoV-2 uses ACE2 (angiotensin-converting enzyme-2) receptors to enter the cell and is responsible for both human to human and cross-species transmission of SARS-CoV-2

[3]. No intrauterine transmission of SARS-CoV-2 has been reported [4].

II. EMERGING OF SARS-CoV-2

The early reports of SARS-CoV-2 infected individuals date back to late December 2019, in the capital, Wuhan, of Hubei province of China. The local health care facilities reported a number of pneumonia patients of unknown etiology. The epidemiological investigations linked the cases to Huanan seafood market, where many aquatic and non-aquatic animals like rabbits and birds were being sold. Using next generation sequencing (NGS), a human-infecting, novel-coronavirus (2019-nCoV) belonging to beta-coronaviruses was identified, forming a clade in sarbecovirus, subgenus in Orthocoronavirine subfamily, to be associated with these pneumonia cases and named the disease as “novel coronavirus-infected pneumonia (NCIP).” [5]. The first genomic sequence of SARS-CoV-2 was released on January 10, 2020. On January 30, 2020, WHO declared the virus as ‘public health emergency of international concern’ [6].

On February 11, 2020, the virus was named SARS-CoV-2 (severe acute respiratory syndrome-coronavirus-2) by the International Committee on Taxonomy of Viruses (ICTV), on the basis of its phylogenetic similarities with SARS-CoV [7]. On the same day, the World Health Organization (WHO) named the disease related to SARS-CoV-2 infection as, COVID-19. By the end of February 2020, a total of 82,294 people were reported to be infected from SARS-CoV-2 [6]. Different countries adopted different approaches to minimize the spread of COVID-19 to save lives and decrease the burden on health-care systems. China imposed nationwide lockdown and strict measures of quarantine to slow COVID-

19 spread. Heavy fines were imposed on citizens in Singapore who did not follow the quarantine measures established by the government. Due to unavailability of a proper therapeutic treatment of COVID-19, these measures were considered to be the best practices to reduce COVID-19 infection among individuals [8].

The electron microscopic analysis identified that the SARS-CoV-2 is an enveloped virion having diameter of ~50-200 nm with club-shaped spike glycoproteins giving the virus a coronal or crown-like appearance. The genome of the virus is a single-strand-positive sense RNA.

During the early stages, COVID-19 patients developed symptoms of severe acute respiratory infection with complications of acute respiratory failure, acute respiratory distress syndrome (ARDS), pulmonary edema, cardiovascular diseases, and multiple organ failure. Infection was more common among males with chronic comorbidities like diabetes, cerebrovascular and cardiovascular diseases [9]. It is estimated that a single COVID-19 patient can pass the disease to an average of 2 to 3 healthy individuals in a susceptible population.

Globally, several shifts had been reported in SARS-CoV-2 isolates. The D614G mutation in the S protein of SARS-CoV-2 emerged in March-April 2020 resulting in increased transmissible G-strain. It was the primary shift observed during the first 9 months of COVID-19 pandemic. At the end of December 2020, several new variants of SARS-CoV-2 such as Alpha (B.1.1.7) lineage, Beta (B.1.351) lineage, and Gamma (P.1) lineage, were being reported due to mutations in the receptor binding domain (RBD) of the viral spike protein. Some of these variants had higher transmission rates than that of others. These variants were identified in various countries including the United States, Canada, Brazil, South Africa, the United Kingdom, and Japan. The rapid changes in the S gene of SARS-CoV-2 and enhanced transmissibility of these variants shifted the pattern of COVID-19 and its response to vaccination and antibody therapies [10].

