Abstract

Objectives: To provide an overview of the three major deadly coronaviruses and identify areas for improvement of future preparedness plans, as well as provide a critical assess

ment of the risk factors and actionable items for stopping their spread, utilizing lessons learned from the first two deadly coronavirus outbreaks, as well as initial reports from the current novel coronavirus (COVID19) epidemic in Wuhan, China.

Methods: Utilizing the Centers for Disease Control and Prevention (CDC, USA) website,

and a comprehensive review of PubMed literature, we obtained information regarding clinical signs and symptoms, treatment and diagnosis, transmission methods, protection methods and risk factors for Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS) and COVID19. Comparisons between the viruses were made.

Results: Inadequate risk assessment regarding the urgency of the situation, and limited

reporting on the virus within China has, in part, led to the rapid spread of COVID19 throughout mainland China and into proximal and distant countries. Compared with SARS and MERS, COVID19 has spread more rapidly, due in part to increased globalization and the focus of the epidemic. Wuhan, China is a large hub connecting the North,

1

South, East and West of China via railways and a major international airport. The availability of connecting flights, the timing of the outbreak during the Chinese (Lunar) New Year, and the massive rail transit hub located in Wuhan has enabled the virus to perforate throughout China, and eventually, globally.

Conclusions: We conclude that we did not learn from the two prior epidemics of corona

virus and were illprepared to deal with the challenges the COVID19 epidemic has posed. Future research should attempt to address the uses and implications of internet of things (IoT) technologies for mapping the spread of infection.

Key words: Coronavirus, epidemiology, epidemic, outbreak, MERS, SARS, nCoV, COVID19

Introduction

The novel coronavirus (COVID19) was first identified in Wuhan, China, in December 2019 among a cluster of patients that presented with an unidentified form of viral pneumonia with shared history of visiting the Huanan seafood market.1 Patients were assessed for viral pneumonia through the ascertainment and testing of bronchoalveolarlavage fluid utilizing whole genome sequencing, cell cultures and polymerase chain reaction (PCR). The virus was isolated from biologic samples and identified as genus betacoronavirus, placing it alongside other Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS).1 At the time of writing, the number of persons infected by the virus has now surpassed 67 091 and Chinese authorities have reported 1527 deaths from the virus, most in Hubei, the provincial epicenter of the outbreak.2 Over 25 countries have confirmed cases to date, including countries from Asia, Europe, North America and the Middle East (see Figure 1).2 The virus spread internationally within 1 month of the first identification, and can be transmitted via close humantohuman contact.3 The World Health Organization (WHO) declared COVID19 a Public Health Emergency of International Concern as of 1 February 2020.

Another betacoronavirus was first identified in Southern China (Guangdong province) in November 2002. The WHO did not receive an update from the Chinese government until the end of March, with 792 cases and 31

deaths reported. The lack of transparency of the Chinese health ministry has been cited as one of the largest contributors to the spread of the virus globally.4 At the end of the

epidemic, China reported >8,000 cases of the disease and

774 deaths, and a casefatality rate of 7%.5 The reservoir host of the disease was thought to be the Asian civet cat (Paguma larvata). The foci of transmission from host to human were thought to be the open markets, much like the COVID19 outbreak currently ongoing.5 The SARS global outbreak was contained in July 2003 and since 2004 there have not been any known cases of SARS reported.6

After the emergence of SARS, MERS was the second coronavirus resulting in a major global public health crisis. It first emerged in 2012 in Saudi Arabia when a 60 yearold man presented with severe pneumonia.7 An outbreak of the virus did not occur until 2 years later, in 2014, with a total number of identified cases of 662 and a 32.97% casefatality rate.8 From 2014 to 2016, 1364 cases were observed in Saudi Arabia. A total of 27 countries were affected by MERS during the outbreaks spanning Europe, Asia, the Middle East and North America. Cases that were identified outside of the Middle East, including the outbreak in South Korea in which 186 individuals were infected as a result of a super spreader, were transplanted individuals that had previously been infected in the Middle East.9 Since 2012, 2494 laboratory confirmed cases of MERS have been reported, and 858 associated deaths have occurred (34.4% casefatality ratio).8,10

