Introduction

Influenza, commonly referred to as the flu, is an infectious disease caused by RNA viruses of the family Orthomyxoviridae (the influenza viruses), that affects birds and mammals. The name influenza is Italian and means "influence" (Latin; influentia). The most common symptoms of the disease are chills, fever, sore throat, muscle pains, severe headache, coughing, weakness, fatigue and general discomfort Sore throat, fever and cough are the most frequent symptoms ***(Eccle, 2005).***

In more serious cases, influenza causes pneumonia, which can be fatal, particularly for the young and the elderly. Although it is often confused with other influenza-like illnesses, especially the common cold, influenza is a much more severe disease than the common cold and is caused by a different type of virus Influenza may produce nausea and vomiting, particularly in children but these symptoms are more common in the unrelated gastroenteritis, which is sometimes called "stomach flu" or "24-hour flu" ***(Eccle, 2005).***

Types of influenza virus in virus classification influenza viruses are RNA viruses that make up three of the five genera of the family Orthomyxoviridae:

- Influenza virus A
- Influenza virus B
- Influenza virus C

Reasonably effective ways to reduce the transmission of influenza include good personal health and hygiene habits such as: not touching your eyes, nose or mouth frequent hand washing (with soap and water, or with alcohol-based hand rubs) covering coughs and sneezes; avoiding close contact with sick people; and staying home yourself if you are sick. Avoiding spitting is also recommended ***(Kappagoda et al., 2000).***

Treatment

People with the flu are advised to get plenty of rest, drink plenty of liquids, avoid using alcohol and tobacco and, if necessary, take medications such as acetaminophen (paracetamol) to relieve the fever and muscle aches associated with the flu. Children and teenagers with flu symptoms (particularly fever) should avoid taking aspirin during an influenza infection (especially, because doing so can lead to Reye's syndrome, a rare but potentially fatal disease of the liver. Since influenza is caused by a virus, antibiotics have no effect on the infection; unless prescribed for secondary infections such as bacterial pneumonia. Antiviral medication can be effective, but some strains of influenza can show resistance to the standard antiviral drugs ***(Kappagoda et al., 2000).***

Anise is one of the common beverages in Egypt during winter season specific. Known to all Egyptian there is relation between common cold and Anise drinking.In 2005, in response to the SARS avian flu, there was a temporary shortage of star anise due to its extensive use in creating Tamiflu ***(Matheson et al., 2003).***

Biology of Anise

Anise (Pimpinella anisum), also anise (stressed on the second syllable) and aniseed) is a flowering plant in the family Apiaceae native to the eastern Mediterranean region and Southwest Asia. It is known for its flavor, which resembles liquorice, fennel and tarragon. Anise is an herbaceous annual plant growing to 3 ft (0.91 m) tall. The leaves at the base of the plant are simple, 0.5–2 in (1.3–5.1 cm) long and shallowly lobed, while leaves higher on the stems are feathery pinnate, divided into numerous leaves ***(Arts and Hollman, 2005).***

A study conducted to assess the efficacy, safety and tolerability of herbal neuraminidase inhibitors in the treatment and prophylaxis of influenza infection in children they performed this study on three randomised controlled trials reporting data from 1500 children with a clinical case definition of influenza, of whom 798 had laboratory confirmed influenza infection ***(Matheson et al., 2003).***

Shikmic acid is used for synthesis for potent antiflu drug tamiflu. Shikimic acid can be rapidly separated (ca. 5 min) from Chinese star anise with hot water extraction at temperatures of 120°C or higher to obtain recoveries of 100%. Extraction recoveries of shikimic acid close to 97% were obtained with water at 70 °C using slightly longer extraction times (ca. 10 min) than those at 120 °C. For 0.5 g Chinese star anise raw material that contained 8% shikimic acid, 100% recoveries of shikimic acid could be obtained with 60 g water at 150 °C at 15 MPa in 4 min for star anise material having a particle size range from 355 to 600 μm ***(Ohira and, Torri. 2009).***

The effects of the essential oil of Foeniculum vulgar and Pimpinella anisum and three lignin-carbohydrate-protein complexes (LC1, LC2, and LC3) with antiviral and immunostimulating activity were isolated from a hot water extract of seeds of Pimpinella anisum by combination of anion exchange, gel filtration, and hydrophobic interaction column chromatographies. These complexes showed antiviral activities against herpes simplex virus types 1 and 2, human cytomegalo virus, and measles virus ***(Lee, et al., 2011).***

Screening of some Iraqi medicinal plants for analgesic activity showed that the extracts of Tribulus terrestris and Pimpinella anisum exhibited significant analgesic activity versus benzoquinone induced writing and in thermal tests ***(Twaij et al., 1998).***

In a study by Tas, essential oil of Pimpinella anisum showed significant analgesic effect similar to morphine and aspirin ***(Tas, 2009).***

Hippocrates theory:

"It is thus regard divine nor more sacred than other diseases, but had a natural cause from the originates like other affections. Men regard it's nature and cause as divine from ignorance and wonder…"

Palestinian study on anise seeds

This study was conducted to determine the extent of herbal self-therapy among university students, investigate the different types of herbal remedies used and investigate the correlates and reasons associated with such practices.

