A REVIEW OF SPREADING WAYS, FEATURES OF DIAGNOSIS AND TREATMENT OF CORONAVIRUS INFECTION

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A REVIEW OF SPREADING WAYS, FEATURES OF DIAGNOSIS AND TREATMENT OF CORONAVIRUS INFECTION


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Abstract

In December 2019 Coronavirus begin to spread first in China than COVID-19 quickly crossed whole European countries and spreads to the US, South America. Coronavirus also came to Uzbekistan through Europe. COVID-19 evokes risky clinical features such as: pneumonia in the lung and acute respiratory distress syndrome which leads to breathlessness and multi organ damage. On March 11, WHO declared the COVID-19 a pandemic. Members of this virus can cause respiratory, enteric, hepatic, and neurological diseases in human body. Laboratory analysis such as decreased total white blood cell count, decreased lymphocyte count, lymphopenia, increasing of liver enzymes, C-reactive protein, Increased D-dimer were common in COVID-19 patients. Standard radiographic Imaging examination Chest X-Ray were useful for monitoring of the treatment, especially ICU care patients and patients with severe pneumonia who always on SPAP portable X – Rays were method of choice. Multi detector computed tomography very sensitive for lung changes in COVID-19 is the method of choice in the study of COVID-19 pneumonia, even in the initial stages.

Key words: Coronavirus, pneumonia, acute respiratory distress syndrome, epidemiology, pandemic, diagnosis, chest radiography, computed tomography
INTRODUCTION

Since the first suspected case of coronavirus disease-2019 (COVID-19) on December 1st, 2019, in Wuhan, Hubei Province, China, a total of 40,235 confirmed cases and 909 deaths have been reported in China up to February 10, 2020, evoking fear locally and internationally. Here, based on the publicly available epidemiological data for Hubei, China from January 11 to February 10, 2020, we provide estimates of the main epidemiological parameters. In particular, we provide an estimation of the case fatality and case recovery ratios, along with their 90% confidence intervals as the outbreak evolves (Data-based analysis, modelling and forecasting of the COVID-19 outbreak [1].

It was officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the international committee on taxonomy of viruses (ICTV) and the disease's name is COVID-19 for coronavirus disease 2019. SARS-CoV-2 is very contagious and is capable of spreading from human to human. Infection routes include droplet and contact, and aerosol transmission is currently under investigation. It is associated with a respiratory illness that may cause severe pneumonia and acute respiratory distress syndrome (ARDS). SARS-CoV-2 became an emergency of international concern [2].

A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), associated with severe respiratory illness emerged in Wuhan, China, in late 2019 [3].

By Marco C., et.al. this new virus is very contagious and has quickly spread globally. In a meeting on January 30, 2020, per the International Health Regulations (IHR, 2005), the outbreak was declared by the WHO a Public Health Emergency of International Concern (PHEIC) as it had spread to 18 countries with four countries reporting human-to-human transmission. An additional landmark occurred on February 26, 2020, as the first case of the disease, not imported in China, was recorded in the United States (US). The potential for these viruses grow to become a pandemic worldwide and represents a serious public health risk. Concerning COVID-19, the WHO raised the threat to the CoV epidemic to the "very high" level, on February 28, 2020. On March 11, as the number of COVID-19 cases outside China has increased 13 times and the number of countries involved has tripled with more than 118,000 cases in 114 countries and over 4,000 deaths, WHO declared the COVID-19 a pandemic [4].

World governments are at work to establish counter measures to stem the devastating effects and it has been estimated that strict shutdowns may have saved 3 million lives across 11 European countries [5]. Health organizations coordinate
information flows and issues directives and guidelines to best mitigate the impact of the threat.

