

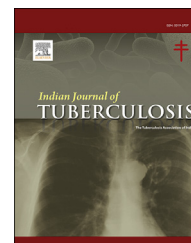


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Review Article

Lessons to be learnt from 100 year old 1918 influenza pandemic viz a viz 2019 corona pandemic with an eye on NTEP

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ABSTRACT

The article is about the 1918 H1N1 flu pandemic also called the “Spanish flu” which killed 50 million plus people worldwide, and the coronavirus pandemic (Covid-19) which has spread in the world at an alarming pace. As of now there are 11,327,790 cases and 532,340 deaths globally. Aim of this article is to draw conclusions and share knowledge from both the pandemics and apply these lessons in other health programmes.

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1. Introduction

The 100-year anniversary of the 1918 pandemic/10-year anniversary of the 2009 H1N1 pandemic are milestones that provide an opportunity to reflect on the vast work that lead to the discovery of sequencing and reconstruction of the 1918 pandemic flu virus. The effort has helped the public health community to prepare for pandemics, like 2009 H1N1, and future pandemic threats.¹ The 1918 H1N1 flu pandemic also called the “Spanish flu,” killed 50 million plus people worldwide, and almost 675,000 people in the United States. More than half of the world's population had been infected. Examining the 1918 influenza pandemic is an opportunity to

consider the current corona virus (SARS CoV-2 or COVID-19) crisis from a different perspective, and draw conclusions for other health programmes like NTEP so that the country is better prepared to deal with such situations in the future.

Corona virus is the first pandemic of this scope where we have known the exact pathogen (complete genome) and the place of its origin from the very start. With social distancing in place, herd immunity building and collaborative work underway to develop treatments and a vaccine. It can be followed by an economic recession like that seen in 1929, as sharp decline in working hours globally due to the COVID-19 outbreak means that 1.6 billion workers stand in immediate danger of having their livelihoods destroyed, warns the International Labor Organization.²

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1.1. Influenza and corona virus

The influenza virus are RNA viruses of the genus Orthomyxoviridae which circulate in humans in yearly epidemics and antigenically novel virus strains emerge sporadically as pandemic viruses^{3,4}—3 waves of Spanish Influenza of 1918–1919 killed more than 50 million people worldwide over the course of two to four years. Origin of the 1918 influenza pandemic is unknown. Spain was the first country to publicly report on the health crisis and Spanish Influenza became a popular term. Spain was an unlikely candidate as some suggested, it originated in Kansas in the spring of 1918.⁵ As per records, influenza pandemics have occurred regularly every 30–40 years since the 16th century.

Similarly the initiation of Covid-19 was also abrupt. On December 31, 2019, hospitals in Wuhan, Hubei province, China reported a cluster of cases suffering from pneumonia of unknown cause. A new variant of corona virus was identified after 2 weeks, which was named 'severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). On January 30, 2020, the World Health Organization declared the outbreak to be a Public Health Emergency of International Concern.^{6,7} On 11th March, it was declared a pandemic as it had spread to 113 countries.

Corona virus are a family of viruses that can cause respiratory infections ranging from common cold to more severe conditions like MERS (Middle East respiratory syndrome/ SARS. In terms of fatality, though the case fatality rate of SARS-CoV-2 is 3.44%, lower than MERS-CoV (34.4%) and SARS-CoV (9.19%). Statistical models on the spread of SARS-CoV-2 suggested that, due to lack of herd immunity in the population and high contagiousness of the virus, 40–70% of the population can be infected unless strong containment measures are timely taken.^{6,8,9}

1.2. The virus can affect the front line staff (HCWs) due to lack of understanding

Due to limited knowledge regarding Influenza impact, infection control actions, effective treatment and prevention methods were not fully utilized.¹ As per an article from US, the number of influenza patients that needed physicians attention during the influenza pandemic overwhelmed St. Paul and Minneapolis clinicians. Due to the war, movement of medical personnel was affected. Another challenge was to keep the staff healthy while taking care of patients. This was observed during the Covid 19 pandemic also whereby many ground level staff and physicians contracted the disease. During that period too, many health-care providers fell ill, and some died.

