

# A Narration: 20th v/s 21st Century: Pandemic v/s Another Pandemic: Virus v/s Another Virus (Spanish Flu V/S COVID-19)

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## ABSTRACT

**Pandemic leads to major mortality and morbidity. Many pandemics occur over the centuries, but the mother of all pandemic was "Spanish Flu" and nowadays we are facing another huge uncontrollable "Covid 19" pandemic of the current century. The purpose of this comparative review is to help and provide guidance for frontline medical staff in dealing with this current outbreak to differentiate and seek information with the previous pandemic and get knowledgeable guidance for future dealings of COVID-19. Peer-reviewed literature on the outbreaks of infectious disease has steadily increased in recent years, but the major pandemics should be compared to find out the similarities and differences. To do so, we provide step by step contents of both diseases.**

**Keywords:** infection control and management, respiratory illness, SARS CoV-2, Spanish Flu.

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## I. INTRODUCTION

Throughout history, nothing has executed human beings more than infectious diseases. The deadly "Spanish flu" pandemic had last from January 1918 to December 1920. The mortality was estimated to have been anywhere 17 million to 50 million [1], [2]. It was late December 2019, hospitals in Wuhan, Hubei, China, reported a cluster of cases with pneumonia of unknown cause, another pandemic, attracting great attention worldwide. The number of PCR-confirmed cases has touched the threat level and within one month, WHO declared COVID-19 to be a Public Health Emergency of International Concern (PHEIC) and declared an epidemic has occurred. We reviewed the published clinical features, symptoms, complications, and treatments of patients with Spanish flu and COVID-19 to help health workers around the world combat the current outbreak.

## II. LITERATURE SEARCH

This narrative review discusses the relevant literature, including updated studies, and the implications for practice concerning Spanish flu and COVID-19 infections. We performed a literature search using Pub Med and UpToDate. The search was restricted to articles between 1997 and 2020. Keywords used were "COVID-19," "2019 novel coronavirus", "SARS-CoV-2", "2019-nCoV", "Wuhan coronavirus" "Spanish Flu", "1918 H1N1", "Pandemic".

## III. HISTORY

Spain is not the geographical origin of the Spanish flu. The Spanish government was the first one to accept that unusual and strange pathogen, since then the name stuck to it. The outbreak occurred in three waves. It was World War I, during which the first wave started in early March 1918 [17]-[19]. It was benign comparatively and resembled typical flu epidemics; sick and elderly were at risk mostly, although young and healthier communities recovered easily. However, in August 1918, the second wave of a more lethal type of disease had fully emerged. Pneumonia often developed rapidly, with high mortality within two days after the first indications of the symptoms. When the second wave began in, the Spanish flu had mutated to a much deadlier form when it reached France and the United States [20]. The third wave occurred in winter, and by the spring the virus had over its course [21]. About half of the deaths were among the younger age group, which was an unusual mortality age pattern recognized with the latter two waves.

### A. End of Deadliest Pandemic

The Spanish flu pandemic came to an end by the summer of 1919, as those that were infected either developed immunity against the virus or no more. Despite the very high mortality with this influenza pandemic, the memories began to fade away and to be called as "forgotten pandemic". Over time, the public awareness wane off until the new bird flu and other pandemics recalled the memories once again in the 1990s and 2000s, although with not much cruelty.

## B. Beginning of New Pandemic

It was on 31 Dec. 2019, when China, the most populated country of East Asia, was informed to WHO regarding mysterious pneumonia of unknown etiology [22], [23].

On 7 Jan 2020, from the seafood market in Wuhan city, Chinese research authorities mentioned that they isolated a new virus; named as 2019-nCoV, that closely related to bat coronavirus [24], Pangolin coronaviruses [25] and SARS-CoV. Official names have been announced latter for the virus responsible for COVID-19 (“coronavirus disease”) and the virus is “Severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2) [26], [27].

Considering this deadly virus is of zoonotic origin as many of the cases had linked to the seafood wholesale market in China [28]-[30].

On 30 January 2020, Public Health Emergency of International Concern had declared the outbreak [31], [32].

As per WHO, too- date 29 November 2020, there have been 61,869,330 confirmed cases of COVID-19, including 1,448,896 deaths, reported to WHO [33].