At the moment, the therapeutic strategies to deal with the infection are only supportive, and prevention aimed at reducing transmission in the community is our best weapon. Aggressive isolation measures in China have led to a progressive reduction of cases. From China, the disease spread to Europe. COVID-19 quickly crossed the ocean and as of June 20, 2020, about 2,282,000 cases (with 121,000 deaths) recorded in the US, whereas Brazil with more than 1,000,000 cases and about 50,000 deaths is the most affected state in South America and the second in the world after the US. Although over time the lethality rate (total number of deaths for a given disease in relation to the total number of patients) of COVID-19 has been significantly lower than that of the SARS and MERS epidemics, the transmission of the SARS-CoV-2 virus is much larger than that of the previous viruses, with a much higher total number of deaths. It is estimated that about one in five individuals worldwide could be at increased risk of severe COVID-19 disease if they become infected, due to underlying health conditions [6-8].

In general, estimates suggest that 2% of the population are healthy carriers of a CoV and that these viruses are responsible for about 5% to 10% of acute respiratory infections [9].

Thus, SARS-CoV-2 belongs to the beta CoVs category. Like other CoVs, it is sensitive to ultraviolet rays and heat. In this regard, although high temperature decreases the replication of any species of virus. Currently, the inactivation temperature of SARS-CoV-2 must be well elucidated. It seems that this virus can be inactivated at about 27°C. On the contrary, it may resist the cold even below 0°C. Furthermore, these viruses can be effectively inactivated by lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid, and chloroform except for chlorhexidine.

Based on data from the first cases in Wuhan and investigations conducted by the China CDC and local CDCs, the incubation time could be generally within 3 to 7 days (median 5.1 days, similar to SARS [10] and up to 2 weeks as the longest time from infection to symptoms was 12.5 days (95% CI, 9.2 to 18) [4].

Public health managers tend to monitor and evaluate epidemic responses by looking at the overall mortality rates and where available, specific mortality rates among children and ‘healthy’ adults.

Older people in general though identified to have higher susceptibility to the effects of epidemics. This is likely owing to their dwindling immunity, contributed partly by the physiology of the ageing process and more specifically due to any existing co-morbid conditions [11].
It is important for stakeholders to acknowledge that older people are a special group and that their lives are as precious as other physiologic age groups. It is critical to be able to design health campaigns and messages that are tailored to their needs during epidemics. There is little evidence on how older people receive information during epidemics and whether behavior change campaigns were successful or not. Theories generated from behaviour and psychosocial epidemiology of old age would recommend that the messaging be limited, focused and unambiguous with the intention of not overwhelming or confusing them [12].

Using stories and illustrations which draw on previous experiences are more likely to attract the attention of older people than complex data, statistics and scientific explanations. In simpler words, what happened to a neighbor and what happened during previous epidemics is likely to attract more attention from older people.

COVID-19 average incubation period is 5.2 days (95% confidence interval (CI), 4.1–7.0) with the 95th percentile at 12.5 days [13]. Another study estimated it at 6.4 days (95% CI, 5.6–7.7) [14]. The median age of COVID-19 cases ranges from 49 to 57 years and median time from the first symptom to death is 14 days [15].

Incubation period was defined as the time interval between exposure and onset of disease symptoms. To obtain an accurate estimate, only the cases with an exposure period spanning 3 days or less were included in the analysis. For those exposed for three continuous days and those exposed on two dates with one day apart (i.e., exposed on the first and third days), the second day was uniformly used as the exposure date in estimation. For those exposed for two continuous days, the first day was uniformly used as the exposure date in estimation. This approach ensured the upper limit of error in the estimated incubation period be smaller than 1 day for the cases with a 2-day or 3-day exposure, regardless of when exactly (i.e., first, second, or third day) the transmission actually occurred. In reality, the overall error was bound to be much smaller than 1 day, as most included cases were exposed for only 1 day which would dilute the overall error [16].

Epidemiologic data indicate that the virus can cause a wide spectrum of clinical disease (mild-to-severe illness), including death [17, 18, 19], and spreads through direct contact and droplets. Estimates are 5–6 days (range 2–14 days) for the incubation period and 2.2–3.6 for the reproduction rate; this rate is higher than those for seasonal and pandemic influenza [20, 21].

