VOLUME - 9, ISSUE - 12, DECEMBER - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Medical Science

INFLUENZA : A COMPLETE OVERVIEW

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KEYWORDS :

THE BACKGROUND

Origin of disease /outbreak :

- At first haemophilus influenza was considered as the causative agent for influenza but after the research it has been found that it caused various other types of infections but not influenza. Influenza was caused by some flu virus which was first isolated from pigs in 1931 and from humans in 1933.[4]
- The 1918 influenza pandemic was the most severe pandemic in recent history it was caused by an H1N1 virus with the genes of avian origin although there is not universal consensus regarding where the virus originated it spread worldwide during 1918 and 1919. [3]
- It was first identified in military personnel in spring 1980 it is estimated that about 500 million people or one third of the world's population became infected with this virus.[3]
- The number of deaths was estimated to be at least 50 million worldwide with about 6,75,000 deaths occurring in the United States. [3]
- Mortality was high in people younger than five years old ,20 to 40 years old and in 65 years and older. The high mortality in healthy people including those in the 20 to 40 year age group was a unique feature of this pandemic. [3]
- There was no vaccine to protect against influenza infection and no antibiotics to treat secondary bacterial infections that can be associated with influenza infection control efforts worldwide were limited to non-pharmaceutical intervention such as isolation quarantine good personal hygiene use of disinfectants and limitations of public gathering which were applied unevenly.[3]
- In the northern and southern parts of the world outbreaks occur mainly in the winter while around the equator outbreaks may occur at any time of the year .In the northern and southern parts of the world outbreaks occur mainly in the winter while around the equator outbreaks may occur at any time of the year.[7]
- In the 20th century three influenza pandemics occurred Spanish influenza in 1918 where the death toll ranged from 17- 200 million deaths, Asian influenza in 1957- 2 million deaths and Hong Kong influenza in 1968 -1 million deaths.
- The world health organisation declared an outbreak of a new type of influenza A or H1N1 to be a pandemic in June 2009.
- influenza may also affect other animals including pig horses and birds.[9]
- The name "influenza" originated in 15th century Italy, from an epidemic attributed to "influence of the stars." The first pandemic that fits the description of influenza was in1580. At least four pandemics of influenza occurred in the 19th century, and three occurred in the 20th century. The pandemic of "Spanish" influenza in 1918–1919 caused an estimated 21 million deaths worldwide. The first pandemic of the 21st century occurred in 2009–2010. Historically, influenza viruses of three HA subtypes (H1, H2 and H3) have acquired the ability to be transmitted efficiently between humans. Currently, influenza viruses of the H1 and H3 subtype co-circulate in humans, however influenza viruses of the H2, H5, H6, H7 and H9 subtype are also considered to represent a pandemic threat. In 1997, a large outbreak of highly pathogenic avian influenza (HPAI) H5N1 virus in poultry in Hong Kong resulted in the first documented cases of direct transmission of HPAI H5N1 virus from poultry to humans, with a fatal outcome in 6 out of 18 cases [17]. As a result, this outbreak warranted the mass culling of 1.5 million chickens. In 2003, a large outbreak of an HPAI H7N7 virus in poultry in the Netherlands resulted in 89 cases of human infections, one of which was fatal [21]. HPAI H7N7 virus displayed an unusual tissue tropism; the virus targeted the conjunctiva, resulting in conjunctivitis, a symptom rarely reported for other influenza virus subtypes.[1]

Important viral properties:

A. Influenza is considered one of the most infectious diseases which is highly contagious airborne disease that occurs in seasonal epidemic and manifests as an acute febrile illness with various degrees of systemic symptoms ranging from mild fatigue to respective period ended influence or cause a significant loss of workdays human suffering and mortality .

B. Waterfowl are important reservoirs for many influenza subtypes. In mammals influenza is transmitted through the air by coughing and sneezing, by direct contact with nasal discharges or contaminated objects.

