Clinical management and supervision of Influenza – systematic review

Michał Głoźnik
Przychodnia Bracka Bielszowice, Ruda Śląska
glodzimichal@gmail.com
https://orcid.org/0009-0009-4751-1784

Marek Miśkiewicz
Wojewódzki Szpital Podkarpacki im.Jana Pawła II w Krośnie
miskiewiczkeram@gmail.com
https://orcid.org/0000-0002-3691-343X

Martyna Łęcka
Szpital Murcki Sp z o.o. Katowice
martyna.lecka@gmail.com
https://orcid.org/0009-0007-1473-8400

Aleksandra Ogiegło-Kowalczyk
SPZOZ Okręgowy Szpital Kolejowy w Katowicach
aleksandra.ogieglo@gmail.com
https://orcid.org/0009-0008-8773-7123
Julia Samborska
SPZOZ Okręgowy Szpital Kolejowy w Katowicach
julia.samborska.med@gmail.com
https://orcid.org/0009-0001-2157-7015

Karina Stelmaszak
SPZOZ Okręgowy Szpital Kolejowy w Katowicach
stelmaszak1259@gmail.com
https://orcid.org/0009-0006-3877-2753

Katarzyna Stencel
Specjalistyczny Zakład Opieki Zdrowotnej "MULTIMED" Sp. z oo
katarzynastencel96@gmail.com
https://orcid.org/0009-0006-9574-9277

Paweł Więckowiak
Śląski Uniwersytet Medyczny w Katowicach
pawew36@gmail.com
https://orcid.org/0009-0004-6610-1792

Monika Wojtasik
Przychodnia Wielospecjalistyczna w Mikołowie
monika.wojtasi95@gmail.com
https://orcid.org/0009-0008-6723-3841

Katarzyna Żak
Uniwersyteckie Centrum Kliniczne w Gdańsku
lek.katarzyna.zak@gmail.com
https://orcid.org/0009-0000-7056-1960
Abstract
The main aim of the following study is to review current knowledge on Influenza. Influenza, also known as the flu, is an acute, infectious disease which attacks the respiratory system. The disease is caused by the influenza virus, of which there are 3 types. The most common is type A of influenza virus. It is transmitted between people by the droplet route, with cases occurring particularly frequently during seasonal epidemics. This is why the most important form of prevention is maintaining personal hygiene and isolation of sick people. Another form of prevention is a vaccine for the influenza virus developed with new variants every year. The flu causes a variety of symptoms from many systems but can also be asymptomatic. Diagnosis of the illness is based on clinical criteria and the results of diagnostic tests for which there are established criteria of legitimacy. Most common and sufficient curation for an illness is a symptomatic treatment but there is also a causal treatment for influenza. However certain conditions are required for its implementation. Influenza is usually a mild disease, but there are present cases of serious complications. Groups particularly exposed to severe and complicated courses of the disease are pregnant women, children and patients with multimorbidities. Currently, the co-occurrence of influenza with Covid-19 infection is particularly dangerous, which constitutes a new challenge for the global health care system.

Key words: “Influenza”, “Flu”, “Pathogenesis”, “Epidemiology”, “Prevention”, “Diagnosis”, “Symptoms”, “Treatment”, “Complications”, “SARS-CoV-2”

Introduction and historical background:
The influenza virus has coexisted with mankind for centuries, taking with it a deadly toll of successive generations. One of the earliest descriptions of influenza was provided by
Hippocrates himself, dubbed the father of medicine. He described an upper respiratory tract infection in the fifth century BC in his work 'Corpus Hippocraticum', which he called 'Perinthos cough'.

Influenza has haunted the world for centuries. We can distinguish two types of influenza cases from an epidemic perspective. Seasonal influenza covers annual illnesses during the epidemic period caused by typical types of viruses. This is a milder kind of disease, with less intensity and potential to spread. Pandemic influenza, on the other hand, is characterized by the occurrence of dangerous global epidemics caused by new, previously unknown subtypes every several dozen years. It spreads very quickly and is hard to control.

The most virulent influenza pandemic scientifically documented occurred between 1918 and 1920 and swept through Europe, Asia, Africa and North America. The Spanish flu, as the epidemic was called, killed between 50 and 100 million people [1], representing between 3 and 5% of the world's population at the time.

Later epidemics, due to the development of human immunity, vaccines and drugs, such as the Asian flu of 1957, were no longer as deadly [2].

The last influenza pandemic took place in 2009-2010 and was caused by the H1N1 virus [3]. The disease caused huge public fear and economic losses, but was brought under control, particularly through vaccination.[4]

**Etiology and transmission**

Influenza is caused by three types of viruses belonging to the orthomyxovirus family [5]. We distinguish A, B and C viruses.

Influenza A virus occurs in humans and animals. Its genetic material is single-stranded RNA divided into 8 segments [6]. It is characterized by very high genetic variability due to the huge number of possible subtypes of proteins that make up its protein shell and the enzymes necessary for replication. In total, there are approximately 180 possible combinations of gene segments of this virus, which makes it the most common variety of the influenza virus.

The influenza B virus occurs only in humans and is characterized by low genetic diversity due to the small number of subtypes of its single-stranded RNA. Its incidence is very low.

The influenza C virus occurs in humans and pigs, causes only mild infections and does not have the ability to cause an epidemic. Its single-stranded RNA has only 7 segments and lacks the neuraminidase enzyme.

Infection with the influenza virus occurs through droplets during contact with an infected person. There are many factors that facilitate infection. These include: staying in close
proximity to a sick person for a longer period of time, direct contact with him, insufficient hand hygiene and frequent stay in closed rooms with a high concentration of people. Individual factors, such as immunocompromised states, also predispose to infection.