III. SPREAD OF COVID-19 IN CHINA

Several cases of pneumonia of unknown cause have been reported in Wuhan, China, since December 8, 2019. Most of these patients lived round or worked at local wholesale Huanan seafood market. On January 7, 2020, the Chinese Centre for Disease Control and Prevention (CDC) identified a novel coronavirus from the throat swab specimen of a patient from Wuhan [3]. COVID-19 started to spread quickly in Wuhan and exported to other provinces in China. The clinical picture of the COVID-19 patients resembled that of SARS-CoV infection and patients with comorbidities required oxygen therapy and ICU admission. A total of 835 laboratory confirmed SARS-CoV-2 infections and 25 deaths were reported on January 24, 2020. A cohort study of 41 laboratory confirmed COVID-19 patients found a mortality rate of 15% in COVID-19 patients. Most of the patients in this cohort study had been to wholesale Huanan seafood market [2]. Human to human transmission of SARS-CoV-2 was confirmed by several reports involving clinical, epidemiological, laboratory, microbiological and radiological investigations of COVID-19 patients. A study involving 6 COVID-19 patients in a family-cluster provided evidence for

person-to-person transmission of COVID-19 in family and hospital settings. Five patients had returned from Wuhan to Shenzhen, Guangdong province of China and one patient did not travel to Wuhan and became infected with SARS-CoV-2 through several days of contact with other family members. These findings also suggested inter-city spread of COVID-19 by air travel and supported reports of infected Chinese travelers being detected in other geographical regions [11]. A study documented a history of travel to Wuhan and contact with people of Wuhan in 31.3% and 71.8% respectively, in 1099 patients from 552 hospitals in 31 province-level municipalities and provinces across China. They found a mortality rate of 1.4% in the study population [12]. The total crude death rate of COVID-19 in China was higher during the early stages of outbreak and was decreased to 0.7% in patients with clinical presentation after February 1, 2020 [13].

After January 10, 2020, the number of confirmed cases increased rapidly and reached to peak on February 12, 2020. No confirmed cases were reported in the provinces, Qinghai, and Tibet, until the end of February 2020. Data from China's CDC demonstrated that COVID-19 patients were majorly concentrated at 30 to 79 years of age accounting for 89.8% confirmed cases in Wuhan, 88.6% in Hubei and 86.6% in mainland China [14]. Owing to the implementation of strict public health measures the daily reported new COVID-19 cases started to decline. As of March 2020, COVID-19 transmission in China was effectively controlled.

IV. SPREAD OF COVID-19 IN THE FAR EAST

The first case of COVID-19 reported outside of mainland China was in Thailand on January 11, 2020, and the disease spread to other countries including Japan, North Korea, Hong Kong, South Korea, Malaysia, Indonesia, Singapore, Malaysia, and Philippines. COVID-19 cases in Korea, Japan and Thailand were exported from Wuhan, China. By 21st February 2020, the confirmed cases of COVID-19 in Thailand were 35 cases [15]. A boxing match at Lumpinee Boxing Stadium, Thailand, on March 6, 2020, resulted in 143 new COVID-19 cases and was considered a key event in the spread of disease. Thailand responded to COVID-19 pandemic by implementing Integrated Plan for Multilateral Cooperation for Safety and Mitigation of COVID-19 and minimized the disease rate early in the pandemic [16].

The first three cases in Malaysia were identified on January 25, 2020, and were related to travel history of patients. The number of cases rose to 22 by February 15, 2020. The first wave of COVID-19 outbreak was from January 25 to February 15, 2020. No new cases were reported in Malaysia for next 11 days. The second wave of COVID-19 was from February 27 to April 29, 2020. The second wave started when individuals who had returned from foreign travels started to develop COVID-19 symptoms. A Tablighi Jamaat religious conference that took place at the 'Masjid Jamek Sri Petaling' in Kuala Lumpur's Sri Petaling district from February 27 to March 3, 2020, resulted in the largest cluster of COVID-19 and caused local transmission in Malaysia. On March 18, 2020, Malaysia implemented Movement Control Order (MCO) to minimize spread of COVID-19 by social distancing. On March 19, 2020, Malaysia reported 900 confirmed cases of COVID-19 which ranked Malaysia at the

fourth position among Asian countries with highest number of cases. Several subclusters of COVID-19 cases were also generated in other states due to Sri Petaling Tabligh. On May 21, 2020, cases from these clusters rose to 3,347. Sri Petaling Tabligh cluster ended on July 11, 2020. More clusters were reported from Sarawak, Puhang, Kuantan, Kluang and Sungai Lui villages. The third wave of outbreak started from October 8, 2020 and is still ongoing till the publication of this paper. From September 1 to October 19, 2020, highest number of cases were recorded in Selangor, Kedah, Sabah, and Kuala Lumpur. In the next 2 months by December 3, 2020, the total number of cases increased to 69,095 (381%) [17].

