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AN UPDATE ON INFLUENZA - A DEADLY SEASONAL VIRAL INFECTION

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ABSTRACT

Background: Influenza (Flu) is one of the most common infectious diseases which is a highly contagious airborne disease that occurs in seasonal epidemics and manifests as an acute febrile illness with variable degrees of systemic symptoms, it ranges from mild fatigue to respiratory failure and death. Influenza can be defined as the acute contagious respiratory infection, which is caused by orthomyxoviruses A, B, and C, occurs in local outbreaks, epidemics, and pandemics. Influenza causes severe effects on human mankind, which include significant loss of workdays, human suffering, and mortality. The flu virus can spread from person to person via respiratory secretions. Flu spreads when a person inhales a droplet in the air that contains the flu virus, makes direct contact with respiratory secretions via sharing utensils, or handles items contaminated by an infected person. The flu virus on the skin can infect the person when they touch or rub their eyes, nose, or mouth. Influenza A is virulent, Influenza B is mild, and Influenza C is

nonvirulent. Vaccination is the most effective measure to prevent infections, non-pharmaceutical public health measures like physical distancing, using hand rubs, and sanitizers, and wearing proper masks can also be effective in preventing transmission and allowing suppression or mitigation of influenza pandemics and epidemics. **Conclusion:** In this review, we focused on the latest findings in the etiology, epidemiology, transmission, clinical manifestation, diagnosis, prevention, and treatment of influenza and the incidence and severity profile of influenza virus infections in populations.

KEYWORDS: Influenza, types of influenza, Flu, Infectious Diseases, prevention, and treatment of influenza.

INTRODUCTION

Influenza can be defined as acute viral respiratory disease caused by infection of the respiratory tract with influenza viruses (seasonal influenza A and B viruses) that circulate among people worldwide. Seasonal influenza is a human disease caused by infection with seasonal influenza A or B viruses. Globally, annual influenza epidemics have variable severity and typically occur during colder periods in temperate climates.[1,2]

Influenza (flu) is a contagious respiratory illness caused by influenza viruses that infect the nose, throat, and lungs, especially people 65 years and older, young children, and people with comorbidities, are at higher risk of serious flu complications. Influenza (flu) can cause mild to severe illness, which may lead to death. Flu symptoms usually arrive suddenly and include fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue (tiredness), vomiting, and diarrhea.[3]

Globally, more than hundreds of millions of influenza virus infections occur each year, but immunity against reinfection with the same strain can last for several years, rapid antigenic change in circulating strains allows influenza viruses to escape the population immunity that builds up after an epidemic.[4]

Usually, influenza pandemics occur when a novel strain emerges from animals and is able to spread among humans.[5] Whereas most infections are associated with mild and self-limiting disease, older individuals and those with underlying medical conditions can be more vulnerable to more serious diseases and influenza epidemics tend to have the greatest impact on these groups. Influenza can also cause serious disease in neonates and infants, most people

who are infected with flu recover completely in 1-2 weeks, but some people develop severer symptoms and potentially life-threatening medical complications, such as pneumonia.[6]

Types of influenza

Influenza viruses can be divided into 3 general categories: types A, B, and C. All three types of influenza viruses can mutate or change into new strains.[7] Influenza D is seen only in animals, not infect humans.

Type A mutations are responsible for major flu epidemics and rarely major pandemics, type influenza mutates often, yielding new strains of the virus every few years, and Type A strain causes avian flu.[8]

Type B is less common and generally results in milder cases of flu, but major flu epidemics can occur with type B every three to five years.[8]

Type C causes infection but it is usually asymptomatic.[8]

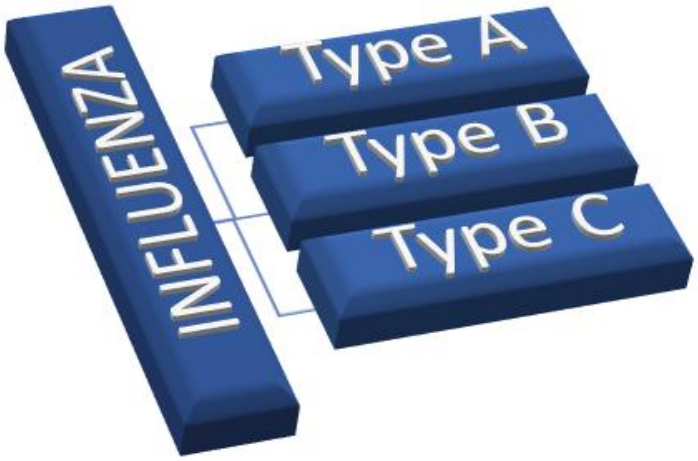

Fig. 1: Types of influenza.