Spanish flu	Corona
50 million people died	532,340 (till date)
Etiology was not known during 1918	Known Etiology
Originated in US	Originated in China
Lack of information	Excess of information due to multimedia
Vaccine developed at a later stage	Vaccine still not developed

A Minneapolis's City Hospital reported that "nearly half of the nursing staff had influenza symptoms in a period of 3 weeks.^{5,10} 2 major hospitals in the US were solely devoted to treating influenza patients. Non-influenza patients were transferred to other hospitals.¹¹ Covid-19 is the greatest challenge humanity has faced since World War Two. The virus has spread to every continent and cases are rising daily. Countries are racing to slow the spread of the virus via testing/ treating patients, contact tracing, limiting travel, quarantining citizens, and avoiding large gatherings Medical masks and respirators like N95, FFP2 are being recommended for health care workers while giving care to patients.^{5,12}

COVID-19 Global Pandemic

"The pandemic is accelerating. It took 67 days from the first reported case to reach the first 100,000 cases, 11 days for the second 100,000 cases, and just 4 days for the third 100,000 cases. You can see how the virus is accelerating" - Tedros Adhanom Ghebreyesus, Director General, WHO

World Health Organization. Director-General's opening remarks at the media briefing on COVID-19 .

1.3. Confusion regarding the mutation of organism and guidelines for prevention

In 1918, physician claimed that influenza was bacterial in origin. Physicians claimed "bacillus influenza of Pfeiffer," which is today known as Haemophilus influenza, was the cause of Spanish Influenza. Despite this lack of understanding about viruses, advice to curb infection was quite accurate. The Minnesota State Board of Health (US) recommended the use of handkerchiefs to cover sneezes and coughs, plenty of fresh air, avoidance of the sick and of crowds, and to contact a physician if ill.^{4,13,14}

Influenza A viruses have the unique ability to evolve by the mechanisms of antigenic drift and shift. They should be considered emerging infectious disease agents Importance of predicting the emerging new virus strains for annual vaccine development is equally important.

Pandemic influenza viruses have emerged three times:

- ✓ 1918 (Spanish" influenza, H1N1)
- ✓ 1957 (Asian" influenza, H2N2), and in 1968
- ✓ Aavian H5N1 viruses in Asia from 1997 to 2004

How/when influenza viruses emerge as pandemic virus strains and how they cause disease is still not understood.⁴

For Covid-19 control measures applied at the time of SARS are no longer adequate in these days, and more vigorous actions are required. Moreover, during SARS viral shedding peaks only when the patient's illness is advanced and respiratory symptoms occur, but in case of SARS-CoV-2, transmission can occur in the early phase of the illness, when the patients are asymptomatic (40%). Spread in case off Covid-19 is wider due to urbanization and increase in international travel during the last two decades. Hence, isolation after the onset of symptoms and temperature screening might be

ineffective in preventing virus transmission. SARS-CoV-2 has been proven to hold higher transmissibility and wider community spread when compared with other betacoronaviridae. Severity of SARS-CoV-2 is much less when compared to SARS.^{6,8,15–17}

1.4. Steps taken for disease containment

Confusion prevailed during Influenza pandemic, whether to isolate the cases or not, -An article¹ stated that a closing order was introduced for the whole city in the same way as with Covid -19 pandemic. A 15 member Committee recommended this policy change. The number of new cases began to decline after 10 days¹.

Measures taken were as follows

- ✓ limiting crowding in places with restricted access to fresh air
- ✓ Street car regulations aimed to keep the air in the street cars fresh by mandating open windows and limiting the number of passengers to 84 (streetcars had a seating capacity of 46).^{5,18,19}
- ✓ Regulating business hours of stores/theaters to keep street car congestion to a minimum.⁵
- ✓ Buildings with less than six stories were no longer permitted to use their elevators. The hospitality/hotel industry was affected. Later the authorities started operating the elevators although only one person per 5 square feet was permitted.