V. COVID-19 IN AUSTRALIA AND NEW ZEALAND

Initially, SARS-CoV-2 was identified in Australia in a 58-year-old male who had returned from Wuhan, China to Melbourne, Australia on January 19, 2020. Compared to other countries around the globe, fewer COVID-19 cases had initially been reported in Australia. Almost 140 confirmed COVID-19 cases and 3 fatalities were reported in Australia till March 2020 [18]. The number of reported cases started to double after every 3.4 days by the end of March and reached to about 100,000 till mid of April. Australia reported first peak of confirmed 527 COVID-19 cases on March 29, 2020. Later on, the number of confirmed COVID-19 cases and the doubling time continuously decreased up to 112 days in Australia. The doubling time of COVID-19 cases was lower in Australian Capital Territory, South Australia and New South Wales as compared to that of the national average. The lowest doubling time was reported in Tasmania. This was possible due to early implementation of lockdown and non-pharmaceutical control measures for COVID-19 by the Australian Government [8].

The first case of COVID-19 was identified in New Zealand in February 2020. Community transmission of COVID-19 was reported in mid-March 2020. Alert level 4 comprising a strict lockdown was implemented across the country by the government of New Zealand. Within 5 weeks, the number of COVID-19 cases declined rapidly, and the government shifted to alert level 3 for the next two weeks. In July, New Zealand reported a total of 1,569 confirmed COVID-19 cases and 22 fatalities. The mortality rate was 4-per-million COVID-19 individuals, and it was the lowest among 37-Organization for Economic Cooperation and Development countries during the first wave [19]. COVID-19 cases started to rise again from mid-August 2020, due to cluster of infected patients identified in Auckland. COVID-19 confirmed cases increased once again in late October 2020. The number of infected individuals again started to decrease from the end of April 2021. As of June 20, 2021, the total number of confirmed cases in New Zealand were 22 cases [20].

VI. COVID-19 SPREAD IN INDIA

The spread of COVID-19 to India was initially reported on January 30, and February 3, 2020, when 3 infected persons returned from Wuhan, China to Kerala, India. A month later, 2 additional individuals with travel history from Dubai and Italy, were identified to be positive for SARS-CoV-2

infection. By March 15, 2020, a total 107 cases of COVID-19 were reported, and the number kept on increasing [21]. At the end of first lockdown, by April 14, 2020, number of positive cases increased exponentially and reached to 11485 including 396 fatalities. At the same time, more cases were identified in Jaipur. Immediate measures like travel restrictions, social distancing of almost one meter and lockdown were implemented to control the spread of COVID-19 in the region. A total of 190,648 confirmed COVID-19 cases including 5,407 fatalities were reported till the end of all lockdown periods. Almost 75% positive cases were present in six major states of the country. These included Tamil Nadu, Maharashtra, Delhi, Gujrat, Rajasthan, and Madhya Pradesh. The Northeastern States reported low number of positive cases is Manipur, Arunachal Pradesh, Mizoram, Tripura, Meghalaya, Sikkim, and Nagaland with >1% confirmed cases. Major outbreak clusters of COVID-19 were reported in Southern, Western and Northwestern regions of India [22]. The spread of COVID-19 started to decline in September 2020 but started to increase in March 2021. During the third week of April 2021, the already high number of COVID-19 cases in India raised the daily global cases to 899,755. On April 25, 2021, the Indian government reported 352,991 new COVID-19 cases. Recently, the Alpha (B.1.1.7) and Delta (B.1.617) lineages of SARS-CoV-2 are prevalent in Punjab and Maharashtra states of India and are the main variants responsible for the spread of COVID-19 [23].