## IV. ETIOLOGY

According to the Centers for Disease Control and Prevention, there are 18 H subtypes and 11 N subtypes identified with variations [34]. But H1, H2, and H3 have substantial human-to-human transmission [35].

H1N1 virus with genes of avian origin was identified as Spanish flu, a member of the family Orthomyxoviridae (a group of RNA viruses) with 2 surface antigens (hemagglutinin (H) and neuraminidase (N)). These antigen shows drift by mutation. Antigenic drift produces new strains of H1N1 that causes epidemic [36], [37]. During the last century, there were four pandemics of influenza strain had been observed; the H1N1 Spanish flu (1918), the H2N2 Asian flu (1957), the H3N2 Hong Kong flu (1968), and the H1N1 swine flu (2009).

Coronaviruses are enveloped RNA viruses. Not so often, Animal coronaviruses can spread to humans and subsequently spread among humans, SARS and MERS were the examples. SARS-CoV-2 is among the Sarbecovirus subgenus of the family Coronaviridae, known to infect humans. This virus has been isolated and found to be similar to SARS-like coronaviruses from bats, but it is found to be different from SARS-CoV and MERS-CoV [38], [39]. There are two subtypes (L and S) of the SARS-CoV-2 strains found in China. The L type was found to be more prevalent and more aggressive during the early stages of the outbreak in Wuhan City [40]. It has been confirmed that the virus binds to the angiotensin-converting enzyme-2 (ACE2) receptor in humans, which suggests similar pathogenesis to SARS [41], [42]. However, there is a unique structural feature of the spike glycoprotein receptor binding domain which offers a higher binding affinity of SARS-CoV [43]. A furin-like cleavage site does not exist in other SARS-like coronaviruses [44]. Because of the ACE2 expression level, lungs, heart, esophagus, kidneys, bladder, and ileum are considered more vulnerable to SARS-CoV-2 infection [45]. And due to a down regulating ACE2 receptor level, it induces acute respiratory distress syndrome and myocarditis [46].

## V. PREVALENCE

Despite poor or nearly absent data for many countries, the pandemic mostly killed young adults. It was thought to be due to the cytokine storm (an overreaction of the immune system). This may be the reason for its surprising effect on younger and healthier people [47]-[50]. 99% of deaths in the U.S. occurred in people under 65, and nearly half of deaths were in young adults between 20 to 40 years old [51].

Data from the largest case series in China found that 3% were aged around 80 years and more, 87% cases were aged around 30 to 79 years, 1% was around aged 9 years or less and, 1% was aged between 10 to 19 years. In this case series, 51% of patients were male and 49% were female. Healthcare workers were involved in 4% of cases with 23 deaths [53]. Children were infected less which accounts for only 1% to 5% as compared to adults, with the median age of 7 years [54].

## VI. DIAGNOSIS

To check Spanish flu virulence and understanding the deadly virus, reconstruction of the entire 1918 virus was begun in August 2005 [56] but there is no data available for the detection of H1N1 in past like nowadays (rapid molecular assays, RIDTs)

Detection of SARS-CoV-2 RNA by reverse transcription-polymerase chain reaction (RT-PCR) is the gold standard for the diagnosis of COVID 19 [57]. It is better in nasopharynx samples compared to throat samples [58].

There may be the availability of urgent and convenient detection of virus by saliva sampling, although it's not the gold standard [59].

There is also the detection of SARS-CoV-2 RNA in stool and blood [60] and it may be the marker of severity of illness [61].

## VII. MODE OF TRANSMISSION

Like any other influenza viruses known, Spanish flu was also transmitted from person to person through airborne respiratory secretions. World War I hastened the pandemic and as well as a denial by the government and public was not prepared to handle another problem [62].

The risk of transmission is thought to be greatest when patients are symptomatic since viral shedding is greatest at the time of symptom onset and declines over several days to weeks. Novel Coronavirus can spread with respiratory droplets, so the close contacts 1 to 2 meters (3 to 6 feet) [63] is recommended, while both sputum and saliva can carry the heavy viral load [64]-[66].

The virus can also stay prolonged in the air and can be the source of transmission [67]. Therefore, some have proposed that precautions should be used everywhere [68]. However, the proportion of SARS-CoV-2 transmission in the population due to asymptomatic or pre-symptomatic infection compared to symptomatic infection is unclear [69]. There is an estimate of one infected person may transmit and infect the other person of the population for COVID-19 is 2.2% [70].