During the present time various businesses have been affected due to the Covid 19 pandemic. Worst affected are the tourism/airline/hospitality industry etc. As per the protocols of Covid -19 a patient with mild symptoms like muscle aches, cough, sore throat/fatigue, should be isolated at home and use a medical mask.¹³ WHO suggested measures like frequent hand washing with an alcohol-based hand rub/soap and water, avoiding touching eyes, nose, and mouth, and practicing respiratory hygiene, use of face masks for personnel.

1.5. Public response to disease containment

Measures implemented to contain 1918 Pandemic affected the day-to-day lives of citizens. Closure of public places in Minneapolis was announced in advance, so people rushed to complete those activities that would soon be banned, resulting in the very same crowded conditions the ban wanted to prevent. Similar sequence of events followed during the covid-19 pandemic. Various businesses struggled to pay their the ground level staff/employees. This was seen in the Covid epidemic also.

Disease Notification Era: Isolation and surveillance along with official's apathy.

All influenza cases in 1918 were to be reported to a physician, who in turn had to isolate the case in his/her home and notify the health department. Various issues came up. Physicians as well as the patients were hesitant to bring attention to cases. The physicians were not reporting the cases to prevent homes from being quarantined. Symptomatic cases wanted to escape isolation by not

seeking medical attention/seeking medical attention when they became very ill. They did not approach the health authorities for many days and many cases developed pneumonia. During Covid 19 pandemic also, people were hesitant to approach the health authorities due to the fear of being quarantined. Due to shortage of inspectors, houses were not released promptly from isolation.

As per an article¹ telephone operators went on strike due to which reporting of cases, isolation, as well as their release from such a measure were affected.⁸

1.6. Fear and discrimination

People in the 1918 pandemic did not approach the health authorities for many days and many cases developed pneumonia (cut and paste elsewhere).

Physicians/Nurses who fell ill and even died as a result of assisting in the fight against the pandemic scared other nurses and physicians away.

As per the article linking a disease with the name of a foreign/minority community is closely related to the desire to separate those who are viewed as threats of contagion.

During this process Air travel bans are implemented for disease control. Xenophobia, helps to explain the call for travel bans. As per the article air travel plays a less important role in the spread of pandemics than is commonly believed.

The fear a pandemic affects the population more than public health responses. It affects how physicians and other health care workers respond during an emergency. Similarly With the spread of corona virus has come a wave of anti-Asian backlash in cities across the globe, driven in part by the fact that the illness emerged in the Chinese city of Wuhan and swept through the Chinese population first.^{6,8}

1.7. Case fatality due to co-morbidities

Studies show that the 1918 virus could spread to other tissues beyond the respiratory tract, resulting in more widespread damage. Moreover the virus had mutations that allowed it to be more easily transmitted between humans. Unlike in 1918, scientists today can evaluate the pandemic potential of new viruses, both in animals and humans.²⁰

In 1918, people suffering from malnutrition and other conditions, like tuberculosis were more likely to die from the infection. Future pandemics will also face the challenge of diabetes, obesity, etc which increases the risk of dying from influenza.

Young adults were the most affected groups during the influenza pandemic. Researchers thought that the elderly were spared due to previous exposure to other viruses, giving them immunity to the 1918 viral strains. However, given that seasonal flu typically kills the very old, today's aging population will be another challenge in future pandemics.

Researchers reported that banning public gatherings/hand washing helped to reduce levels of infection and death during the 1918 pandemic but only if they were applied early and for the entire duration of the pandemic.

1.8. Infection control and vaccination

In 1918, the use of gauze masks, more stringent sanitation laws, and vaccination campaigns were deployed. Directions for wearing the masks were issued to the public. An acute shortage of masks was observed.²¹ Fabric masks were used by the public as seen in the present pandemic. Sanitation laws were introduced that called for the sterilization of dishes and cups in restaurants, bars and the banning of roller towels and common drinking cups in public restrooms.