Methodology: This cross-sectional, descriptive study was carried out using a structured questionnaire that contained five sections: demographics; medication knowledge and self-care orientation; types of herbal remedies used; clinical conditions treated; and finally, the reasons reported by students for herbal self-therapy practice. **Results:** 33.9% of the respondents reported using herbal remedies in self-therapy. Female gender, students at medical colleges and those with high self-care orientation were significant predictive model for herbal, anise (Pimpinella anisum L.), and thyme (Thymus vulgaris L.) were the most commonly utilized herbal remedies. The types of herbal remedies selected were significantly influenced by gender, but not by the level of medication knowledge or self-care orientation. Herbal remedies were used primarily for the prophylaxis from headache, flu, and sore throat. The main motivating factor for using herbal remedies reported for using herbal remedies was simplicity of symptoms ***(Sawalha et al., 2008).***

Conclusions: Herbal self-therapy was a common practice among university students. Health care providers need to be aware of the students' self-therapy practices and need to have sufficient knowledge regarding herbs not simply because of the widespread use, but also because of significant reported side effects. Academics need to consider offering courses about herbal remedies to students in both the medical and non-medical faculties to broaden their treatment capabilities during this time of increased unregulated medical interventions such as herbal therapy ***(Sawalha et al., 2008).***

Aim of the Work

Evaluation of the role of anise in protection from the influenza symptoms.

Influenza

Influenza, commonly called "the flu," is an illness caused by RNA viruses that infect the respiratory tract of many animals, birds, and humans. In most people, the infection results in the person getting fever, cough, headache, and malaise, some people also may develop a sore throat, nausea, vomiting and diarrhea. The majority of individuals has symptoms for about one to two weeks and then recovers with no problems. However, compared with most other viral respiratory infections, such as the common cold, influenza (flu) infection can cause a more severe illness with a mortality rate (death rate) of about 0.1% of people who are infected with the virus ***(Conrad, 2012).***

The above is the usual situation for the yearly occurring "conventional" or "seasonal" flu strains. However, there are situations in which some flu outbreaks are severe. These severe outbreaks occur when a portion of the human population is exposed to a flu strain against which the population has little or no immunity because the virus has become altered in a significant way. These outbreaks are usually termed epidemics. Unusually severe worldwide outbreaks (pandemics) have occurred several times in the last hundred years since influenza virus was identified in 1933. By an examination of preserved tissue, the worst influenza pandemic (also termed the Spanish flu or Spanish influenza) occurred in 1918 when the virus caused between 40-100 million deaths worldwide, with a mortality rate estimated to range from 2% to 20% ***(Conrad, 2012).***

In April 2009, a new influenza strain against which the world population has little or no immunity was isolated from humans in Mexico. It quickly spread throughout the world so fast that the WHO declared this new flu strain (first termed novel H1N1 influenza A swine flu, often later shortened to H1N1 or swine flu) as the cause of a pandemic on June 11, 2009. This was the first declared flu pandemic in 41 years. Fortunately, there was a worldwide response that included vaccine production, good hygiene practices (especially hand washing) were emphasized, and the virus (H1N1) caused far less morbidity and mortality than was expected and predicted. The WHO declared the pandemic's end on Aug. 10, 2010, because it no longer fit into the WHO's criteria for a pandemic ***(Conrad, 2012).***

Antigenic shift and drift

Influenza type A viruses undergo two kinds of changes. One is a series of mutations that occurs over time and causes a gradual evolution of the virus. This is called antigenic "drift." The other kind of change is an abrupt change in the hemagglutinin and/or the neuraminidase proteins. This is called antigenic "shift." In this case, a new subtype of the virus suddenly emerges. Type A viruses undergo both kinds of changes; influenza type B viruses change only by the more gradual process of antigenic drift and therefore do not cause pandemics. The 2009 pandemic-causing H1N1 virus is a classic example of antigenic shift. The U.S. Centers for Disease Control and Prevention (CDC) has indicated that novel H1N1 swine flu has an RNA genome that contains five RNA strands derived from

various swine flu strains, two RNA strands from bird flu (also termed avian flu) strains, and only one RNA strand from human flu strains. They suggest mainly antigenic shifts over about 20 years have led to the development of novel H1N1 flu virus ***(Conrad 2012).***

