SCREENING CHILDREN WITH RESPIRATORY SYMPTOMS FOR INFLUENZA A VIRUS INFECTION DURING POST WINTER SEASON IN EL GHARBIA GOVERNORATE

Thesis

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List of Abbreviations

Abbrev.	Full term
ACTH	Adrenocorticotropic hormone
ARIs	Acute respiratory infections
BMI	Body mass index
CI	Confidence interval
EBV	Epstein-Barr virus
GABHS	Group A beta-hemolytic streptococcus
HA	Hemagglutinin
HBoV	Human bocavirus
HCoV	Human coronavirus
Hib	Haemophilus influenza type B
HMPV	Human metapneumovirus
HSV	Herpes simplex virus
ICAM1	Inter-cellular Adhesion Molecule 1
ILI	Influenza like illness
IV	Influenza virus
NA	Neuraminidase
NCHS	National center for health statistics
NP	Neucleoprotein
OR	Odd ratio
PIgA	Polymeric immunoglobulin A
PIgR	Polymeric immunoglobulin receptor
PIV	Parainfluenza virus

List of Abbreviations (Cont...)

Abbrev.	Full term
RIDTs	Rapid influenza diagnostic tests
RSV	Respiratory syncytial virus
RT-PCR	Reverse transcriptase-polymerase chain reaction
SC	Secretory component
S-OIV	Swine-origin influenza virus
TIV	Trivalent influenza vaccine
URTIs	Upper respiratory tract infections

INTRODUCTION

Acute respiratory infections (ARIs) continue to be the leading cause of acute illness worldwide and remain the most important cause of infant and young children mortality. It accounts for about two million deaths each year *(Mizgerd et al., 2006).*

Although upper respiratory infections (URIs) are very frequent but seldom life threatening, lower respiratory infections (LRIs) are responsible for more severe illnesses such as influenza, pneumonia, tuberculosis, and bronchiolitis that are the leading contributors to ARIs mortality ***(Scott et al., 2008).***

Influenza virus is highly contagious and is readily transmitted via aerosols and droplets from the respiratory tract of infected persons by direct contact, through coughing or sneezing, or by hands contaminated with respiratory secretions *(Musher et al., 2003).*

Three times in the past century, pandemic influenza viruses circulated globally and caused increased morbidity and mortality among persons who were not generally at risk for severe seasonal influenza ***(Simonsen et al., 2005).***

In March 2009, a new strain of pandemic influenza A **(H1N1)** virus emerged in Mexico, where it caused extensive disease in young adults. Deaths that were associated with 2009 **(H1N1)** influenza occurred predominantly in young children, two thirds of fatal cases were attributed to refractory hypoxemia and bacterial co- infection in few patients from cultures of blood or pleural fluid ***(Chowell et al., 2009 and Perez-Padilla et al., 2009).***

The recent appearance and worldwide spread of novel influenza A virus has highlighted the need to commercially available, widely used rapid influenza diagnostic tests (RIDTS) for their ability to detect these viral antigens in respiratory clinical specimens ***(Dawood et al., 2009).***

Testing for influenza A with real-time reverse transcriptase-polymerase chain reaction (RT-PCR) is important in making a diagnosis, but it is both expensive and of limited practicality on a very large scale. In addition people are likely to remain PCR-positive for several days after they stop shedding viable virus and are infectious ***(Witkop et al., 2009).***

AIM OF THIS WORK

A cross sectional study designed to screen children with respiratory symptoms for influenza A virus infection during post winter season in El Gharbia governorate using "One Step Influenza A Rapid Test".

INFLUENZA A VIRUSES

Influenza viruses are one of RNA viruses that make up three of the five genera of the family Orthomyxoviridae (Influenza virus A, Influenza virus B, Influenza virus C) ***(Kawaoka, 2006).***

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. 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.

(Hay et al., 2001)

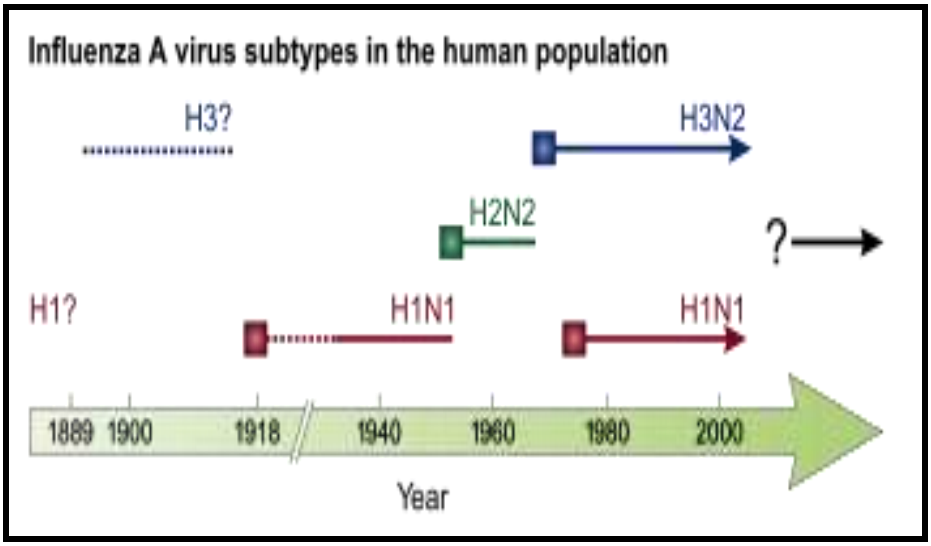

Figure (1): The main types of influenza viruses in humans: Solid squares show the appearance of a new strain, causing recurring influenza pandemics. Broken lines indicate uncertain strain identifications ***(Palese, 2004).***