Influenza A and B may develop Reye's syndrome which is a potentially fatal complication that usually affects children and teens under age 18. Widespread outbreaks of Reye's syndrome have been associated with influenza type B and also with chickenpox, but other viruses have been implicated. The risk of Reye's syndrome is increased when taking aspirin, so people under age 18 should not take aspirin if they have any viral symptoms or are recovering from the flu or any other virus.[9]

Epidemiology

Influenza affects all age groups, especially it affects people at greater risk of severe disease or complications when infected, pregnant women, children under 59 months, the elderly,

individuals with chronic medical conditions (such as chronic cardiac, pulmonary, renal, metabolic, neurodevelopmental, liver or hematologic diseases) and individuals with immunosuppressive conditions (such as HIV/AIDS, receiving chemotherapy or steroids, or malignancy). Due to increased exposure to the patients, Health care professionals are at high risk of acquiring influenza virus infection.[8]

Transmission

Seasonal influenza spreads easily, with rapid transmission in crowded areas including schools, collages, malls, theaters and other crowded areas. When an infected person coughs or sneezes, virus spreads via infectious respiratory droplets, which are dispersed into the air and can spread up to one meter, and infect persons in close contact who breathe these droplets in. The virus can also be spread by contaminated hands with influenza viruses.

To prevent transmission, people should cover their mouth and nose with a sterile tissue, when coughing or sneezing and wash their hands regularly. Peoples should wear proper face mask and maintain one-meter physical distance in crowded areas to prevent the transmission. The time period from infection to illness is known as the incubation period**,** which is about 2 days to four days.[8]

Pathogenesis of influenza

Most influenza viruses that infect humans are originated in parts of Asia, Due to close contact between livestock and people, it creates a hospitable environment that leads to mutation and transmission of viruses.[10]

Influenza viruses infect the columnar epithelium lining in the respiratory tract, which causes infection in both the upper and lower airways. The incubation period of influenza is 2 days (with a range of 1–4 days).[11] Primary infection in young children is usually symptomatic, but overall, ~50% of influenza infections may be asymptomatic. Infected persons can become contagious (i.e., they can spread detectable amounts of the influenza virus) the day before symptoms begin. Adults usually shed the virus for ~3–5 days, whereas young children can shed the virus for up to 3 weeks.[12]

Pathogenesis of influenza virus infection induces exacerbation of bronchial asthma and COPD and infection-induced pneumonia and ARDS, and the inhibitory effects of the serine protease inhibitors.[13] Influenza viral replication induces cytokine production and cell lysis in

the airway epithelium, which is the first target of infection. Infection-induced production of inflammatory cytokines, includingIL-6 and tumor necrosis factor (TNF)-α, and proteases may cause damage to airway and alveolar epithelial cells and to vascular endothelial cells. This damage may subsequently exacerbate bronchial asthma and COPD and develop into pneumonia and acute respiratory distress syndrome (ARDS).[13]

Patients infected with highly pathogenic influenza viruses experience increased viral replication and subsequent hypercytokinemia.[14] Influenza viral infection-induced cell damage is partly related to the magnitude of viral replication, as well as NF-κB-p65-mediated IL-6production and caspase-3 activation. Furthermore, a large number of CD8+ T cells and granzyme B+ cells have been found to be expressed in autopsy lung tissue specimens from patients infected with the pandemic A/H1N1 influenza virus.[15] Granzymes are granule-stored lymphocyte serine proteases, and CD8+ cells exert their cytotoxic functions by releasing granzymes in response to influenza viral infection.[16] Because IL-6 induces granzyme production, hypercytokinemia during influenza virus infection may activate CD8+cells, resulting in lung damage through the cytotoxic activities of granzymes.[17]