VII. COVID-19 SPREAD IN AFRICA

Africa was the last continent to be infected by SARS-CoV-2. The first case of COVID-19 in Africa was reported in Egypt on February 14, 2020, in an individual with travel history from China. During the first week of March 2020, more than 40 cases of COVID-19 were reported in Egypt, Algeria, Senegal, Tunisia, South Africa, Nigeria, Cameroon, and Togo. The highest number of COVID-19 cases reported in Europe during March 2020, were responsible for the initial spread of the pandemic in Africa. More than 100,000 confirmed cases and 3,100 fatalities were reported from 54 African Union Member States by May 22, 2020 [24]. The most severely affected areas were Djibouti and Sao Tome with 230 and 118 confirmed cases respectively per 100,000 population. To reduce the spread of COVID-19 in the region, over 40 African countries closed their borders during April and May 2020. Most of the COVID-19 cases in Africa were imported from the United States and Europe rather than China [25].

The Beta (B.1.351) and Eta (B.1.525) lineages of SARS-CoV-2 were found in February 2020 in South Africa and December 2020, in Nigeria, respectively. The Beta lineage of SARS-CoV-2 had been reported in over 48 countries and was responsible for majority of COVID-19 cases in these countries [26]. The limited testing capacities for COVID-19 in Africa resulted in the detection of lower number of confirmed cases in the region. According to the United Nations COVID-19 spread to all African countries were due to improper mitigation strategies [27].

VIII. COVID-19 IN EUROPE AND RUSSIA

The initial cases of COVID-19 spread to Europe were identified in France in January 2020. Three confirmed cases of COVID-19 were reported in France in patients returning from Wuhan to France [28]. By February 28, 2020, COVID-19 cases also spread outside of mainland China to European countries including France, Italy, and Germany. Initially, the hardest hit country in Europe was Italy followed by Spain and Netherlands. The returning of tourists from skiing holidays transmitted COVID-19 in neighboring countries of Austria and Italy in Europe [29]. An outbreak of COVID-19 was also reported in a high school in France with 41% infected students and staff in early February 2020 confirming the spread of COVID-19 in school settings. The COVID-19 attack rates were 59.3% in non-teaching staff, 43.4% in teachers and 38.1% in pupils [30].

The zoonotic and anthroponotic transmission of SARS-CoV-2 further spread COVID-19 in Europe. Denmark reported 214 COVID-19 patients infected with SARS-CoV-2 related to mink having Y453F mutations in the spike protein. The same mutations were also observed in Netherlands in various clusters related to mink farms, but both the strains of SARS-CoV-2 were not closely related and were grouped in different clades. Variants with this mutation were also reported sporadically from other European countries including Switzerland, Russia, Spain, Italy and Sweden. During the period of April 23 to November 5, 2020, Netherlands reported spread of COVID-19 infection at 69 mink farms in 3 regions. Similar reports of COVID-19 infection in mink and mink farm workers were also found in Sweden, Spain, and Italy. So far, only cluster 5 variant of mink related SARS-CoV-2 variants, raised specific concern because of its impacts on antigenicity of the virus [31].

The COVID-19 outbreak in Russia occurred later than that in neighboring European countries. Since 11 May 2020, Russia was among the four countries with the highest number of SARS-CoV-2 infection cases. Initial case reports of COVID-19 in Russia were considered to be imported from China and later the virus spread through Moscow and Saint Petersburg. A nosocomial outbreak corresponding to a major transmission cluster of COVID-19 was reported at the Vreden Russian Research Institute of Traumatology and Orthopedics in Saint Petersburg. Despite various surveillance and strategic plans for minimizing the spread of COVID-19 in Russia, the virus spread locally infecting large number of populations [32].

