

Overview of Influenza on Older Patients

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Abstract

Introduction: A respiratory viral infection that affects people around the globe. Usually this viral infection is self-limiting in young and healthy individuals, but for the elderly it leads to hundreds and thousands of death and even more hospitalizations around the globe. Many antiviral drugs and vaccines are present to treat the infected and prevent the spread respectively. Despite the advancements, elderly population still remains at risk due to their weaker immunity and comorbidities associated with old age.

Aim of Work: The study aims to write a generalised review on Influenza flu affecting the elderly.

Materials and Methods: The review is comprehensive research of PUBMED from the year 1959 to 2019.

Conclusion: According to the literature reviewed for this article, Influenza is one of the leading causes of infectious death among the elderly population. Due to difficulty in diagnosis in the elderly, antiviral therapy is often not timely given. Even vaccines in the elderly do not work as effectively as they would in the younger population. Nevertheless, vaccination of a community against Influenza reduces the hospitalization and mortality rate quite significantly. Research to improve diagnosis, treatment and prevention must go on to counter the effects of Influenza in the elderly population.

Keywords: Influenza; Flu; Elderly; Immunosenscence; Viral Infection

Introduction

Influenza is an acute respiratory infection seen globally and it infects humans, mammals, and birds. Influenza appears seasonally from December to March in the Northern Hemisphere. It is a mild disease in most people but remains the leading cause of death due to infections among elderly people, largely due to diminishing immune competence with age. Despite advances in its prevention and control, Influenza continues to be important due to the exceptional ability of the virus to undergo antigenic variation [1].

Methodology

A comprehensive and systematic search was conducted regarding influenza in elderly, epidemiology, clinical picture and managements. PubMed search engine and Google Scholar search were the mainly used database for search process. All relevant available and accessible articles of all types were reviewed and included.

The term used in search were: influenza, elderly, immunosenscence, viral infection, flu, antiviral.

Epidemiology

CDC estimates that the burden of illness during the 2018 - 2019 season included an estimated 35.5 million people getting sick with Influenza, 16.5 million people going to a health care provider for their illness, 490,600 hospitalizations and 34,200 deaths from Influenza [2].

	Symptomatic illness	Medical visits	Hospitalization	Death
8 - 49 years	33.5	26.7	13.6	7.2
50 - 64 years	26.0	24.0	20.0	16.6
5 - 17 years	21.6	24.1	4.3	0.6
0 - 4 years	10.2	14.7	5.2	0.8
65 and older	8.7	10.4	57.0	74.8

Table 1: Percentage of Influenza-related burden by age group, 2018 - 2019 Influenza Season [2].

Influenza can produce a significant functional decline in elderly patients. In general, over one-third of hospitalized patients age 70 or older leave the hospital more disabled than when they arrived. Since influenza-related hospitalizations are more frequent and prolonged among elderly patients, Influenza likely contributes significantly to this functional loss [3].

In contrast to seasonal Influenza, the majority of symptomatic infections during pandemic influenza occur among young adults. Experts attribute this relative sparing of older adults to persistent immunological memory from prior exposure to similar viruses decades earlier. Indeed, 34% of the adults born before 1950 had cross-reactive antibodies to the pandemic H1N1 virus at the beginning of the 2009 pandemic [4]. Although disproportionately fewer elderly people developed clinical Influenza, their mortality during the 2009 H1N1 pandemic remained substantial [5].

Virology

Influenza belongs to the orthomyxoviridae family and is a segmented RNA virus that appears annually. Two types A and B are known to cause disease in humans. It can make minor changes (called antigenic drift) or major changes (called antigenic shift) in its genome. This possible because the virus is a segmented RNA virus, causing seasonal or pandemic outbreaks of disease [6].