In the US two vaccines were administered, and neither of them were effective as neither contained influenza virus. One made by bacteriologists at the University of Minnesota was to prevent pneumonia. The Mayo Clinic in Rochester, Minnesota, made another vaccine to prevent pneumonia and influenza. This latter vaccination was composed of *Streptococcus pneumoniae* types I, II, and III, *S. pneumoniae* group IV, hemolytic streptococci, *Staphylococcus aureus*, and “influenza bacillus.”

1.8.1. Influenza vaccine

In 1935, Sir Frank Macfarlane Burnet (1899–1985) and Smith individually discovered that the flu virus could be grown on the chorio-allantoid membrane of embryonated hens eggs. In 1936 the first neutralized antibodies generated by infection by human influenza virus were isolated. In the next few years it was demonstrated that the virus inactivated by formalin was immunogenic in humans, purification of the virus by means of high-speed centrifugation and influenza virus grew easily in fertilized hen eggs.

According to researchers, providing emergency vaccines during future pandemics should take in account different age groups, viral and host factors.

1.9. Importance of IEC in a pandemic

A health education campaign was conducted in (US) involving school teachers (who were out of jobs), Postal workers and Boy Scouts. Similar efforts are being seen during the Covid-19 pandemic. Mass media and digital platforms are playing a major role in disseminating the information about spread and prevention of the flu.

1.10. Stigmatization/disinformation/infodemic: epidemic of wrong information

The Covid outbreak was first identified in the Chinese city of Wuhan, so it was labeled as Chinese virus. Stigmatizing a group/nation for its responsibility in a calamity is not a new trend. Spanish Flu -The Spanish press covered the spread of the virus, creating incorrect assumptions that the epidemic originated in Spain. Rumors spread wrong information about the origin of the disease. During the war time in 1918, all sides accused one another of being responsible for the epidemic. Accusations were made against German pharmaceutical company Bayer of having deliberately introduced the pathogen into aspirin tablets. War censorship/propaganda also had adverse effects on efforts to mitigate the pandemic. After years of war propaganda, some of the population no longer

believed in government's health policies. Clear information is crucial at all times. To implement public health measures, population needs to trust the authorities. After four years of conflict/propaganda, trust was broken. What was true then is even more so in 2020. Recent development of digital social networks makes it even harder.

1.11. Pandemic and conflict: inextricably intertwined

No evidence suggests that the First World War led to the outbreak of the H1N1 virus. Switzerland and the US were affected even though no fighting took place on their territory. Due to underdeveloped health systems various countries suffered. Like the present COVID-19 pandemic, the 1918–1919 influenza spread without distinction and did not spare heads of state. Both developed as well as developing countries have been affected by Covid-19.

War played a major role during the influenza pandemic. Factors like gathering of men, circulation of troops, the mobilization/demobilization of soldiers, crowded barracks, internment camps, and meetings related to war propaganda created a favorable environment for a pandemic. Bad decisions were made, like avoiding quarantine and travel bans for military advances. The absence of skilled manpower further contributed to increased mortality. The pandemic further compounded the effects of destroyed infrastructure, poor sanitation, famine, overcrowding, or other infectious diseases such as typhus, tuberculosis. As per ICRC,²² the Covid -19 is an additional threat in war-affected countries, in places where factors like unhygienic conditions, weak medical infrastructures, and displaced people in camps are present.