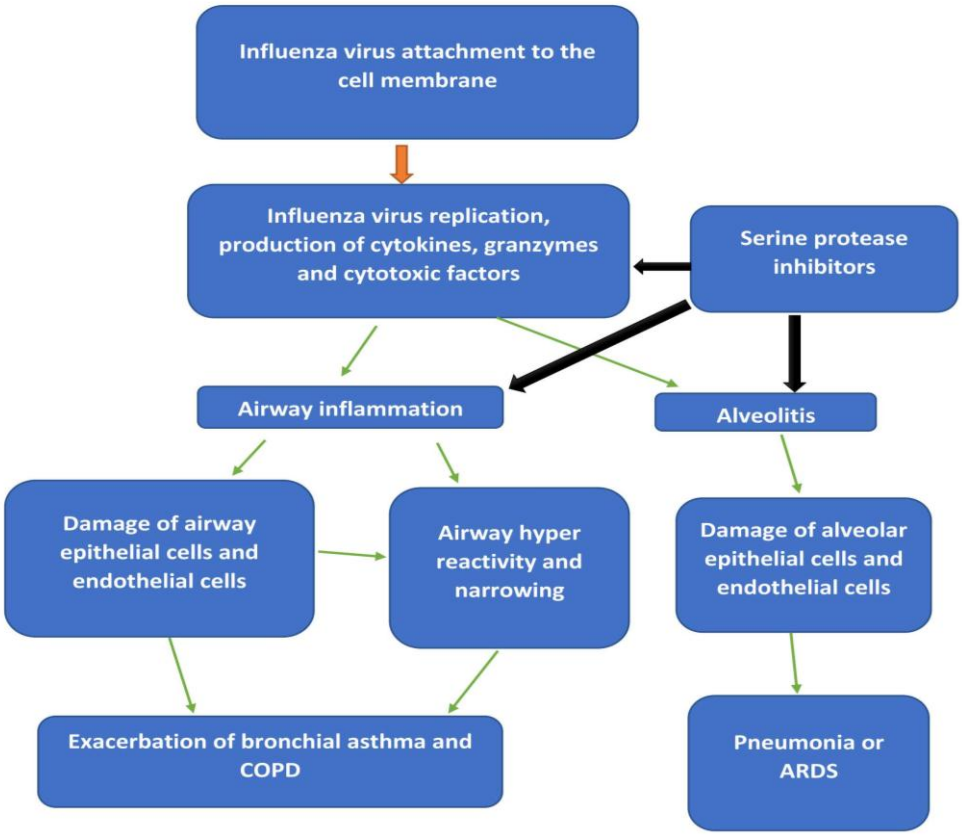

Fig. 2: Pathogenesis of influenza.

Clinical manifestations of influenza

The typical influenza symptoms include fever, cough, and body aches for 3 to 7 days, but lassitude, cough, sneezing and evidence of small-airways disease may persist for weeks. Pneumonia, laryngotracheobronchitis, and unexplained fever are prominent clinical manifestations of influenza that lead to the hospitalization of young children. Adults may have complications of bacterial pneumonia and worsening of chronic pulmonary disease or congestive heart failure. Less frequent complications include myositis, various neurologic disorders, and Reye's syndrome.[18]

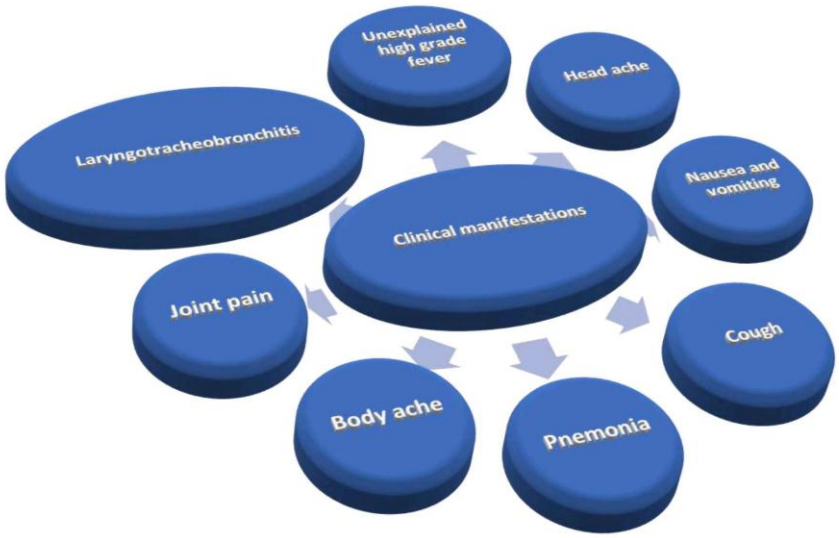

Fig. 3: Clinical manifestations of influenza.