Influenza A subtypes can be distinguished by the type of hemagglutinin and neuraminidase seen on their outer surfaces (e.g. H1N1 and H3N2 subtypes). Hemagglutinin and neuraminidase are proteins that help enter and exit the host cells, respectively. These surface proteins can undergo mutations and thus escaping the detection from host immunity. There are two main lineages of influenza B that circulate in the human population, B/Yamagata and B/Victoria. Several viruses can spring up in a season, and a person may get infected by more than one [7].

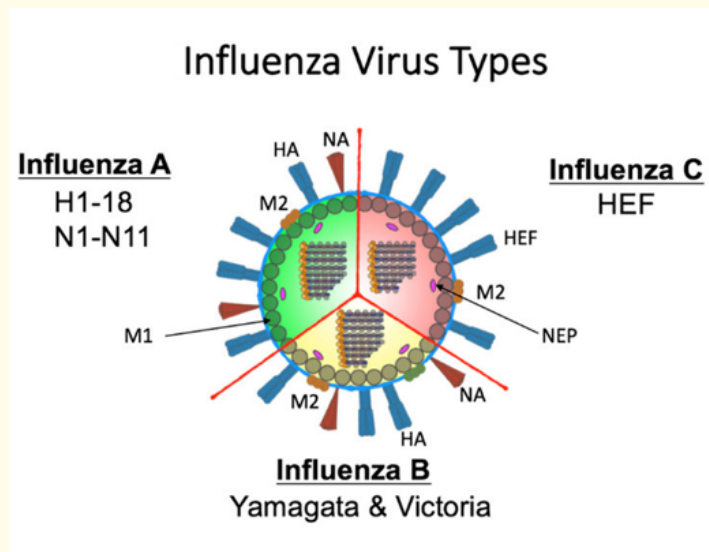


Figure 1: Schematic of influenza A, B, and C virus structure. Influenza A is defined by its surface proteins hemagglutinin (HA) and neuraminidase (NA) of which there are 18 HA and 11 NA. Influenza B viruses are categorized into two lineages (B/Yamagata and B/Victoria) Influenza C viruses have only one external spike protein (HEF) which functions both in viral entry and egress and an ion channel M2 protein [8].

Transmission and viral shedding

Influenza is spread largely through droplet aerosols produced by sneezing, coughing or spitting. Viral shedding normally begins within 24h before the symptoms arise and last for approximately five days in healthy adults. In elderly adults with comorbidities, viral shedding can last even longer. Viral shedding can be reduced with antiviral drugs [9].

Pathogenesis and host defense

Once viral particles are inhaled, they attach to epithelial cells of the respiratory system. Mechanical defense includes mucociliary clearance and cough, both of which are frequently diminished in the elderly population. Animal studies imply that fever may hasten viral clearance, but fever is suppressed in the old age and may be associated with prolonged viral shedding. Host antibody responses are strain-specific and are absent unless previously exposed to it. Influenza viruses frequently mutate; therefore, annual vaccinations are recommended. Cellular responses, especially from cytotoxic T cells, promote viral clearing, and also help protect against pneumonia [10].

Toll-like receptors on macrophages recognize a broad array of antigens and forms part of the innate immunity. Experiments in aged mice have revealed a reduction in Toll-like receptors on macrophages, and a decline in the number of proinflammatory cytokines produced by antigenic stimulation with Influenza compared with young mice. This decline in inflammatory response helps explain the milder early clinical presentation of disease, the lesser prevalence of fever in older patients and possibly the lessened vaccine responsiveness [11].

Cell-mediated immunity response also declines with advancing age, which explains why influenzas lasts longer in older individuals. Together, these changes in the innate and adaptive immunity make the elderly population more vulnerable to the detrimental effects of Influenza. Moreover, it also amounts to lesser protective response post influenza vaccination [12].