Total deaths (Other Locations)

Total deaths (Source Country)

Total cases (Other Locations)

Total Cases (Source Country)

Total Deaths

Total Cases

0 10000 20000 30000 40000 50000 60000 70000

MERS SARS COVID19

Figure 1 Examining relationships between coronaviruses overall and by country, 15 February 2020. Source country: MERS (Middle East Respiratory Syndrome), Saudi Arabia; SARS (Severe Acute Respiratory Syndrome), Hong Kong (China); and COVID19 (novel coronavirus), China.2

The objectives of our study are to provide an overview of the three major deadly coronaviruses and identify areas for improvement of future preparedness plans, as well as provide a critical assessment of the risk factors and actionable items for stopping their spread, utilizing lessons learned from the first two deadly coronavirus outbreaks, as well as initial reports from the current COVID19 epidemic in Wuhan, China. Although the epidemic is still ongoing, initial lessons from its spread can help inform public health officials and medical practitioners in efforts to combat its progression.

Methods

Utilizing the Centers for Disease Control and Prevention (CDC, USA) website, and a comprehensive review of PubMed literature, we obtained information regarding clinical signs and symptoms, treatment and diagnosis, transmission methods, protection methods and risk factors for MERS, SARS and COVID19. Additionally, the Chinese Center for Disease Control and Prevention (CCDC) was accessed for uptodate information on COVID19. Furthermore, verified news articles were also of interest in obtaining uptodate case and fatality numbers on COVID19. The Johns Hopkins University website was also utilized to access maps and spatiotemporal information regarding the virus.2 SARS and MERS data were compiled from the WHOs latest situation report for

creation of graphs and maps to compare the spatial distribution of the three coronaviruses.

Patient and public involvement

Patients and the public were not involved in this research.

Results

Diagnosis and treatment

With respect to COVID19, diagnosis was conducted initially by assessing clinical characteristics of the presenting patient, chest imaging and the ruling out of common bacterial and viral pneumonia. Once common bacterial and viral pathogens were ruled out, lower and upper respiratory tract specimens were obtained for cell culture and deep sequencing analysis. These specimens indicated a novel coronavirus initially known as 2019nCoV.3 PCR, using the RespiFinderSmart22kit (PathoFinder BV) realtime reverse transcription PCR (RTPCR) assay, was used to detect viral RNA by targeting a consensus RNA dependent RNA polymerase region of pan bCoV.3 A diagnostic test was developed soon after viral isolation. Treatment in some hospitals involves prophylactic antibiotics to prevent secondary infection.3 To date, no antiviral agent has been proven effective against COVID19. Initial reports showed that oseltamivir was given to 93% of patients (orally administered 75 mg 2x/day) in combination with antibiotics.3

Patients experiencing severe illness (22%) were given corticosteroids (40 120 mg/day) to reduce lung inflammation due to high levels of cytokines caused by the virus, as part of a combined regimen for cases that were communityacquired and diagnosed at the designated hospital.3 Since the combination of lopinavir and ritonavir was already available in the local hospital, a randomized controlled trial was initiated quickly to assess the efficacy and safety of combined use of lopinavir and ritonavir in patients hospitalized with COVID19 infection.3

A suspected case according to the WHO is a patient with severe acute respiratory infection (fever, cough and requiring admission to hospital), and with no other etiology that fully explains the clinical presentation and at least one of the following: a history of travel to or residence in the city of Wuhan, Hubei Province, China in the 14 days prior to symptom onset, or the patient is a health care worker who has been working in an environment where severe acute respiratory infections of unknown etiology are being cared for.11 A confirmed case is a person with laboratory confirmation of COVID19 infection, irrespective of clinical signs and symptoms.11 On February 13 2020 the Hubei National Health Commission said it would include cases confirmed by clinical diagnosis using CT scans in addition to rtPCR, adding several thousand new cases to the total count.