The virus can survive on surfaces for up to 72 hours. Fomites, though not certainly, are suspected as the source of

infectious particles [71].

There is the potential of fecal-oral transmission of this disease as a virus has been detected from stool sample [72]. Vertical transmission is less likely to occur based on little research data available [73].

### VIII. CLINICAL MANIFESTATIONS

Uncomplicated Spanish flu symptoms were quite similar to seasonal influenza as often described in the clinical records [74].

These symptoms include high fever, malaise, cough but muscle ache, vomiting, fatigue, and headache were also common. In contrast to seasonal influenza, epistaxis often appeared. In serious cases, cyanosis was described as the most important predictor of a worse outcome [75].

Complications like "Post influenza pneumonia" developed sooner after the onset of the influenza symptoms in most of the infected people. A prolonged duration of high fever was the first indication of a secondary infection [76]. Other most commonly reported pathological findings were endocarditis and hemorrhagic pulmonary disease. The mortality becomes evident within 9.6(SD 3.3) days [77]. The incubation period is around 14 days, with a median time of 4-5 days [78]-[81]. The most contagious period of this virus is during the first three days with the start of symptoms although it can spread earlier [82]-[84]. There is a diversity of range of intensity of this disease reported so far. Fever is the main clinical manifestations of COVID-19 (90% or more) then cough (75%), and shortness of breath (50%) [85]-[88]. Older individuals with co-morbidities can present with delayed onset of symptoms [89], [90].

There is some extrapulmonary or atypical clinical presentations are also noted like vomiting, and diarrhea before respiratory symptoms [91]. Headache, confusion, pink eye, conjunctivitis is also reported. Anosmia or ageusia before the onset of respiratory symptoms [92], [93]. Acute kidney injury of various severity is also seen with the critically ill patient, either due to the overall patient's critical illness or a direct effect of virus attack ACE2 receptors present on the kidney, although many types of research are ongoing [94], [95].

### IX. COMPLICATIONS

Spanish flu initially misdiagnosed and due to its extremely high infection rate, complications and mortality became so high [96], [97].

The observed complication was hemorrhage from the nose and upper gastrointestinal. Bleeding from ears and petechial hemorrhage in the skin was also observed. Most of the death occurred due to secondary bacterial pneumonia [99].

Spanish flu has been linked to the outbreak of encephalitis lethargica in the 1920s [100].

There is an association between differences in age and prevalence of underlying conditions (cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer) with increased mortality associated with COVID-19 [101].

A high inflammatory response results in a variety of cardiovascular complications like myocarditis, heart failure,

arrhythmias, acute coronary syndrome [102].

Cytokine release syndrome results in multiple-organ failure that leads to death [103]. ARDS was reported in 15% to 33% of patients [104] and children are more prone to develop ARDS [105]. Critically ill patients may more likely to develop an acute liver injury, although it's not routinely seen [106].

There are high chances of thromboembolic complications in COVID-19 as it has prothrombotic properties [107].

25% to 69% of patients have been reported with venous thromboembolism in severe COVID-19 [108].

Cerebrovascular thrombosis has been reported in a few patients younger than 50 years of age in New York [109].

Acute Guillain-Barre syndrome as initial presenting symptoms in a few patients with COVID-19 has been observed [110].

Acute kidney injury by the virus itself rather than in complicated disease is the emerging new finding and reported in 3% to 8% of patients in case series [111]-[113].

Secondary infections are also associated with COVID 19 and the major cause of morbidity and mortality [114]. A conclusion section is not required. Although a conclusion may review the main points of the paper, do not replicate the abstract as the conclusion. A conclusion might elaborate on the importance of the work or suggest applications and extensions.

#### A. Reinfection or Immunity

There are more upcoming researches about the immunity or reinfection. Initially, it was thought that there was no data concerning the possibility of re-infection after recovery. Clinical recovery has been correlated with the detection of IgM and IgG antibodies which signal the development of immunity [115], [116].

But as more researches are coming and the exploring of this surprising virus, new and future outcome can be predicted. Recently Geneva-based UN health agency stated that more evidence needed about the effectiveness of antibody-mediated immunity to guarantee the "risk-free certificate". WHO also stated that there is currently no evidence that antibodies produced in recovered patients are enough to keep them protected against re-infection.