2. Conclusions

Prior planning could have made a significant difference in the number of cases and deaths due to influenza in 1918. There was no planning for the 1918 pandemic though various current recommendations were implemented, like use of masks, the use of vaccines, increased sanitation measures, limiting crowding and trying to coordinate hospitals, nurses, physicians, and medical students to maximize resources. Disagreements between various agencies could have been discussed in advance. Supplies could have been stockpiled, business leaders/community members could have provided input on controversial disease containment policies, and medical students could have been put to work in hospitals and communities that lacked physicians. These disputes arose and continued throughout the pandemic. To maximize human resources during an influenza pandemic, it is important that the safety of health-care workers should be ensured. **Orders** were not being given clearly to public health officials; the public in turn was not receiving transparent and consistent advice and information. The public had to decide for itself. So, the effect of the messages that were communicated served to contradict each other. **Isolation:** Clear explanations of the reason for isolation, employer support, and providing food, medicine/social service to those in isolation may mitigate fears and increase cooperation. During the Covid 19 pandemic, ILO and UNICEF are calling on governments to

support employers and strengthen social protection, Family-friendly policies and practices, including employment and income protection, flexible working arrangements, paid leave to care for family members and access to quality, emergency childcare.² **Transparent information to the Public:** Public must be educated about the reasoning behind other health measures (i.e., closures), should those methods be implemented.⁸ Today in spite of having high end technology it remains ineffective in preventing influenza. Other factors like poverty, limited access to healthcare, cultural barriers support the rapid spread of infectious diseases. It was believed that the borders of a nation can be sealed during pandemics which would prevent the infection. Health experts reject this approach. A public health event in any part of the world can create a public health threat everywhere. Airplane travel facilitates the rapid spread of pathogens, and even communication technology enables the spread of fear and misinformation. Public health capacity building and disaster preparedness are the key elements which have to be strengthened and refined for preventing epidemics. Another area of concern is the circulation of unreliable news on digital platforms which may prove dangerous during any epidemic. At this juncture the role of governments is to remove these misconceptions and provide correct information.

2.1. *Lessons learned, lessons still to learn*

Consequences of 1918 Pandemic were political, social, economic and emotional. The viruses of 1957, 1968, and 2009 are descendants of the H1N1 virus that caused the 1918 pandemic. Similarly Covid-19 has the potential to create devastating social, economic and political crises for a long period of time.

Influenza pandemic led to enormous improvements in public health. Strategies, like Health education, Isolation, Sanitation, and Surveillance were adopted which further led to improvement in knowledge regarding transmission and are still being implemented. The influenza Pandemic led to creation of health ministries in France and Great Britain, Role of medical staff was majorly recognized.

Wars weaken the ability of a country to prevent, detect, or fight outbreaks of infectious disease, and leave the population incredibly vulnerable. Though, the COVID-19 outbreak did not originate in a country at war; but its impact is disastrous wherever there are armed conflicts or other situations of violence. Since the 'Spanish Flu', medical advances have been tremendous. COVID-19 pathogen was quickly identified and sequenced. Researchers around the globe are working to understand its mechanism and find effective therapies.

2.2. *Lessons we can learn from the past*

- The Spanish flu did not originate in Spain, but got its start at a military base in Fort Riley, Kansas. Conclusions have been drawn on the same lines like "Wuhan flu" and "Chinese flu" to describe Corona virus. Social distancing: Just like in 1918, in 2020, travel spread the virus. In 1918 the reason it was so deadly and passed quickly across the world was that it took place during war time unlike today. Without latest technologies, researchers then, wrongly assumed it was bacterial, and efforts to treat it/vaccinate