C. Inside the virus the genetic material contains the information to make more copies of the same virus. A protein shell provides a hard protective enclosure for the genetic material as the viral travels between the people or the animals it infects.

D. Outer envelope allows the virus to infect cells by merging with the cell's outer membrane. Projecting from the envelope are spikes of protein molecules. The flu virus uses its h spikes like a key to get inside your cells. N spikes allow copies of the virus to break away from the infected cells to infect more cells. 17 known types of H spikes and nine known types of N Spikes scientists used to name different types of flu viruses such as the virus H5N1 you get the few by touching an object that has the flu virus on it or through exposure to the body fluids from people or animals infected from the virus.[5]

E. Once it has entered the body the influenza virus comes into contact with cells in your nose throat or lungs and causes it infection by infecting the cells .

F. The H spike on the virus inserts into a receptor molecule on your cell membrane like a key in a lock. This action allows the virus to get inside your cell. And the N spike help release the virus from the infected cell and move freely in the body and go and infect new other healthy cells.

G. Due to multiple different types of H and N spikes in the virus structure the development of vaccine and treatment against these viruses is very rudimentary.

H. Continuous ability of viruses to get mutated and develop more abilities to infect human cells has caused an increasing concern against these viruses.[2]

I. One of the best-known virulence determinants of HPAI viruses is the multi basic cleavage site (MBCS) in HA.

Human influenza viruses harbours a monobasic cleavage site that is cleaved by trypsin-like proteases. These trypsin-like proteases are only present in the respiratory tract of humans and the respiratory and/or intestinal tract of birds, thereby restricting virus replication to these tissue.[1]

Epidemiological data on influenza:

I) A type - infect birds and humans and cause pandemics
II) B & C types - infect only humans

- Estimates suggest that the world population in 1918 was 1.8 billion. Based on this, the low estimate of 17.4 million deaths by Spreeuwenberg et al. (2018) implies that the Spanish flu killed almost 1% (0.95%) of the world population.[1]
- From April 12, 2009 to April 10, 2010, CDC estimated there were 60.8 million cases (range: 43.3-89.3 million), 274,304 hospitalizations (range: 195,086-402,719), and 12,469 deaths (range: 8868-18,306) in the United States due to the (H1N1)pdm09 virus.[1]

History :

- The word influenza comes from the Italian language meaning influence and refers to the cause of disease initially this ascribed illness to unfavourable astrological influences. It was introduced into English in the mid-18th century during a pan-European epidemic . archaic term for influenza include epidemic catarrh, la grippe (from the French in first used in 1694; also used in German), sweating sickness and Spanish fever(particularly for the 1918 flu pandemic strain.[8]

Impact of outbreak in population:

- 1917 the United States entered World War I. US life expectancy is 54 years of age for women and 48 for men.[10]
- In 1918 Spring and fall waves of influenza that is flu activity caused the average life expectancy in the United States to fall by 12 years.[10]
- In 1919 a third wave of pandemic flu activity occurred and pandemic subsides but virus H1N1 continued to circulate seasonally for 38 years.[10]
- In 1930 isolation of influenza proving that flu is caused by a virus is not a bacteria .[10]
- In 1957 H2N2 flu virus emerged to trigger a pandemic replacing the 1918 H1N1 virus..[10]
- In 1960 the US public health service recommend annual flu vaccine for people at higher risk of serious flu complications.[10]
- 1960 H3N2 flu virus emerges to trigger a pandemic replacing H2N2 virus.[10]
- In 2005 the genome of 1918 pandemic flu virus was fully sequenced..[10]
- In 2009 H1 N1 virus distantly related to 1918 virus emerged to trigger a pandemic.[10]
- The US Centres for CDC documented that seasonal influenza was responsible for 34,400 to 57,300 deaths during the 2018-19 season mortality is highest in infants and elderly patients.[10]
- In the 20th century three influenza pandemics occurred Spanish influenza in 1918 where the death toll ranged from 17- 200 million deaths, Asian influenza in 1957- 2 million deaths and Hong Kong influenza in 1968 -1 million deaths.[10j]
- The world health organisation declared an outbreak of a new type of influenza A or H1N1 to be a pandemic in June 2009.[10]