IX. COVID-19 IN THE UNITED STATES AND CANADA

The initial reports of COVID-19 in the United States and Canada can be linked to the travel history of the patients to Wuhan, China. On January 20, 2020, the first confirmed case of COVID-19 was reported in the United States. The patient was 35-year-old male with a history of dry cough, fever, nausea, and vomiting. The patient had returned from Wuhan to Washington State on January 15 [33]. Between February 12 to April 9, 2020, a total of 49,370 confirmed COVID-19 cases involving 9,282 health care workers were reported to CDC from all states of the United States. Initially, new cases of COVID-19 peaked around late March with a subsequent

increase in new fatalities in late April. On April 11, 2020, the United States exceeded Italy with the highest reports of COVID-19 deaths reaching to ~24,000. COVID-19 began to spread all over the United States piling up 5.04 million total number of cases and 162,919 fatalities. The spread of COVID-19 started to decrease in August [34]. By the end of December 2020, the variants B.1.1.7 and B.1.351 lineages were identified in the United States with increased transmissibility and severity of the disease.

A total of 1,406,253 confirmed COVID-19 cases and 26,012 deaths have been reported in Canada till June 17, 2021 [36]. The first case of COVID-19 in Canada was identified on January 23, 2020, when a person tested positive for SARS-CoV-2 after returning from Wuhan to Toronto [35]. All COVID-19 cases till March 2020 were linked to recent travel history of patients to a country with high COVID-19 cases. On March 5, 2020, the first community transmission case of COVID-19 was reported in British Columbia [36]. Till July 2020, the majority of COVID-19 cases were reported from the most populous, Quebec and Ontario, provinces of Canada with 56,407 and 36,594 cases, respectively. Reports of new COVID-19 cases and fatalities were higher in early May which later decreased steadily in many regions of the country. However, few low-grade community transmission cases persisted [36]. The variants of SARS-CoV-2 that constitute majority cases of COVID-19 in Canada include Beta (B.1.351), Alpha (B.1.1.7), Delta (B.1.617.2) and Gamma (P.1) lineage. Among these variants, Alpha lineage is most commonly infecting the Canadian population [36].

X. COVID-19 IN LATIN AMERICA

Brazil was the first country in Latin America to report the first case of COVID-19 on February 25, 2020. Due to rapid spread of COVID-19 across various regions in the world, other countries across the territory restricted their borders and imposed lockdowns. Latin America registered approximately 65,000 COVID-19 cases till April 14, 2020. Pandemic control measures varied much across the continent with many countries affected badly by the pandemic [37]. Brazil declared COVID-19 as a health emergency on March 19, 2020, Mexico on March 23, 2020, Argentina on March 20, 2020, Colombia on March 24, 2020, Peru on March 15, 2020, and the remaining 3 countries imposed partial closure by March 15, 2020 [38]. A preliminary analysis by a study reported an increase in infection rate and fatalities across Latin America from the start of pandemic till February 2021. Furthermore, detection of new variants of lineage Gamma (P.1) and Zeta (P.2) were reported in the start of February 2021 in Brazil. Currently, 3 variants of SARS-CoV-2 are circulating in Latin America. These include Alpha (B.1.1.7), Gamma (P.1), and Zeta (P.2) lineages [39].

XI. CONCLUSION

COVID-19 spread rapidly around the globe resulting in a large number of infected people and fatalities. The pandemic is far from ending in various regions of the world. The emergence of several variants of SARS-CoV-2 further enhanced the infectivity and transmissibility of SARS-CoV-2 from animal to human and human to human. Countries like

Russia and New Zealand, which implemented early strategies and measures to reduce spread of SARS-CoV-2 succeeded to contain COVID-19 spread. On the other hand, countries of Latin America and Malaysia which stayed behind in implementing an early strategic plan for control of COVID-19 faced large number of COVID-19 cases and deaths. Vaccination and non-pharmaceutical therapies are currently the best approaches to reduce the spread of COVID-19 around the world.

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