Diagnosis

Differential diagnosis

Influenza typically has an acute onset with high-grade fever, headache, body aches, joint pain, dry cough, nausea, vomiting, pneumonia, and laryngotracheobronchitis (Figure 3).[18]

Diagnostic tests

Influenza can be suspected based on the clinical presentation and physical exam, it can be diagnosed by rapid antigen detection testing, reverse transcriptase-polymerase chain reaction (RT-PCR), and viral culture. Rapid antigen detection tests provide the quickest results, but the sensitivity of this test is generally low and does not exclude influenza in a symptomatic patient. RT-PCR test is the most sensitive and specific test for influenza and it can be used for

differentiating between influenza types A and B. Viral cultures can be used to confirm a diagnosis of influenza, but they are more frequently used for surveillance during viral outbreaks.[19]

Prevention

Vaccination is the most effective measure to prevent infections, Nonpharmaceutical public health measures like physical distancing, using hand rubs, and sanitizers, wearing a proper mask, and maintaining personal hygiene can also be effective in reducing transmission, allowing suppression or mitigation of influenza epidemics and pandemics.[20]

Multiple formulations of the influenza vaccine are available, which include inactivated influenza vaccines (IIV), recombinant inactivated vaccines (RIV), and live attenuated influenza vaccines (LAIV).[21]

Among influenza vaccines, IIV or RIV is suitable for most patients. LAIV is contraindicated in pregnant women, immunosuppressed people, children younger than 2 years, children two to four years of age who have had asthma or wheezing in the past 12 months, and adults 50 years and older.[22]

For children six months to eight years of age, two doses of IIV administered at least four weeks apart are recommended if the child has not received at least two doses of the influenza vaccine previously.[22]

Treatment

Anti-influenza drug is the treatment option, with the decision to prescribe based on balancing potential benefits, harms, cost, and patient preferences. When treatment is initiated within 24 hours of symptom onset, the clinical benefit will be higher. The primary aim of treatment is to decrease the symptom duration by approximately 24 hours when treatment is initiated within 36 hours, and a reduction in disease severity.[23]

The CDC and the IDSA recommends the patients with severe or progressive illness, who are at high risk of influenza-associated complications, and who are hospitalized should follow the antiviral therapy. Early treatment is most beneficial and highly recommended, which the treatment should be initiated in high risk patients regardless of symptom duration. The IDSA also recommends that treatment be considered for household contacts of people at high risk

of influenza-associated complications. Healthcare professionals caring for high-risk patients can also be considered for treatment.[23]

Four antiviral drugs have been approved for the treatment of influenza, which include NA inhibitors oseltamivir, zanamivir, and peramivir, and the cap-dependent endonuclease inhibitor baloxavir. Baloxavir is indicated for the treatment of uncomplicated influenza in patients 12 years and older.[24]

Oseltamivir is the preferred treatment for patients with severe influenza. Intravenous peramivir is an option for these patients if there are contraindications or concerns about the reduced bioavailability of oral oseltamivir. Administration of zanamivir via inhalation is not recommended for patients with severe disease because it is not yet well studied. It is contraindicated in patients requiring mechanical ventilation and in those with underlying lung disease because of the risk of bronchospasm. Adamantanes (amantadine and rimantadine) are approved for influenza treatment but are not currently recommended. These medications are not active against influenza B, and most influenza A strains have shown adamantane resistance for the past 12 years.[24]

Supportive treatment and management of complications, including potential secondary bacterial pneumonia, are paramount. Corticosteroids are not recommended, but it can be used on the patient who has another approved indication for their use. Treatment resistance should be considered in patients who take antivirals and develop lower respiratory tract disease, although this is less likely than natural disease progression and more common in immunosuppressed patients.[23,24]

Pregnancy is an independent risk factor for complicated influenza. The risk of maternal death increases with each trimester and continues for four weeks postpartum. Oseltamivir has good safety data in pregnancy, and the CDC recommends it as a first-line treatment for pregnant women.[24]

CONCLUSION

In this review, we focused on the latest findings in the etiology, epidemiology, transmission, clinical manifestation, diagnosis, prevention, and treatment of influenza and the incidence and severity profile of influenza virus infections in populations.

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