- **So overall:**

1. Behavioural changes with less commuting of people.
2. Economic crisis due to mortality and morbidity of populations.
3. Increased investment in the health industry and restructuring of health institutions[1]

Impact in low and middle income countries:

- when the epidemics or pandemics hit they usually hit the poor first and worst.
- Pandemics such as influenza hit the worst of the low income population because of their economic structures which make outbreak prevention impossible.[1]
- As we note the effects of 1918 flu pandemic in India it was the outbreak of an unusual deadly influenza pandemic in India between 1918 and 1920 as a part of worldwide Spanish flu pandemic also referred to as the Bombay influenza or the Bombay fever in India.[11]
- The pandemic is believed to have killed up to 14 to 17,000,000 people in the country, the most among all countries . David Arnold estimated at least 12 million dead about 5% of the population; in India the decade between 1911 and 1921 was the only sentence period in which India's population fell most due to the devastating situation of theSpanish flu pandemic. The death toll in India's British rule districts was 13.88 million in India. The pandemic broke out in Bombay in June 1918 with one of the possible routes being via ships carrying troops returning from the first world war from Europe .The outbreak was spread across the country from west and south to east and north reaching the whole of the country. [11]
- The pandemic has a significant influence in the freedom movement in the country . The healthcare system in the country was unable to meet the sudden increase in the demand of medical attention; the consequent toll of death and misery and economic fallout brought about by the pandemic led to an increase in emotion against colonial rule in India.[11]

SUCCESSES AND FAILURES

FAILURES:

- All influenza cases were supposed to be reported to a physician, who in turn was required to isolate the case in his or her own home and notify the health department. Several problems sprung up with these requirements that hampered surveillance, the care of patients and protecting people from getting sick. For one, physicians were not reporting their cases to prevent homes from being quarantined.[13]
- The ill sought to evade isolations in their homes by not seeking medical attention, or only seeking medical attention when they became gravely ill, and in many cases, pneumonia had already developed when treatment is first given.[13][17]
- The limited scientific knowledge negatively impacted on the infection control actions, effective treatment and prevention methods were not fully utilized.[14]
- The World War 1 led to a considerable drain on the medical profession, many health care providers fell ill and some died. This meant that there were more infection but this staff to treat them was very limited.[16]
- The government would give warnings of the public to stay indoors to counter the further spread of the illness but did not heed to the measures.[13][15]
- During the 1918 influenza pandemic, symptoms of the illness were so unusual that the influenza cases were misdiagnosed as dengue, cholera or typhoid. With the misdiagnosis came very many infections due to quick and further spread of the influenza virus.[23]

SUCCESSES:

- Non-medical interventions such as isolation and cutting a community from the outside world did work if done early enough. This measure failed when and where these measures were carelessly applied but did some good when they were rigidly carried$_{out.}$(14)(15)
- Developing new vaccines and sera that were later studied

and d were considered to have prophylactic value but not therapeutic value was major success during the past pandemics.[14]

- During the last influenza pandemic occurred which is in 2009.On5 October the same year, the first monovalent H1N1 pandemic vaccine was administered. The vaccine also proved to be a major success to ending the pandemic.[24]

Influenza pandemics have occurred regularly every 30 to 40 years since the 16th century. Today influenza experts consider the possibility of another influenza pandemic, not in terms of if but when.[25]

The World Health Organization and international experts believe that an influenza pandemic may occur any time sooner that we may ever think. The highly pathogenic H5N1 avian influenza virus which has been circulating in poultry in parts of Asia since mid-2003has infected more than 200 humans in 10 countries but remains primarily a disease of birds. Should the virus acquire an ability to spread efficiently and sustainably among human, a pandemic is expected to begin.[25]