COVID-19 is a highly contagious disease. Its clinical manifestations range from mild to severe but most infected cases present a mild form of the disease and therefore have no severe clinical features [22].
Extensive control efforts are now in place as part of a global containment strategy to minimize exportation from China and rapidly identify and stop international spread.

In the World Health Organization European Region, Rome, Paris, London, Istanbul, and Moscow have direct flights to Wuhan, China, and the risk for importation was considered high [23]. SARS-CoV-2 was reported to have been introduced into Europe by a person from France who had traveled to Wuhan, China, for work, became ill on January 16, and returned ill to France on January 22 [24].

In Uzbekistan disease first registered in 15th of March 2020 among arrivals from France. From this period all travelers were isolated till May 2020. In spite of strict isolation June 2020 Covid-19 spreads among population [25].

First identified patient in Uzbekistan was a doctor who travels to France for 2 weeks. After coming back home she went to work meets with friends and relatives. 5-6th day she feels chills and common cold, and she suspect to catching corona virus. She got positive PCR test on 15th of March. But until these days she meets with a lot of friends. Already lot of people suspected to caching this disease. First admissions were mild to moderate cases. Strict isolation were the best choice for control this disease in our country.

Next group of patients came from Turkey before 15th of March but symptoms of one member occurred only end of March month. All her relatives and friends were severe ill and her mother died in ICU care after 45 days of the disease. That means more exposure time reveals to more serious disease.

As part of the investigation, the countries the tour visited identified low-risk (<15 min, >1–2 m) and high-risk (>15 min, <1–2 m) contacts [40].

In Italy, because seat numbers on the flight from Wuhan to Rome, during which 1 tour group member had a cough, were not reported in the passengers list, authorities contacted and informed all passengers (n=176) and crew members (n=17). The information provided was to watch for development of symptoms and call if any developed. No other high-risk contacts of the symptomatic group member in Italy were identified [4].

In France, the group visited several tourist attractions and used public transportation; contacts in the shops and hotel were interviewed and defined as low-risk contacts. Only 1 high-risk contact was identified. This person was the physician.

The physician was not wearing a mask during the consultation because he was not informed of the risk of COVID-19. He became ill on January 28 and stopped seeing patients. He went to a designated referral hospital on January 29
and showed a positive PCR result for SARS-CoV-2 for 12 days; he has since recovered. A total of 58 contacts (20 low risk and 38 high risk) of the physician were identified, including patients and their family members he saw during home visits the day before onset of symptoms. All involved persons were investigated and followed-up for 14 days; none showed development of illness.

Authorities in China were notified of symptomatic persons on the flight from Paris to Guangzhou. However, we were unable to confirm whether any contact tracing was performed.

As of February 10, the tour guide remained hospitalized, but had a normal chest radiograph and was clinically well. She remains in isolation because of a virus-positive sputum test result 19 days after illness onset. The other 3 tour members who were ill reportedly experienced mild illness, and all are now well. Because the first 2 symptomatic persons were never tested, we cannot conclude that they were the source of infection. However, given that the virus was not circulating in France, the source was most likely in the tour group. It is also possible that additional transmission resulting in mild illness occurred, particularly in the tour group, but was not identified. This event represents early introduction of SARS-CoV-2 into Europe, before implementation of extensive travel restrictions in Wuhan on January 23, and could explain additional chains of transmission in France, where the disease has now spread widely. The event was characterized by clinically mild illness in 6 persons; 2 showed documented prolonged virus shedding [40]. Excluding members of the tour group, 1 of 40 high-risk and 0 of 216 low-risk contacts became ill. The 1 high-risk exposure event was short but entailed close contact during a clinical examination. Assuming this was the sole exposure, the incubation time was 5 days, which is consistent with reported data.

This event represented a coordinated international effort and highlights the effectiveness of working through the established mechanisms of the European Union Early Warning and Response System and the International Health Regulations. This effort will be key to the effective implementation of the current global containment strategy [26].