Diagnosis of MERS by the WHO is defined initially as

patients presenting with a fever, cough and hospitalization with suspicion of lower respiratory tract involvement.12 Patient history was obtained upon hospitalization and prominent considerations for diagnosis involved a history of contact with probable or confirmed cases of the illness, or a reported history of travel or residence within the Arabian Peninsula. Severe cases were subjected to laboratory testing.13 Similar to COVID19, RTPCR was used for diagnosis. Additional serum tests for antibodies of the virus were developed. In Saudi Arabia, a clinical trial revealed that a combination of lopinavir ritonavir and interferon beta1b was shown to be effective among MERS cases.14 Additionally, a broadspectrum antiviral nucleotide prodrug named remdesivir presented potent efficacy for the treatment of MERS coronavirus and SARS coronavirus in preclinical studies.15,16

A patient was considered to have laboratoryconfirmed

SARS if there was a positive RTPCR result from two or more clinical specimens, either from different sites or tested in different laboratories, obtained from patients before or after death, or if there was seroconversion by enzymelinked immunosorbent assay, indirect fluorescent antibody test or neutralization assay.17 Similar to MERS, serologic testing for IgG antibodies was developed for SARS coronavirus. Treatment of SARS involved combination therapy of

lopinavir and ritonavir and was associated with substantial clinical benefit with fewer adverse clinical outcomes.18 A broadspectrum antiviral nucleotide prodrug named remdesivir presented potent efficacy for the treatment of MERS coronavirus and SARS coronavirus in preclinical studies.15,16

There are several similarities between these viruses in their diagnosis and treatment. All three viruses are definitively diagnosed by utilizing cell cultures of respiratory fluids, serum antibody analysis or RTPCR analysis of respiratory fluids from patients. All three viruses cause pneumonia, and radiography of the lungs is an important diagnostic tool for preliminary and broad identification of the severity of the disease. These viruses are similarly treated with antiviral therapies, although no specific antiviral therapy has yet been approved for COVID19, with clinical trials underway. The major difference between COVID19 and its predecessors is that this virus rarely produces runny noses or gastrointestinal symptoms in those infected, which are commonplace in MERS and SARS cases.3

Mode of transmission

There is limited knowledge regarding the transmission of COVID19. Transmission has been confirmed to occur from human to human, and it is thought to be spread through respiratory droplets from coughs or sneezes.3 Primary cases of COVID19 have been traced back to the Huanan seafood market, with secondary cases occurring at hospitals among nurses and physicians who had extensive contact with COVID19 patients. Furthermore, several individuals who did not have direct contact with the Huanan seafood market were diagnosed with the disease.

MERS is also transmitted from close persontoperson contact (primarily in health care settings during the symptomatic phase of the disease), although instances of this transmission were significantly less during the height of the MERS epidemic. The transmission occurs through respiratory secretions from coughing and sneezing, whereas primary cases of the virus have been traced to close contact with infected dromedary camels, the animals identified as the reservoir host for MERS.19

Similarly, the transmission of SARS occurred during close persontoperson contact, via respiratory droplets from sneezing or coughing at a rapid rate, although not as quickly as the current outbreak of COVID19. Furthermore, fomites, fecal transmission and handling of animals (killing, selling or preparing wild animals) were less common methods of transmission.20

The modes of transmission, although still in part unclear regarding COVID19, are thought to be the same

mechanism for all three viruses. Infection via respiratory droplets or secretions of infected individuals are thought to be the predominant mode of transmission from human to human. The spread of infection for the current outbreak is occurring more rapidly than in the SARS epidemic. Rates of humantohuman transmission were generally lower for MERS, possibly in part due to the higher case fatality ratio (CFR) among those diagnosed with the disease.