



COVID-19 – Lessons Learned

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Abstract

Modern society has not forgotten yet epidemics that killed millions in the last millennium and the COVID-19 pandemic caused by the SARS CoV-2 has recently emerged. With the onset of the Wuhan epidemic in the Chinese province of Hubei, the initially called new corona virus due to the similarity of 80 % to the 2002 SARS virus was renamed to SARS CoV-2. The virus was originally isolated from bronchoalveolar aspirate specimens. Viral RNA was detected in 6 of 41 blood samples with clinical signs of infection. A senior Chinese expert told to the media that the median incubation period was 7 days, ranging from 2 - 12. The International Health Regulations Emergency Committee for Epidemics gives a preliminary estimate basic reproduction number R_0 of 1.4 - 2.5. COVID-19 is mainly transmitted by close contact with the infected by drops due to sneezing and coughing. Fever, cough, myalgia and fatigue are the predominant initial signs and symptoms. The clinical picture is non-specific. Exacerbation occurs suddenly, as bilateral interstitial pneumonia that requires admission to intensive care. Initial lethality in hospitalised cases was 15 %, but these estimates had to be taken with reserve as the situation evolved. According to recent data, the global fatality rate is 3.7 %, the lethality rate in China is 3.9 % and in Italy 6.8 %. According to data from the Chinese Centre for Disease Control and Prevention, of 44,672 confirmed cases 1,023 people died, therefore lethality was 2.3 %. In the absence of specific prevention and control measures, mankind is limited to general prevention measures.

Key words: Covid-19, SARS CoV-2, pandemic, lethality.

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Introduction

Modern society have not yet forgotten the epidemics that killed millions in the last millennium and the COVID-19 pandemic caused by the SARS CoV-2 virus has emerged. According to the World Health Organization (WHO), as of the end of December 2019, 153,517 persons had been laboratory-confirmed by 15 March 2020, of which 81,048 or 52.79 % of the total number of patients became ill in China. At the same time, 5,735 people died, 3,204 in China.¹

The epidemic was first reported in Wuhan, Hubei, China, and quickly spread to 143 more countries. While the epidemic in China is gradually dying out, new hotspots centred in Europe

are opening up around the world. Italy was particularly affected with 21,157 patients and 1,441 deaths, as well as about 3,500 patients and over 170 deaths on a daily basis. The situation is continuing to deteriorate in Spain, France, Germany and the United Kingdom.

The first death outside China occurred on 2 February 2020 in the Philippines. On 15 February 2020 France reported the first death outside Asia, a person who had been to China. The first two Europeans to die from COVID-19 were reported in Italy on 23 February 2020.

The first two cases of infection in the Republic of

Srpska were confirmed in a man who returned from Italy, as well as in his school-age son. As of 16 March, 20 cases of COVID-19 were confirmed in the laboratory in the Republic of Srpska. No case with severe clinical picture was recorded yet.

The epidemic is spread across the continents of Europe, Asia, Africa, America and Oceania and the WHO has declared a pandemic. The whole world has come together to fight this global epidemic. All countries implement the same measures, with differences in the implementation of measures and levels of restrictions. It is very important to summarise the known facts on the epidemiological characteristics of COVID-19 disease.

SARS CoV-2 virus

With the onset of the Wuhan epidemic in the Chinese province of Hubei, the causative agent was designated as a new corona virus, but over time, after 80% sequence similarity with the 2002 SARS virus mankind is, this virus was designated SARS CoV-2. Coronaviruses were known since the mid-1960s. It has been known that they have ability to infect humans and many birds and mammals. Two outbreaks involving coronaviruses with animal reservoirs were noted: SARS-CoV in 2002, caused by a *Betacoronavirus*, subgenus *Sarbecovirus*, and MERS-CoV in 2012, caused by *Betacoronavirus*, subgenus *Merbecovirus*).²

In the previous decade, two pandemic viruses, SARS and MERS, affected several thousands of people with very high fatality ratio. Known facts regarding SARS virus identified in 2002 are: 8,096 affected people, mostly having pulmonary infections, 774 deaths, fatality ratio 10%.³ Most likely, bats were origin of the virus, which was spread further to Himalayan palm civets, Chinese ferret badgers and raccoon dogs sold for food at the markets of Guangdong, China. The 2012 MERS virus had ever greater fatality rate than SARS, it was around 35.7%. It was spreading among the people, particularly in healthcare settings. Besides that, dromedary camels were animal reservoirs of the virus.⁴

In December 2019, a new coronavirus caused pneumonia in three patients connected to the cases of acute respiratory illness from Wuhan. After genetic analyses of the new coronavirus were performed, it was discovered that it was closely related to SARS-CoV and genetic clusters within the genus *Betacoronavirus*, forming a distinct clade in lineage B of the subgenus *Sarbecovirus* together with two bat-derived SARS-like strains.⁵ It was later confirmed that the COVID-19 shares with SARS-CoV a property binding to the angiotensin-converting enzyme-2 (ACE-2), a membrane exopeptidase that acts not only as the receptor for these viruses, but also enables them to enter into the human cells.⁶

The virus was originally isolated from broncho-alveolar aspirate specimens.⁷ Virus RNA was detected in the blood samples in six of 41 cases in a study on the clinical characteristics of infection.⁸ At present, it remains unknown whether the virus is excreted in faeces or urine.