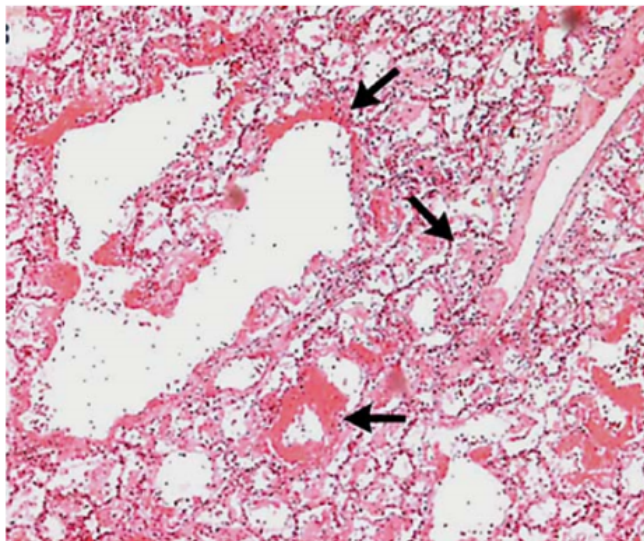


Figure 2: Hematoxylin and eosin stain of lung tissue from a patient who ultimately died of H1N1 influenza pneumonia. Note necrosis of bronchiolar walls (top arrow), a neutrophilic infiltrate (middle arrow) and diffuse alveolar damage with prominent hyaline membranes (bottom arrow) [13].

Clinical manifestations

Incubation typically lasts 1 day to 2 days. A typical symptom is a fever, which usually 3 - 7 days. Chills, headache, myalgia and malaise are usually seen along with fever. Once initial symptoms subside, respiratory symptoms such as dry cough, sore throat, and nasal discharge, become more evident. Signs seen of clinical examination are the flushed face, moist skin hyperemic mucosa, and small but tender cervical lymphadenopathy. Older adults usually present with cough, fatigue and confusion, whereas fever is relatively very mild [14].

Primary influenza viral pneumonia: It is not usually encountered in seasonal flu epidemics, but it is prominent in influenza pandemics and is accountable for much of the associated mortality. It starts like regular Influenza but may rapidly progress into severe acute respiratory distress without any bacterial pathogen involved. Nasopharyngeal specimens typically have high influenza viral titers. Laboratory and radiological examination often show hypoxemia and bilateral interstitial infiltrates typical of acute respiratory distress syndrome. Primary influenza viral pneumonia during history of pandemics was seen more frequently in younger population [15].

Secondary bacterial pneumonia in influenza cases is responsible for much morbidity and mortality of elderly population. It usually presents with biphasic illness. It starts with typical influenza like symptoms, few days of improvement followed by severe cough with purulent discharge. Chest x-ray reveals pulmonary consolidation. *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae* are common bacterial pathogens involved [16].

Exacerbation of existing chronic pulmonary and cardiovascular diseases due to Influenza may also increase the morbidity and mortality of old age adults. Existing asthma and chronic bronchitis can impair pulmonary function in influenza patients. Myocardial infarction has shown higher incidences during winter season and influenza activity has been suggested as a possible reason for it [17].

Diagnosis

Epidemiological diagnosis: During an influenza outbreak, the presence of fever and cough within 2 days symptom onset has a positive predictive value of 79%. In seasons where influenza outbreaks are not expected, specific tests must be done to rule out possible infections from rhinovirus or coronaviruses [18].

Rapid antigen tests: It is used to detect virus antigens in the sample. Throat swab is used to collect the specimen from nasopharyngeal mucosa. The advantage of rapid antigen testing is that they are easily available at various health care settings and can provide test results within minutes. Despite its availability, the sensitivity of the test remains limited to both seasonal and pandemic Influenza [19].

Molecular diagnostics: During molecular diagnostics, samples are collected in a similar format as rapid antigen tests. Reverse transcriptase-polymerase chain reaction (RT-PCR) is the most sensitive and specific diagnostic test available and has the ability to differentiate various influenza types. This test, however, remains unavailable at most health care centers and is mostly used in laboratories [20].