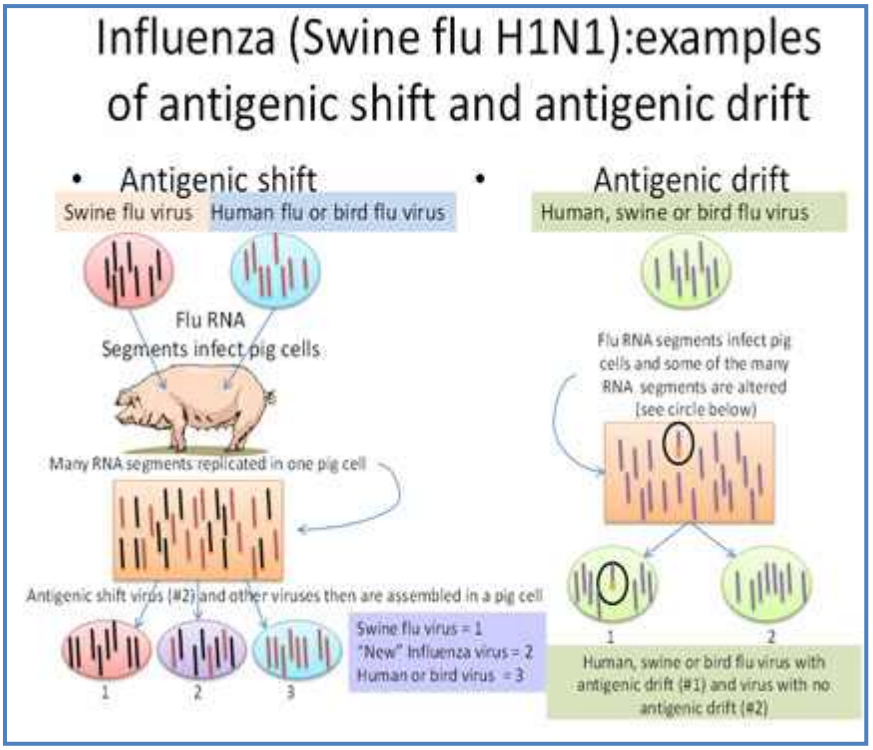

Fig. (1): An example of influenza antigenic shift and drift ***(Johnson and Mueller, 2002).***

Signs and symptoms

Symptoms of influenza, with fever and cough the most common symptoms ***(Call et al., 2005).***

Symptoms of influenza can start quite suddenly one to two days after infection. Usually the first symptoms are chills or a chilly sensation, but fever is also common early

in the infection, with body temperatures ranging from 38 to 39 °C (ed for sea proximately 100 to 103 °F) ***(Suzuki et al., 2007).***

Many people are so ill that they are confined to bed several days, with aches and pains throughout their bodies, which are worse in their backs and legs ***(Kerr et al., 1975)***

[1] Symptoms of influenza may include:

- Fever and extreme coldness (chills, shivering, shaking [rigor])
- Cough
- Nasal congestion
- Runny nose
- Body aches, especially joints and sore throat
- Fatigue
- Headache
- Irritated, watering eyes

[2] Signs of influenza

- Reddened eyes, skin (especially face), mouth, throat and nose
- Petichial rash

In children, gastrointestinal symptoms such as diarrhea and abdominal pain, (may be severe in children with influenza B) ***(Kerr et al., 1975).***

It can be difficult to distinguish between the common cold and influenza in the early stages of these infections, but a flu can be identified by a high fever with a sudden

onset and extreme fatigue. Influenza is a mixture of symptoms of common cold and pneumonia, body ache, headache, and fatigue. Diarrhea is not normally a symptom of influenza in adults ***(Call, et al., 2005).***

Although it has been seen in some human cases of the H5N1 "bird flu" and can be a symptom in children. The symptoms most reliably seen in influenza are shown in the table to the right ***(Richards, 2005).***

Most sensitive symptoms for diagnosing influenza ***(Call S, et al., 2005)***

Symptoms:	Sensitivity	Specificity
Fever	68-86%	25-73%
Cough	84-98%	7-29%
Nasal congestion	68-91%	19-41%

All three findings, especially fever, were less sensitive in people over 60 years of age.

