# Research paper on comparative analysis of h1n1 influenza virus hemagglutination i...

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## Background and Significance

Influenza, a viral infectious disease caused by influenza viruses, primarily affect the respiratory system and result in hospitalization and death among both the young and the elderly, as well as the pregnant women and chronically ill; epidemics cause an average of 25, 000 deaths annually in the United States alone. (1).

The human influenza virus has three types: Type A, type B, and type C. Influenza A has subtypes, classified by surface antigens, hemagglutinin (HA) and neuraminidase (NA). Influenza A has 16 different hemagglutinin subtypes and 9 different neuraminidase subtypes and strains have a nomenclature of H (1-16) N ( 1-9) (2).

According to Murphy, Travers, and Walport (2008), the “ Influenza virus undergoes antigenic variation by two mutational mechanisms called antigenic shift and antigenic drift.” Antigenic drift are small changes that continually happen in the virus which results in the production of new virus strains. Antigenic shift, on the other hand, is a major change in the type A virus that “ results in new hemagglutinin and/or new hemagglutinin and neuraminidase proteins in the virus,” quickly spreading in humans and causes pandemics. These new antigenic phenotypes created by these mutational mechanisms allow reinfection of the host by bypassing its immunity.

Yearly vaccine against flu is recommended for protection. The vaccine typically encodes the three main flu strains that the World Health Organization (WHO) believes will cause the most illness during the upcoming flu season in the Northern and Southern Hemispheres. (3)

Other than annual flu vaccine, another form of defense is antiviral drugs. There are currently four prescription antiviral drugs in the United States approved for use in the prevention and/or treatment of the influenza virus. These antiviral drugs are grouped into two categories: the adamantanes, which includes the antiviral drugs rimantadine and amantadine, and neuraminidase inhibitors, zanamivir and oseltamivir. (3) However, many influenza strains have developed widespread resistance to these drugs and effective treatment and prevention options are often limited.

Influenza pandemics have occurred throughout history. The most recent pandemic occurred in the spring of 2009 caused by a novel H1N1 (Influenza A) virus commonly referred to as " swine flu” or AH1N1 (5). The AH1N1 virus is comprised of four strains of influenza virus: two swine strains, one human strain, and one avian strain. The Centers for Disease Control (CDC) estimates that in the United States from April 2009 to April 2010, between 43 million and 89 million people were infected with 2009 AH1N1, of which 195, 000 to 403, 000 cases resulted in hospitalizations with about 8, 870 to 18, 300 reported deaths (6).

The AH1N1 virus is resistant to matrix protein-2 inhibitors but is susceptible to neuraminidase inhibitors. WHO recommends treatment with oseltamivir as soon as possible for patients who initially present with severe illness or whose condition begins to deteriorate (7).

Convalescent plasma may offer a new treatment option for seriously ill influenza patient, and for other new and emerging infectious diseases (8). A meta-analysis has suggested that early administration of convalescent blood products might have reduced the risk by 50 % in patients with Spanish

influenza pneumonia during the 1918 pandemic (9). A recent study conducted in Hong Kong demonstrated that patients with severe H1N1 2009 infection treated with convalescent plasma with neutralizing antibody titer (NAT) of ≥1: 160, collected by apheresis from patients recovering from H1N1 2009 infection, reduced the viral load, dampened the cytokine response and resulted in a 50% reduction in mortality (10).

The hemagglutination inhibition (HI) assay is the gold standard method used to detect serological responses to influenza virus infection or vaccination (11, 12). The hemagglutinin (HA) protein in the influenza virus agglutinates erythrocytes. Antibodies to a specific influenza virus will bind virus HA and prevent attachment between the viral HA and receptors on the erythrocytes inhibiting hemagglutination (11, 13, 14). The HI assay is based on this effect. The HI antibody titer of the serum is the highest dilution that prevents hemagglutination. If the assay indicates that dilutions 1: 10, 1: 20 and 1: 40 are able to prevent agglutination but dilutions of 1: 80 and 1: 160 do not then the antibody titer will be 40. The higher the amount of antibody in the serum, the higher the dilution in which hemagglutination is first observed. Currently, only serum samples have been used to determine the presence of antibodies to the influenza virus in hemagglutination inhibition (HI) assay (11, 12, 13, 14), with no data on performance on plasma samples. The difference of Plasma sample from serum is that plasma sample has contains fibrinogen and clotting factors due to an anticoagulant that prevents clotting. The World Health Organization (WHO) recommends serum for influenza ABC antibody testing (15). To our knowledge, no studies have correlated antibody titers to the influenza virus between simultaneously obtained serum and

plasma samples in HI assays. The ability to use plasma samples obtained from blood banks that produce Fresh Frozen Plasma units and other licensed plasma products to determine the HAI level could simplify the ability to identify those units with an acceptable level of anti-influenza antibodies against a particular strain of influenza.

Therefore, the purpose of this research is to determine whether serum and plasma samples concurrently obtained from the same person would produce comparable results, and whether serum and plasma samples could be used interchangeably in HI assays. This research is part of a phase II study treatment of seriously ill H1N1 2009 influenza patients using high titer H1N1 2009 antibodies convalescent fresh frozen plasma (FFP) as therapy.

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