The involvement of migratory birds in the epidemiology of this disease increases the likelihood of further spread and adds greatly to the complexity of control measures in animals, as elimination of the virus in wild birds is universally considered to be impossible[25]. Neither the timing nor the severity of the next pandemic can be predicted with any certainty. At the same time however, the present threat to international public health is sufficiently serious to call for emergency actions calculated to provide the greatest level of protection and preparedness as quickly as possible.[25]

SWOT ANALYSIS:

It is the source of information which helps us in building strengths and reversing weaknesses. It maximizes firms response to opportunity and identifies the core competencies. It is an important part of the strategic planning process because it helps us to focus on the key issues that we must pay attention to and strengths identified through SWOT analysis can be used as the cornerstones of strategy and the basis on which to build competitive advantage.

ROOT CAUSE ANALYSIS:

The following causes played a major role in the failures associated with ineffective management of the influenza pandemics over the years;

- **Misdiagnosing the disease**

When a pandemic occurs, the trend seen is that the disease occurs in waves. In some disease waves the people infected present with mild symptoms while in another wave people exhibit severe symptoms. This poses a challenge as the health personnel are not sure if they are dealing with the same disease[23]

In the 1918 pandemic people presented with unusual symptoms that could be mistaken for Dengue, Cholera or Typhoid.[23] In addition, victims who succumbed to death at autopsy showed lung characteristics that were very unfamiliar to the pathologists.[22]

- **Spread of infection despite measures put in place**

Despite the government putting up measures like isolation and quarantining of infected people to help curb the spread of the pandemics it was still noted that the disease managed to cross borders between cities. This is attributed to the late implementation as well as lack of strictness in the restrictions put in place.

In the 2009 H1N1 pandemic there was a delay by the WHO declaring that there was influenza pandemic impending as the organization felt that the number of human fatalities as well as the severity of the disease did not meet the criteria of making a declaration of a pandemic. This in turn caused a late implementation of restrictions.[21]

- In the 1968 influenza pandemic there were no restrictive measures put in place as that would have brought about negative economic impact

- **Lack of sufficient public health messaging**

In a health emergency situation, it is the role of every individual to protect themselves from getting infected however if the government doesn't relay a true picture of how severe an outbreak is then the people don't accord the matter the seriousness it deserves.

For instance, in 1918 the media and public health officials were forbidden from relaying information to the public that the influenza disease was serious. It was seen that such information would cause fear among people and thus reducing their motivation in participating in world war.[22]In 2009 WHO officials could not agree on whether to declare a pandemic or not and even went to the extent of removing the influenza pandemic guidelines from their website.[20]

- **Inappropriate labelling of the causative agent**

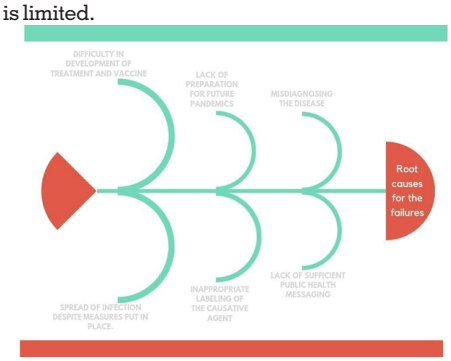
The viruses were initially named after the city the first case was identified and then after the close animal the virus was associated with. Naming the virus after the animal associated with it led to a shift of measures to focus more on the animals rather than humans. An example is the 2009 swine flu which saw culling of pigs in various countries which had devastating effects on the economy.[20]

- **Lack of preparation for future pandemics**

Even though the pattern of influenza viral infections has been studied and can be predicted to certain degree, countries have not equipped themselves with resources to help them fight the pandemic in case it occurred.

- **Difficulty in development of treatment and vaccine**

This is due to constant mutation of the viral proteins. Also, resources available for undertaking molecular biology studies is limited.