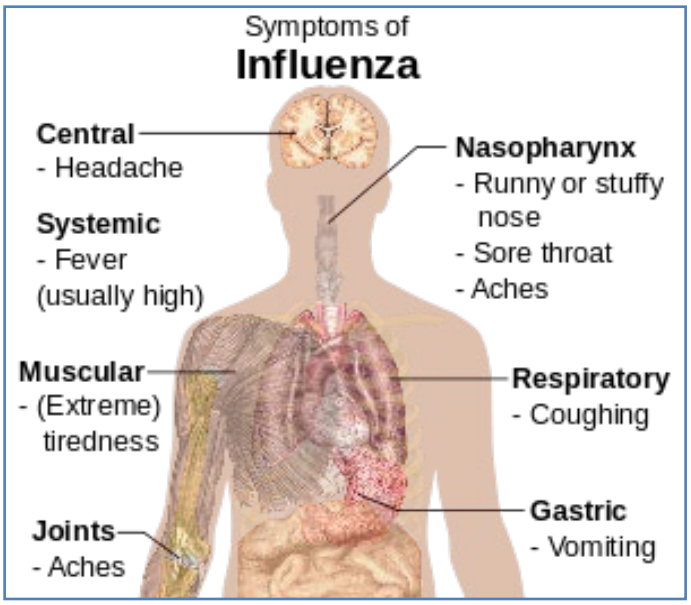

Fig. (2): Symptoms of influenza ***(Call et al., 2005)***

Virology

Types of virus

Structure of the influenza virion. The hemagglutinin (HA) and neuraminidase (NA) proteins are shown on the surface of the particle. The viral RNAs that make up the genome are shown as red coils inside the particle and bound to Ribonuclear Proteins (RNPs). In virus classification influenza viruses are RNA viruses that make up three of the five genera of the family Orthomyxoviridae: ***(Kawaoka, 2006).***

- Influenza virus A
- Influenza virus B
- Influenza virus C

These viruses are only distantly related to the human parainfluenza viruses, which are RNA viruses belonging to the paramyxovirus family that are a common cause of respiratory infections in children such as croup ***(Vainionpää and Hyypiä 1994).***

But can also cause a disease similar to influenza in adults ***(Hall, 2001).***

Influenza virus A

This genus has one species, influenza A virus. Wild aquatic birds are the natural hosts for a large variety of influenza A. Occasionally viruses are transmitted to other species and may then cause devastating outbreaks in domestic poultry or give rise to human influenza pandemics ***(Klenk, 2008).***

The type A viruses are the most virulent human pathogens among the three influenza types and cause the most severe disease. The influenza A virus can be subdivided into different serotypes based on the antibody response to these viruses ***(Hay et al., 2001).***

The serotypes that have been confirmed in humans, ordered by the number of known human pandemic deaths, are:

H1N1, which caused Spanish Flu in 1918, and Swine Flu in 2009

H2N2, which caused Asian Flu in 1957

H3N2, which caused Hong Kong Flu in 1968

H5N1, which caused Bird Flu in 2004

H7N7, which has unusual zoonotic potential

H1N2, endemic in humans, pigs and birds

H9N2

H7N2

H7N3

H10N7

H7N9

(Fouchier et al., 2004).

Influenza virus B

Influenza virus nomenclature (for a Fujian flu virus) this genus has one species, influenza B virus. Influenza B almost exclusively infects humans and is less common than influenza A ***(Hay et al., 2001).***

The only other animals known to be susceptible to influenza B infection are the seal and the ferret. This type of influenza mutates at a rate 2-3 times slower than type A and consequently is less genetically diverse, with only one influenza B serotype ***(Nobusawa and Sato 2006).***

As a result of this lack of antigenic diversity, a degree of immunity to influenza B is usually acquired at an early age. However, influenza B mutates enough that lasting immunity is not possible ***(Webster et al., 1992).***

This reduced rate of antigenic change, combined with its limited host range (inhibiting cross species antigenic shift), ensures that pandemics of influenza B do not occur ***(Zambon, 1999).***

Influenza virus C

This genus has one species, influenza C virus, which infects humans, dogs and pigs, sometimes causing both severe illness and local epidemics ***(Matsuzaki et al., 2002).***

However, influenza C is less common than the other types and usually only causes mild disease in children ***(Matsuzaki et al., 2006).***

Replication

Host cell invasion and replication by the influenza virus. The steps in this process are discussed in the text. viruses can replicate only in living cells ***(Smith and Helenius 2004).***

Influenza infection and replication is a multi-step process: First, the virus has to bind to and enter the cell, then deliver its genome to a site where it can produce new copies of viral proteins and RNA, assemble these components into new viral particles, and, last, exit the host cell ***(Bouvier and Palese 2008).***

Influenza viruses bind through hemagglutinin on to sialic acid sugars on the surfaces of epithelial cells, typically in the nose, throat, and lungs of mammals, and intestines of birds (Stage 1 in infection figure) ***(Wagner et al., 2002).***

The intracellular details are still being elucidated. It is known that virions converge to the microtubule organizing center, interact with acidic endosomes and finally enter the target endosomes for genome release ***(Liu et al., 2011).***

Once inside the cell, the acidic conditions in the endosome cause two events to happen: First, part of the hemagglutinin protein fuses the viral envelope with the vacuole's membrane, then the M2 ion channel allows protons to move through the viral envelope and acidify the core of the virus, which causes the core to dissemble and release the viral RNA and core proteins ***(Bouvier and Palese, 2008).***