against it failed. With no other interventions the cities had to be closed down. Isolation was strictly followed and is of high significance till date. The influenza epidemic was most likely to hit the young and healthy. In contrast to this the coronavirus is targeting older populations and the immune-compromised. Its behavior in the young and healthy is very much similar to that of the virus a century ago. Recent news reports point to immune responses called "cytokine storms" as a likely cause of the collateral damage occurring in younger patients. Inoculation/Early plasma therapy: During smallpox epidemic (North America 1775–1782), war soldiers took an unusual approach to protecting themselves from Variola major. Virus-loaded material from an infected person's smallpox pustule (Variolation) was taken, and they carved an incision into the flesh of a healthy soldier, and rubbed it in. It worked. Today researchers are exploring the idea of using "convalescent plasma" from healed patients as a treatment for serious cases not responding to any other therapy. During the influenza pandemic, mortality ranged from five to twenty times higher than normal. This was as a result of severe infections of the respiratory tract. Waves of influenza activity followed on each other unusually rapidly, resulting in three major outbreaks within a year's time. Each of these unique characteristics may find its explanation in genetic features of the 1918 virus. The challenge will be in determining the links between the biological capabilities of the virus and the known history of the pandemic.⁴ We can expect a second wave or perhaps a third wave of the SARS CoV-2 virus pandemic in the winter/autumn. Till the time a broadly protective vaccine is available, all governments must inform the public on what to expect and how to act during a pandemic "

2.3. *Lessons to be learnt from NTEP and other public health programmes in place*

In a study, a reduced risk of infection for unvaccinated badger pups, was observed suggesting a herd immunity effect. The article also suggested that BCG protects against development of lesions and other disease parameters. There are indications that BCG-induced immunity can lead to bacillary clearance, for natural-transmission settings. Another article quotes that The combination of LTBI treatment and BCG vaccination could target high risk populations like mine workers potentially creating herd immunity.^{25,26}

In case the Tuberculosis and HIV becomes a public health emergency of national concern, following measures may be adopted considering the lessons learnt from the Spanish flu epidemic and the current Covid-19 epidemic

In the event of a public health emergency, TB programs can help to mitigate potential shifts in staff assignments and resources.²³

According to CDC the following measures may be adopted

Contact information for patients is updated, and staff contacts the patients telephonically. Communicate any changes or updates in service to community partners.

Providing additional medications to patients, if health department operations are likely to be affected. If policies and procedures are in place, consider alternative treatment delivery methods, such as **electronic directly observed therapy (e DOT)**. A Module on management of TB patients during Epidemics/pandemics may be compiled by the NTEP programme so that the staff can be accordingly trained. As per an article, A plan is needed which is ahead of time and which incorporates clear lines of responsibilities and roles. Plans for surge capacity/community containment must be discussed with stakeholders and consensus must be achieved. Clear responsibilities may be assigned to all the NTEP staff. NTEP has to ensure that there are sufficient CBNAAT/TruNat machines at all the centers to handle a situation in case an epidemic strikes. The programme also has to ensure that there are spare machines available to handle the high load of patients. The programme has to ensure all reports are being entered on the Nikshay portal which is happening currently. Integrated digital adherence technologies (IDAT) like MERM box, 99 DOTS may be adopted in the programme. Drugs dispensing systems may be made simpler by issuing monthly drugs to patients as is happening now. Other interventions, like getting in touch with patients telephonically to counsel the patients, use of telemedicine/videoconferencing for monitoring of adherence and side effects and time to time training of staff to handle patients during epidemics would prove beneficial. According to an article by WHO²⁴ all measures should be taken to ensure continuity of services for people who need preventive and curative treatment for TB. Health authorities should continue to maintain support for essential TB services, during emergencies like COVID-19.

3. Future of coronavirus

The Covid-19 Pandemic started in the month of December 2019 and presently there are **11,327,790 confirmed** cases in the world till date. Almost **532,340** people have lost their lives. Since the last 7 months the world has an ample of experience in studying the disease/handling the cases. Earlier Hydroxychloroquin was being used for prophylaxis but now evidence has shown that new antiviral, steroids and anticoagulants can substantially decrease the mortality. All countries including India are testing the vaccine and with each passing day new knowledge regarding the disease is emerging. With these new developments and the experience of handling the disease the pandemic can be controlled in the near future. Abbott have recently launched a new inactivated quadrivalent vaccine for influenza, the first of its kind sub-unit vaccine offering protection against four virus strains, in India. It is the only 0.5 ml quadrivalent flu vaccine in India that has been approved for use in children below 3 years²⁷.

Conflicts of interest

The authors have none to declare.

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