#### B. Long Term Effects

As far as the limited data allow us to conclude the long term effects from past pandemics. It causes economic damage, individual behavioral changes; increased rates of physical disability displayed reduced educational attainment [117], [118].

Severe global socioeconomic effects like the cancellation of sporting, religious, political, and cultural events and panic buying result in widespread shortages of supplies [119]. Educational institutes have been closed [120]. Politically unstable countries have been facing increase political stresses. Pandemic control measures such as quarantines, curfew, and lockdown have sparked tension between citizens and states.

## X. CONTROL MEASURE

Preventive measures are a powerful weapon. To prevent the influenza transmission, physicians and public Health Authorities of that time suggested many measures which included cleaning and disinfecting the mouth and nose areas with a mixture of oil and menthol or hydrogen peroxide, avoiding closed settings and direct contact with sick, eating a healthy diet, to ventilate the housing and good sleep and resting. These measures were simple but often hard to carry on [121], [122]. For Coronaviruses, there's currently no vaccine to prevent the disease (COVID-19) [124]. So recommended preventive measures include hand washing regularly for 20 seconds, with soap and water or alcohol-based hand rub, covering one's mouth when coughing, maintaining distance from other people (1 meter or 3 feet), and monitoring and self-isolation of people who suspect they are infected [125]. Contact isolation objects such as masks, gowns, and gloves are also recommended [126]. Transmission via ocular surface can be possible [127], so eye protection should also be considered. The virus is killed by household soap outside the human body, which dissolves its outer envelope [128], [129]. Health officials and authorities across the world have announced to implement quarantines, curfews and stay-at-home orders, workplace hazard controls, lock-down, and travel restrictions [130], [131]. Many household animals have been tested positive for COVID-19 but there is no evidence so far that animals can pass the pathogen to the humans [132], [133].

## XI. MANAGEMENT

In the 1940s, America licensed the first flu vaccine. So earlier to this, there was no preventive vaccine for Spanish flu either. In 1924, Red Cross assembled a team to assess the effectiveness of the treatments used for the biggest pandemic. Later the committee concluded that none of the drug treatments given or trials attempted during the pandemic had any proven effects on the influenza outbreak [134]. But the implementation of non-pharmaceutical interventions resulted in decreased peak mortality rates around 50% [135].

When the Spanish flu hit, it was the time when World War I had left parts of America with a shortage of health workers. Physicians and scientists had no obvious knowledge of etiology and treatments. Symptomatic therapy was practiced like salicylates and quinine and codeine for cough. Complicated therapy was injecting with silver or platinum colloid solutions, digitalis, a camphor oil, or adrenaline. Alternative therapies were also tried. There was no consensus on the effectiveness of the perspiration method, which was thought to reduce mortality in Swedish hospitals [136]. Diphtheria treatments [137] and syphilis treatments [138] were also attempted. Heroin was used as a cough suppressant treatment [139].

Acetylsalicylic acid was used widely with digitalis but latter data showed that there was increased mortality observed with this regimen [140].

At present, most treatment is symptomatic and supportive for Covid-19 [141]. Many drugs are in different stages of being tested as treatments for the Covid-19. The drugs trials being tested, from flu treatments to failed Ebola drugs, to antimalarials and many more; like Antiviral EIDD-2801,

Japan flu drug (favipiravir or Avigan), A blood pressure drug (Losartan), an HIV drug combination drug Kaletra (a combination of lopinavir and ritonavir) [142], [143]. The first reported case with 2019-nCoV infection in the United States of America was treated with remdesivir [144]. A recent study conducted by the "front-line" health care providers combating COVID-19 in Wuhan indicated that systemic corticosteroid treatment did not show significant benefit [145]. Baricitinib has been suggested as a potential drug for the treatment in the hope that it might reduce the process of both virus invasion and inflammation [146], [147]. Steroids use are very common and several researches has been conducted and having good results on severe Covid-19.

Hydroxychloroquine and chloroquine are FDA proved for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection as their research had been done on influenza in past studies [148], [149], [150], [151]. Convalescent plasma for the treatment of patients with COVID-19 is being used as well [152], [153]. Considering the mechanism through which this virus works in the human body, many researchers have given the idea that (ACE) inhibitors or angiotensin receptor blockers (ARBs) or NSAIDs may worsen COVID-19 but currently, no data are suggesting an association between COVID-19 clinical outcomes and the drug uses.