This shows new cases in Europe and USA were with sharp increasing, in Uzbekistan this rate were gradual. In the June Uzbekistan weakened quarantine measures which lead to sharp increasing the disease occurrence. As the result again quarantine measures were re-straightening in Uzbekistan. After achieving some prosperity, in the end of September and October month again increased number of cases as other countries. This wave like occurrence of the disease led to learn more about future of corona virus.
The pathogenic mechanism that produces pneumonia seems to be particularly complex. Clinical and preclinical research will have to explain many aspects that underlie the particular clinical presentations of the disease. The data so far available seem to indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a reaction takes place which as a whole is labeled a 'cytokine storm'. The effect is extensive tissue damage with dysfunctional coagulation. Just a while ago, Italian researchers introduced the term of MicroCLOTS (microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome) for underlying the lung viral injury associated with the inflammatory reaction and the microvascular pulmonary thrombosis [27].

The 2019 novel Coronavirus disease (COVID-2019) has gripped the world with fear, anxiety and confusion, and this is spreading as fast as the virus. With limited age-disaggregated data becoming available, early indications are that the virus, as most other viruses in the past, has been particularly severe on older people [28].

The clinical spectrum of COVID-19 varies from asymptomatic or paucisymptomatic forms to clinical conditions characterized by respiratory failure that necessitates mechanical ventilation and support in an ICU, to multiorgan and systemic manifestations in terms of sepsis, septic shock, and multiple organ dysfunction syndromes (MODS). In one of the first reports on the disease, Huang et al. illustrated that patients (n. 41) suffered from fever, malaise, dry cough, and dyspnea. Chest computerized tomography (CT) scans showed pneumonia with abnormal findings in all cases. About a third of those (13, 32%) required ICU care, and there were 6 (15%) fatal cases [29].

Members of this large family of viruses can cause respiratory, enteric, hepatic, and neurological diseases in human body.

The case studies of Li et al. published in the New England Journal of Medicine (NEJM) on January 29, 2020, encapsulates the first 425 cases recorded in Wuhan [30]. Data indicate that the patients' median age was 59 years, with a range of 15 to 89 years. Thus, they reported no clinical cases in children below 15 years of age. There were no significant gender differences (56% male). On the contrary, in other reports, there is a lower prevalence in the female gender.

Clinical and epidemiological data from the Chinese CDC and regarding 72,314 case records (confirmed, suspected, diagnosed, and asymptomatic cases) were shared in the Journal of the American Medical Association (JAMA), providing the first important illustration of the epidemiologic curve of the Chinese outbreak [31]. There were 62% confirmed cases, including 1% of cases that were asymptomatic, but were laboratory-positive (viral nucleic
acidity test). Furthermore, the overall case-fatality rate (on confirmed cases) was 2.3%. Of note, the fatal cases were primarily elderly patients, in particular those aged ≥ 80 years (about 15%), and 70 to 79 years (8.0%). Approximately half (49.0%) of the critical patients and affected by preexisting comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease, and oncological diseases, died. While 1% of patients were aged 9 years or younger, no fatal cases occurred in this group.

The authors of the Chinese CDC report divided the clinical manifestations of the disease by their severity:

1. Mild disease: non-pneumonia and mild pneumonia; this occurred in 81% of cases.

2. Severe disease: dyspnea, respiratory frequency ≥ 30/min, blood oxygen saturation (SpO2) ≤ 93%, PaO2/FiO2 ratio or P/F [the ratio between the blood pressure of the oxygen (partial pressure of oxygen, PaO2) and the percentage of oxygen supplied (fraction of inspired oxygen, FiO2)] < 300, and/or lung infiltrates > 50% within 24 to 48 hours; this occurred in 14% of cases.

3. Critical disease: respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or failure (MOF); this occurred in 5% of cases [4,31].