Incubation and infectiousness

Since first identified, the epidemic scale of the recently emerged novel coronavirus (2019-nCoV) in Wuhan, China, has increased rapidly, with cases arising across China and other countries and regions. Using a transmission model, a basic reproduction number R_0 of 3.11 (95% CI, 2.39-4.13) was estimated.⁹ The mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution of 12.5 days. In its early stages, the epidemic doubled in size every 7.4 days. With a mean serial interval of 7.5 days (95% CI, 5.3 to 19), the basic reproduction number R_0 was estimated to be 2.2 (95% CI, 1.4 to 3.9).¹⁰ Linton and co-workers¹¹ used the best-fit lognormal distribution method and showed that the incubation period was approximately 5 days (95% CI 4.1 to 7.0 days).

However, these estimates are still only preliminary and will be updated when more information becomes available. The infection correlates with the onset of symptoms and the severity of the clinical picture.⁸

Pathogenesis

In patients with more severe clinical imaging requiring intensive care, a Th1 immune response is enhanced. However, production of IL-4 and IL-10 was also enhanced that stimulates the Th2 immune response that was not observed in SARS and MERS. For researchers in this emerging situation, it remains to be investigated how the use of corticosteroids will affect this balance between Th1 and Th2 immune responses.⁸

Ways of transmission

COVID-19 is mainly transmitted by close contact with the infected person by droplets in sneezing and coughing. It was shown in a study by Ghinai and colleagues¹² that a person-to-person transmission of COVID-19 had occurred between a symptomatic and uninfected subject after a prolonged, unprotected exposure. No further spread of infection was detected, despite the active symptom monitoring and testing with symptomatic and some asymptomatic contacts. Contagiousness is greatest in the period of symptoms. Air is also possible as a transport route. Faecal transmission is not excluded but is unlikely. Transmission is possible through contaminated hands in contact with eyes and saliva of nose and mouth.^{13, 14}

Clinical characteristics

Fever, cough, myalgia and fatigue are the predominant initial signs and symptoms. The clinical picture is extremely nonspecific with a wide range of symptoms, bilateral pulmonary infiltrations and sudden worsening followed by dyspnoea and admission to the intensive care unit. Huang and co-workers⁸ described that the median time since the onset of symptoms to hospital admission had been 7 days, until occurrence of dyspnoea 8 days, until occurrence of acute respiratory distress syndrome 9 days and 10 to 15 days until admission to the intensive care unit.

Age and gender distribution of diseased

Among the first published studies on the epidemic in China there was a study published by Li et al.¹⁰ In a sample of 425 confirmed cases in Wuhan, China, in January 2020, the median age of patients was 59 years (range 15 to 89 years). Out of the total number of patients, 240 (56 %) were men and there were none under the age of 15. This age distribution can be explained by the fact that the first cases consisted of a cluster of non-specific pneumonias. Further follow-up revealed that the disease manifested in children with a lighter clinical picture, so these cases were not registered until the detection of the pneumonia cluster. The slightly milder representation of men can be explained by the exposure to the wholesale market in Wuhan.

According to the Chinese Centre for Disease Control and Prevention, as of 11 February 2020, men represented 63.8 % of the sample of 44,672 confirmed patients. Children between the ages of 0 and 9 accounted for 0.9 % of the total number of patients, but there were no fatalities. The lethality increased with age, thus at the age of 80 and over it was 14.8 %.¹⁵ According to the same source, it was concluded that the number of diseased health workers increased with the increase in the number of patients and accounted for 3.8 % of the total number of patients with a lethality of 0.3 %. Hubei patients accounted for 95.7 % of the total number of patients, an indication of well-implemented control measures in the province and halting further spread across China. Comorbidities were significantly represented, such as hypertension (39.7 %), diabetes (19.7 %), and cardiovascular diseases (22.7 %). In 80.9 % of the confirmed cases, the clinical picture was mild and 4.7 % critical. Wei and co-workers¹⁶ described 9 diseased new-borns (7 girls and 2 boys) in their study who had a mild clinic picture.

Lethality

Initial lethality in hospitalised cases was 15 %, ¹⁷ but these estimates had to be taken with reserve

as the situation evolved and changed. According to recent data, the global fatality rate is 3.7 %.¹ According to the same source, the lethality rate in China is 3.9 % and in Italy 6.8 %. According to data from the Chinese Centre for Disease Control and Prevention, of 44,672 confirmed cases, 1,023 people died, so lethality was 2.3 %. In the same sample confirmed in China, 416 cases of children between the ages of 0 and 9 were registered, with no deaths.¹⁷ Higher lethality in Italy may perhaps be explained by the fact that the Italian population is older than the population in China. Further statistic monitoring and analysis are needed to accurately assess the COVID-19 lethality.

Yang et al¹⁸ have reported that the median time for a radiological confirmation of pneumonia since the onset of symptoms was 5 days (ranging 3-7 days); since the symptom onset until admission to the intensive care unit it was 11 days (ranging 7-14 days) and from admittance to the intensive care unit to death it was 7 days (ranging 3-11 days). The median time from pneumonia confirmation to death was 13 days. In the study of Linton and colleagues,¹⁹ an average of 13 days elapsed from the onset of the disease to death.

In a letter to the editor Wilson et al²⁰ reported on the case-fatality risk estimates by means of a lag time for fatality methodology. Hubei Province was excluded from the clause. The case-fatality risks, when adjusted for a 13-day lag from reporting to death, was 3.5 % in China (0.8% in China, excluding Hubei Province), 4.2 % in the group of 82 countries, territories and areas and 0.6 % for the passengers and crew on a cruise ship.²¹

Conclusion

In the absence of specific prevention and control measures, healthcare systems are limited to general prevention measures. Key measures include limiting travel, quarantining the exposed, minimising social contact, sanitary and hygiene measures, personal hygiene measures and the proper use of personal protective equipment on the exposed. The Chinese authorities pointed to the importance of all these measures.

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Conflict of interest

None.

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