With CoVid 19, several efforts for the development of vaccines are ongoing, but as per WHO, initially it would take 18 months for the COVID-19 vaccines to be available. Huaxia. WHO says vaccines against novel coronavirus 18 months away [154], [155]. Inactivated or weakened virus vaccines, Protein-based vaccines, Viral vector vaccines, RNA and DNA vaccines have been studied but Interim analyses of phase 3 studies have been announced, through press releases, for four candidate COVID-19 vaccines. These are the mRNA platform candidates from Pfizer/Biontech and Moderna, the ChAdOx1 platform candidate from AstraZeneca, and the Ad26/Ad5 platform candidate from the Gamaleya National Centre. Preliminary point estimates of vaccine efficacy all exceed WHO Target Product Profiles and WHO draft EUL criteria. No safety concerns have been identified from the preliminary analyses. Uncertainties remain, however, since the full data have not yet been assessed by regulators nor have peer-reviewed manuscripts yet been published. It is estimated that about 60% of the world population must be vaccinated for the control of virus from spreading (herd immunity).

## XII. DISCUSSION

Ecology is changing; the spillover of viruses from natural hosts to humans continues to be escalating. SARS-CoV, MERS-CoV, H5N1, H7N9, Ebola, and emerging SAR-CoV2, highly lethal viruses should be alarming to the world. We should strive to reduce the probability of invisible viruses' devastating effects on human beings.

Comparability between Spanish Flu and Covid 19: Both diseases share animal hosting before infecting human hosts. Spanish flu virus genes suggested the deadliest wave of the outbreak came from a bird, while health experts suspect an animal hosted the COVID-19, although definite animal host has not been identified. There is an apparent dangerous mutation of both of these pathogens before transferring to

humans. The infection rate of these viruses is another similarity as they are very rapid to spread. Spanish flu infected an estimated 1/3 of the global population and COVID 19 is everywhere on the globe. Assuming the high mortality, we are going through for COVID 19, the death rate is estimated for Spanish flu is greater than 2.5%. The mortality rate may be similar for the Coronavirus but the true case fatality rate remains to be determined based on new information but according to JAMA study published in February, the CFR is 2.3%, which is almost the same to Spanish flu rate.

They may vary in many ways. Historic timing is the most important difference between the two pathogen diseases outbreak. Spanish flu is the mother of the pandemic because it coincided with World War 1, which spread the disease so quickly. Overcrowded army camps and hospitals made the flu more epidemic and people's focus was on war efforts mainly. In contrast, for Covid 19 many nations have travel restrictions and in lock downstate. National Geographic survey suggested that the Spanish flu wiped out the victims very rapidly, although Covid 19 takes a longer time.

The impact of Spanish flu can still be seen, as nearly all the human cases of influenza A are the descendants of it. But Covid 19 is so new that much information is yet to be discovered. During the current century, we benefit from modern resuscitation techniques and the treatment necessary to treat the complications of the disease while in the 20th century; scientific knowledge is not as advanced as today. Spanish flu was found to be more deadly for younger age groups. By contrast, coronavirus is more threatening to different age groups especially elderly and with co-morbid medical conditions.

The COVID-19 pandemic continues. During this, significant progress has been made in virus monitoring, its basic etiology, clinical treatment, drug testing, and efforts of the development of a vaccine. Chinese efforts and contributions from other countries in the world, we believe that this outbreak will subside soon with their occurrence and all the harms.

### XIII. CONCLUSION

Despite the cruel scale of the Spanish flu as it killed more people in 24 weeks than HIV killed in 24 years. There were several outbreaks in decades like SARS in 2003, H1N1 in 2009, and now this Covid-19 era. The WHO asserts that the pandemic can be controlled.

The outbreak duration is uncertain and varies by location. With the strengthening of investigation of animal etiology, the storage of virulent pathogens normalization, reduction of wildlife contact, balancing the barriers between natural reservoirs, and human society will help to control these horrible events in the future. We have learned a lot of lessons from past outbreaks, that we can do competent monitoring and better prepared for the current situation. But meanwhile, we should beware of the subsequent latter waves of this current outbreak as happened with Spanish flu.

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