Treatment

Antiviral treatment given to ambulatory patients within 48 hours of symptoms appearance can lessen the possibility of complications. Also, antiviral treatment given to hospitalized patients can lessen their duration of stay in the hospital. The neuraminidase inhibitors such as oral (Oseltamivir) and inhaled powder (Zanamivir) formulations are the treatments of choice for the pandemic 2009 H1N1 influenza A strain. Zanamivir is another drug but has potential to cause bronchospasm in patients with underlying reactive airway disease. Consequently, Zanamivir is administered to these patients along with bronchodilators [14].

Due to resistance in 98.5% of the seasonal H1N1 isolates from the 2008 - 2009 season, Oseltamivir is no longer recommended for seasonal H1N1 Influenza, although it remains susceptible to pandemic H1N1, H3N2 and influenza B. Fortunately, seasonal H1N1 remain susceptible to Zanamivir, Amantadine and Rimantadine. Amantadine and Rimantadine are M2 inhibitors which at first were active against influenza A, are no longer recommended, as almost all seasonal H3N2 viruses currently have shown resistance to these drugs. Even against influenza B or 2009 H1N1 pandemic, M2 inhibitors are not effective. Nevertheless, M2 inhibitors are effective against seasonal H1N1 influenza A and can be used as an alternative to Zanamivir [21].

Antiviral drug	Pandemic H1N1	H3N2	Seasonal H1N1	Influenza B
Oseltamivir	Susceptible	Susceptible	Resistant	Susceptible
Zanamivir	Susceptible	Susceptible	Susceptible	Susceptible
Amantadine	Resistant	Resistant	Susceptible	No Activity
Rimantadine	Resistant	Resistant	Susceptible	No Activity

Table 2: Antiviral treatment of Influenza according to drug susceptibility of each influenza strain [21].

Prevention

Vaccination is probably the most cost-effective method of preventing Influenza. A systematic review of vaccination against Influenza found a 26% reduction in Influenza related hospitalization and a 42% reduction in all-cause mortality among the elderly in a community [22].

Similarly, in a large scale population of community-dwelling elders from 1996 to 2002, it was found that annual influenza vaccination significantly reduced the risk of death. This risk increased 40% above baseline if annual vaccination was stopped and the mortality risk returned to baseline when annual vaccination was restarted [23]. Despite the success of vaccination, most studies also agree that influenza vaccination is less effective in the old age population when compared to younger individuals. This is probably the result of immunosenes-

cence, where an elderly's body may not be able to respond appropriately to new antigens that it encounters during a vaccination. Adjuvanted influenza vaccines are another possible method to increase immunogenicity in old age population. Adjuvants in immunology are used to enhance the effects of a vaccine by stimulating the immune system to give a more vigorous response. In Italy, an MF59-adjuvant influenza vaccine was more effective in prevention influenza-associated illness compared with a nonadjuvanted vaccine [24].

There are also evidences showing that immunizing children and young adults who respond well to vaccination reduce the risk of influenza exposure among the elderly population. In a US-based study, vaccinating 20% of children aged 6 months to 18 years reduced the total Influenza related hospitalization and mortality by half [25]. Also, vaccination of health care workers in long-term health care facilities reduces the burden on the residing elderly population in such a facility.

Antiviral chemoprophylaxis is another way of preventing influenza outbreaks in high-risk populations. Such chemoprophylaxis is recommended for residents' long-term care facility in an unfortunate event of outbreak irrespective of their vaccination status [26].

Conclusion

Influenza is one of the leading causes of infectious death among the elderly population. Due to difficulty in diagnosis in the elderly, antiviral therapy is often not timely given. Even vaccines in the elderly do not work as effectively as they would in the younger population. Nevertheless, vaccination of a community against Influenza reduces the hospitalization and mortality rate quite significantly. Research to improve diagnosis, treatment and prevention must go on to counter the effects of Influenza in the elderly population.

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