From the subsequent reports, it is estimated that in 70% of patients the disease is asymptomatic or with very mild symptoms, while in the remaining 30% there is a respiratory syndrome with high fever, cough until severe respiratory failure is reached who may require ICU admission. Thus, data obtainable from reports and directives provided by health policy agencies, allow dividing the clinical manifestations of the disease according to the severity of the clinical pictures [32]. The COVID-19 may present with mild, moderate, or severe illness. Among the severe clinical manifestations, there are severe pneumonia, ARDS, as well as extrapulmonary manifestations and Systemic complications such as sepsis, and septic shock. The clinical course of the disease seems to predict a favorable trend in the majority of patients. In a percentage still to be defined of cases, after about a week there is a sudden worsening of clinical conditions with rapidly worsening respiratory failure and MOD/MOF. As a reference, the criteria of the severity of respiratory insufficiency and the diagnostic criteria of sepsis and septic shock can be used [33].

Mild clinical illness - these patients usually present with symptoms of an upper respiratory tract viral infection, including mild fever, cough (dry), sore throat, nasal congestion, malaise, headache, muscle pain, or malaise. New loss of taste and/or smell, diarrhea, and vomiting are usually observed. Signs and symptoms of a more serious disease, such as dyspnea, are not present.
Moderate pneumonia - respiratory symptoms such as cough and shortness of breath (or tachypnea in children) are present without signs of severe pneumonia.

Severe Pneumonia - fever is associated with severe dyspnea, respiratory distress, tachypnea (> 30 breaths/min), and hypoxia (SpO2 < 90% on room air). However, the fever symptom must be interpreted carefully as even in severe forms of the disease, it can be moderate or even absent. Cyanosis can occur in children. In this definition, the diagnosis is clinical, and radiologic imaging is used for excluding complications [4].

In our study, we evaluate 4500 patients (in Specialized “Nazarbek” Covid-19 center in Uzbekistan from 1st of August until 10th of December, 2020): among them 752 patients were with mild diseases with symptoms of fatigue, headache, loss of nasal smell and loss of smell, mild fever. We recommend them isolation at home. Outcome of the mild disease were with normal prognosis.

Other 3748 patients were hospitalized in two departments with moderate disease 2598; severe and critically ill patients were 1241. Some of the critically ill patients initially admitted as a severe but disease progression were negative and they were transfer to the ICU care. The causes of most critically ill patients were their chronic diseases such as diabetes mellitus, obesity, heart failure and kidney failure. Of course as other countries older age patients were in high risk group.

Acute Respiratory Distress Syndrome (ARDS) - the diagnosis requires clinical and ventilatory criteria. This syndrome is suggestive of a serious new-onset respiratory failure or for worsening of an already identified respiratory picture. Different forms of ARDS are distinguished based on the degree of hypoxia [4].

Sepsis - according to the International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), sepsis represents a life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction [34]. The clinical pictures of patients with COVID-19 and with sepsis are particularly serious, characterized by a wide range of signs and symptoms of multiorgan involvement. These signs and symptoms include respiratory manifestations such as severe dyspnea and hypoxemia, renal impairment with reduced urine output, tachycardia, altered mental status, and functional alterations of organs expressed as laboratory data of hyperbilirubinemia, acidosis, high lactate, coagulopathy, and thrombocytopenia. The reference for the evaluation of multiorgan damage and the related prognostic significance is the Sequential Organ Failure Assessment (SOFA) score, which predicts ICU mortality based on lab results and clinical data [35].
1. In the early stage of the disease, a normal or decreased total white blood cell count (WBC) and a decreased lymphocyte count can be demonstrated. Interestingly, lymphopenia appears to be a negative prognostic factor.

2. Increased values of liver enzymes, lactate dehydrogenase (LDH), muscle enzymes, and C-reactive protein can be detected.

3. Unless a bacterial overlap, a normal procalcitonin value is found.

4. The elevated neutrophil-to-lymphocyte ratio (NLR), neutrophil count divided by the result of WBC count minus neutrophil count, and platelet-to-lymphocyte ratio, can be the expression of the inflammatory storm [36]. The correction of these indices is an expression of a favorable trend.

5. Increased D-dimer - in critical patients increased, blood lymphocytes decreased persistently, and laboratory alterations of multiorgan imbalance (high amylase, coagulation disorders, etc.) are found.