INTERVENTION STRATEGIES

1. Reduce human exposure to the virus

The goal of this strategy would be to reduce opportunities for human infections to occur and in so doing, to reduce opportunities for the influenza virus to develop into a form that is readily transmittable to humans. Research is urgently needed to define better the exposure circumstances and behaviours and possible genetic or immunological factors that enhance the likelihood of human infections[25]. To reduce exposure of humans to this virus, the following can be done:

- Improving understanding of the risk factors for human infection[25]
- Ensure that each country affected by outbreaks in poultry has a policy in place supported by appropriate equipment and supplies for protecting defined groups(poultry cullers, veterinarians, health care staff and laboratory workers)considered at high occupational risk exposure to the virus.[25]
- Ensure proper isolation and infection control procedures are followed in hospitals caring for suspected or confirmed cases.[25]

2. Strengthen early warning signs

This would ensure that the affected countries are able to detect and manage cases quickly and an accurate risk assessment in line with the world Health Organizations phases of a pandemic alert[25].to achieves this, these approaches can be used:

- Strengthen the capacity of national and international surveillance systems using existing infrastructures in ways that ensure rapid detection of suspected cases, rapid and reliable laboratory confirmation, rapid and complete reporting the WHO.[25]
- Strengthen mechanism for formal collaboration between human health, animal health and other agricultural sectors. The detection of fresh outbreaks in poultry should trigger heightened vigilance for human cases.[25]
- Routine exchange of information between the veterinary and public health sectors.[25]

3. Intensify rapid containment measures

This ensures rapid detection and investigation of clusters of cases, closely related in time and place, and immediate international intervention aimed at preventing the emergence of a fully transmissible pandemic virus or delaying its international spread[25].This can be done by

- Should assessment indicate that human to human transmission is occurring, intervene immediately, using rapid- response teams and global and regional stockpiles of medications available and supplies[25].
- Quickly ass's situations that potentially signal the start of an efficient and sustained human to human transmission of the virus.[25]

4. Build capacity to cope with a pandemic

This intervention would ensure that all countries have formulated and tested pandemic preparedness plans and identified gaps in core capacities and that THAT is fully able to perform its leadership roles during a pandemic[25].This can be done by:

- Assisting individual countries, particularly those with limited resources in the development plans[25].
- Testing the development plans in individual countries, regions and internationally to identify gaps in core capacities[25].

Based on past experiences, pandemic influenza will not affect all countries or all parts of a country at the same time. If efforts to contain an emerging virus at its source fail, health authorities will at least have some opportunities to intervene to fore stall spread internationally, within a country or an affected community[25].

- wait-and-respond approach is not enough and that the development of systems to prevent novel pandemics *before* they occur should be considered imperative to human health.
- Many studies have highlighted the importance of global travel to spread of pandemic disease. So we need a well developed global surveillance system to tackle this situations and prevent the spread.
- Although global surveillance system is far from reality, some immediate measures can be taken to mitigate risk of transmission.
- In situations where humans and animals are in close contact, behavioural change approaches may be a preventative step to reducing the risk of zoonotic transmission.
- Behavioural modification campaigns can be conducted. Behavioural modification measures may have an enormous impact on curtailing disease emergence and progression in conjunction with other strategies.
- Although it is difficult to predict when and where next pandemic, it will likely due to cross species transmission. This likelihood argues in favour of developing a system specially aimed at detecting the transmission of potentially pathogenic agents from animals to humans early in the zoonotic disease emergence process and identifying ways by which we can diminish the risk of transmission, especially in populations that are highly exposed to animals and their potentially zoonotic agents.
- International organizations such as World Health Organization and Centers for Disease Control and Prevention should have a website that has information on the influenza disease, pandemic. The website should outline the epidemiology, etiology, management, and prevention measures. The information needs to be up to date with emerging issues regarding influenza disease.

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