Structure and properties of influenza virus:

The virus particle is 80–120 nanometres in diameter and usually roughly spherical, although filamentous forms can occur. However, despite these varied shapes, the viral particles of all influenza viruses are similar in composition ***(Bouvier et al., 2008).***

Influenza viruses are made of a viral envelope containing two main types of glycoproteins, wrapped around a central core. The central core contains the viral RNA genome and other viral proteins that package and protect this RNA. RNA tends to be single stranded but in special cases it is double. Unusually for a virus, its genome is not a single piece of nucleic acid; instead, it contains seven or eight pieces of segmented negative-sense RNA, each piece of RNA containing either one or two genes. For example, the influenza A genome contains 11 genes on eight pieces of RNA, encoding for 11 proteins ***(Ghedin et al., 2005 and Bouvier et al., 2008).***

Hemagglutinin (HA) and neuraminidase (NA) are the two large glycoproteins on the outside of the viral particles. HA is a lectin that mediates binding of the virus to target cells and entry of the viral genome into the target cell, while NA is involved in the release of progeny virus from infected cells, by cleaving sugars that bind the mature viral particles. Thus, these proteins are targets for antiviral drugs ***(Wilson et al., 2003 and Suzuki, 2005).***

Furthermore, they are antigens to which antibodies can be raised. Influenza A viruses are classified into subtypes based on antibody responses to HA and NA. These different types of HA and NA form the basis of the H and N distinctions in, for example, *H5N1*. There are 16 H and 9 N subtypes known, but only H 1, 2 and 3, and N 1 and 2 are commonly found in humans ***(Hilleman, 2002 and Lynch et al., 2007).***

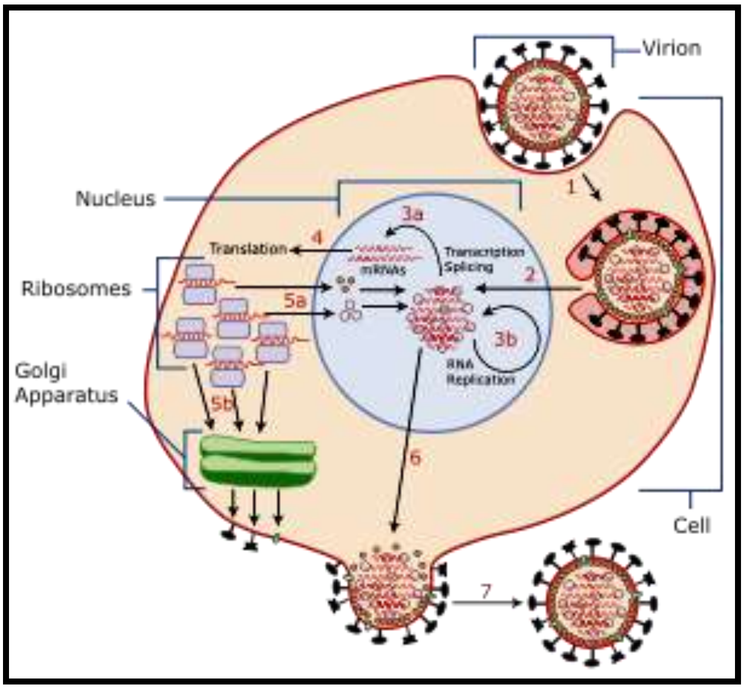

Figure (2): Host cell invasion and replication by the influenza virus ***(Wagner et al., 2002).***

Replication:

Viruses can only replicate in living cells. Influenza infection and replication is a multi-step process: firstly 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 finally exit the host cell ***(Smith et al., 2004 and Bouvier et al., 2008).***

Influenza virus shedding (the time during which a person might be infectious to another person) begins the day before symptoms appear and virus is then released for between 5 to 7 days, although some people may shed virus for longer periods. People who contract influenza are most infective between the second and third days after infection. The amount of virus shed appears to correlate with fever, with higher amounts of virus shed when temperatures are highest ***(Carrat et al., 2006 and CDC, 2010).***

Children are much more infectious than adults and shed virus from just before they develop symptoms until two weeks after infection. The transmission of influenza can be modeled mathematically, which helps predict how the virus will spread in a population ***(Mitamura et al., 2006 and Grassly et al., 2008).***

Route of transmission:

Influenza can be spread in three main ways: by direct transmission (when an infected person sneezes mucus directly into the eyes, nose or mouth of another person), the airborne route (when someone inhales the aerosols produced by an infected person coughing,