In our practice, increasing of liver enzymes mostly associated with drugs such as antivirals and antimicrobials. We also found that the procalcitonin and C-reactive protein several times increased in critically ill patients. D - Dimer were several times increased who already were with coagulopathy or thrombosis.

Imaging of the chest include Chest X-ray Examination -Since the disease manifests itself as pneumonia, radiological imaging has a fundamental role in the diagnostic process, management, and follow-up. Standard radiographic examination (X-ray) of the chest has a low sensitivity in identifying early lung changes and in the initial stages of the disease. At this stage, it can be completely negative. In the more advanced stages of infection, the chest X-ray examination generally shows bilateral multifocal alveolar opacities, which tend to confluence up to the complete opacity of the lung. Pleural effusion can be associated [4].

In our practice – Chest X-Ray were useful for monitoring of the treatment, especially ICU care patients and patients with severe pneumonia who always on SPAP portable X – Rays were method of choice.

Chest Computed Tomography - given the high sensitivity of the method, chest computed tomography (CT), in particular high-resolution CT (HRCT), is the method of choice in the study of COVID-19 pneumonia, even in the initial stages. Several non-specific HRCT findings and patterns can be found. Most of these findings may also be observed in other lung infections. The most common findings are multifocal bilateral "ground or ground glass" (GG) areas associated with consolidation areas with patchy distribution, mainly peripheral/subpleural and with greater involvement of the posterior regions and lower lobes. The "crazy paving" pattern can be also observed. This latter finding is characterized by the presence of GG areas with superimposed interlobular septal thickening and intralobular septal
thickening. It is a non-specific finding that can be detected in different conditions. Other findings are the “reversed halo sign” which is a focal area of GG delimited by a peripheral ring with consolidation, and the finding of cavitations, calcifications, lymphadenopathies, and pleural effusion.

Multi detector computed tomography very sensitive for lung changes in Covid -19, as a first method of choice for diagnosis of coronavirus induced pneumonia. According to Uzbekistan Coronavirus protocols [22] we diagnosed mild if both lung changes composed ≤25%, if changes reach ≥25-50% lung damage we diagnosed as a moderate, if lung changes ≥50% - 70% diagnosed as a severe lung damage and ≥70% were evaluated as a critically ill.

Ultrasound - can allow evaluating the evolution of the disease, from a focal interstitial pattern up to "white lung" with evidence often of subpleural consolidations. It should be performed within the first 24 hours in the suspect and every 24/48 hours and can be useful for patient follow-up, choice of the setting of mechanical ventilation, and for the indication of prone positioning. The main sonographic features are:

1. Pleural lines often thickened, irregular, and discontinuous until it almost appears discontinuous; subpleural lesions can be seen as small patchy consolidations or nodules.

2. B lines. They are often motionless, coalescent, and cascade and can flow up to the square of "White lung".

3. Thickenings. They are most evident in the posterior and bilateral fields especially in the lower fields; the dynamic air bronchogram within the consolidation is a manifestation of disease evolution.

4. Perilesional pleural effusion.

However, during the course of the disease, it is possible to identify the first phase with focal areas of fixed B lines, a phase of numerical increase of the lines B up to the white lung with small subpleural thickenings, and further progress until evidence of posterior consolidations.

There is no specific antiviral treatment recommended for COVID-19, including vaccination. The treatment is symptomatic, and oxygen therapy represents the first step for addressing respiratory impairment [37]. Intensive care is needed to deal with complicated forms of the disease.

In our practice we used oxygenotherapy (if SpO2 < 93-94%, SpO2 < 92% we performed SPAP mask) antiagregants and anticoagulant therapy as a first line treatments. Symptomatic treatment also we used in all cases.

Concerning ARDS treatment, accumulating knowledge on the pathophysiology of lung damage, have gradually induced clinicians to review
strategies for dealing with respiratory failure. As Gattinoni et al. suggested, COVID-19-induced ARDS (CARDS) is not a "Typical" ARDS [2,]. This aspect of the disease is of fundamental importance and has probably negatively affected the therapeutic approach in the early stages of the pandemic.

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