Clinical symptoms
The onset of influenza is preceded by an incubation period that usually lasts 1 to 4 days. After this time, symptoms appear that are characterized by sudden onset. Characteristic symptoms of influenza can be divided into three groups: general, respiratory and others. General symptoms are usually the first to appear. These include: fever, malaise, shivers, general weakness, joint pain, myalgia and headaches. [7] Then, after about 3 days, respiratory symptoms appear, such as sore throat, runny nose, dry cough and a shortness of breath. [8] Other symptoms are rare, such as vomiting, diarrhea and laryngitis. About 50% of infections are asymptomatic.

Diagnosis
In clinical practice, influenza diagnosis does not require detection of the influenza virus in laboratory tests. To implement causal treatment, especially during seasonal infections, it is sufficient to meet appropriate clinical criteria.[9] It assigns 2 points for fever and cough, 2 points for myalgias, 1 point for chills or sweats, and 1 point for symptom onset within the past 48 hours. Taking into account the scores presented above, the probability of developing influenza can be assessed: if the patient scored 4 or more points, the risk is very high and empirical treatment may be considered. However, tests to detect virus infection are also applicable and justified in certain circumstances. According to the CDC, influenza testing can be considered when the results will modify management or when a patient with signs or symptoms of influenza is hospitalized [10]. Testing is also justified by the principle of excluding other diseases and allows for limiting the erroneous overuse of antibiotics and generating unnecessary diagnostic costs for other diseases.

Prevention and treatment methods
Influenza vaccines have been with us for over 60 years. Since then, work has been ongoing to improve them, expanding the scope of protection they offer and increasing their effectiveness
and safety. Currently, we have annual, seasonal vaccines available that offer immunity against virus strains specific to a given region.[11] Vaccination is recommended for anyone who wants to protect themselves against influenza. Particularly recommended groups of people include: elderly people, people with chronic diseases, pregnant women, health care workers. [12][13] The basis of influenza treatment is non-pharmacological treatment. Bed rest and drinking plenty of fluids are recommended. In each case, symptomatic treatment is also applied, tailored to the patient's individual symptoms. [14] The last line of the fight against the influenza virus is causal treatment. The most important group of drugs are neuraminidase inhibitors such as oseltamivir and zanamivir [15]. They act directly on the influenza virus. There are specific indications for including these drugs in therapy. They include patients whose time from the onset of symptoms does not exceed 48 hours and belong to the increased risk group of patients with multimorbidities. Patients with respiratory diseases are particularly at risk. [16] Regardless of the time criterion, causal treatment is also used in patients with a severe, complicated course of influenza infection. The last group covered by targeted treatment are hospitalized patients. Neuraminidase inhibitors are a safe and effective group of drugs according to recent studies. [17]

Complications
Complications of influenza are a very common phenomenon. The occurrence of post-flu complications is more common than post-COVID according to recent studies. [18] Every year we encounter a large number of post-flu complications affecting many different systems. Elderly people, pregnant women and children are particularly vulnerable groups to severe, complicated influenza. [19] [20] The most common complication of influenza is pneumonia. Streptococcal angina is also common. Another complication may also be the exacerbation of a previously existing chronic disease, most often heart failure and diabetes. Neurological complications are also possible, although rare, including epilepsy, which is particularly common in children. [21]

Coexistence of Influenza and SARS-CoV-2 infections
The global COVID pandemic has caused a completely new situation on the map of seasonal infectious diseases. Previously, influenza was the most common disease of this type, currently we are dealing with the overlap of influenza and COVID. This situation causes diagnostic and
therapeutic difficulties. Both diseases are transmitted by the same route and cause similar symptoms. This fact forces doctors to be more vigilant, to constantly expand their knowledge and it complicates the situation for patients, as both diseases may overlap and cause more severe symptoms. Having influenza less than a year before COVID infection is a risk factor for its severe course.[22] Also risk of complications is increased.

Conclusions:
In the 21st century, influenza continues to pose a significant challenge to the global health system. It is caused by new strains of the flu virus, which forces constant medical progress in every aspect of the diagnostic and therapeutic process including the year per year production of seasonal vaccines. Flu symptoms are nonspecific and resemble other acute respiratory diseases which causes difficulties in diagnosis and requires high accuracy in the therapeutic process. Treatment is non-specific and focuses on symptom relief in most cases. There is a causal treatment for influenza, but it requires meeting certain conditions and detecting the influenza virus in material collected from the patient. In most cases, flu is a mild disease, but there are cases of heavy mileage, leading to complications and even death. The most vulnerable to such course are the elderly, patients with chronic diseases, children and pregnant women. In addition, the overlap between influenza and SARS-CoV-2 also poses significant challenges to the healthcare system which is a completely new phenomenon since the global pandemic of COVID-19.

Author contributions:

Conceptualization: Michał Głodzik, Katarzyna Stencel, Monika Wojtasik, Katarzyna Żak

Methodology: Aleksandra Ogieło-Kowalczyk, Julia Samborska, Karina Stelmaszak,

Software: Michał Głodzik, Marek Miśkiewicz, Martyna Łęcka

Form analysis: Michał Głodzik, Marek Miśkiewicz, Martyna Łęcka, Aleksandra Ogieło-Kowalczyk, Julia Samborska, Karina Stelmaszak, Katarzyna Stencel, Paweł Więckowiak, Monika Wojtasik, Katarzyna Żak
Data curation: Aleksandra Ogiełło-Kowalczyk

Visualization: Paweł Więckowiak, Marek Miśkiewicz

Supervision: Michał Głodzik, Marek Miśkiewicz, Martyna Łęcka, Aleksandra Ogiełło-Kowalczyk, Julia Samborska, Karina Stelmaszak, Katarzyna Stencel, Paweł Więckowiak, Monika Wojtasik, Katarzyna Żak

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