Review Article

Journal of Clinical & Experimental Immunology

Emerging Influenza Viruses at Risk in Global Health

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Submitted: 28 Nov 2016; **Accepted:** 02 Dec 2016; **Published:** 07 Dec 2016

Abstract

Since the emergence of a novel aquatic bird Flu agent in humans may be detected in near future, approaches to early diagnosis and prompt therapy are welcome. The swine-origin influenza virus (S-OIV) detected in April 2009 in Mexico, Canada and USA exhibited an unique genome composition not shown before.

The emerging new Flu agent can cause outbreaks of febrile respiratory infection from mild to severe diseases throughout the world. This abstract has the purpose to emphasize the possibility of tracking the new influenza virus in the most affected regions of the world and to avoid a sad toll flu-related deaths that might occur. The possible causes of high incidence and mortality rates are discussed as well as their implications on the public opinion and the prevention campaign.

Keywords: Influenza A, H1N1, Swine-origin influenza virus (S-OIV), Flu virus prevention.

Introduction

The history of flu viruses teaches that influence originates from birds, usually aquatic, then it is transferred to man through the leap into pigs. The promiscuity of the herds, facilitates this transition and then the spread. Three pandemics caused by influenza A viruses, which occurred in the 20th century, have all had this origin: the 'Spanish flu' (1918, H1N1), the 'Asian flu' (1957, H2N2) and the 'Hong Kong flu' (1968, H3N2). The 2009 H1N1 influenza virus acted during the winter in Australia and New Zealand yielding a pattern effect for the treatment of patients during the winter in the Northern Hemisphere [1]. The performance of rapid diagnostic test for the detection of novel influenza A (H1N1) virus was evaluated by the Centers for Disease Control and Prevention [2]. The findings of severe respiratory disease concurrent with the circulation of H1N1 influenza was proved by the aforementioned test [3]. Even the potential impact of pandemic influenza during the Hajj pilgrimage was taken in account to reduce the substantial effect on the crowd to spread the infection [4,5].

Previous observation of hospitalized patients with the 2009 H1N1 influenza in the USA during springtime indicated how to cope with patients showing severe medical conditions [6]. Pregnant women were at increased risk for complication from pandemic H1N1 virus infection [7]. Same critical illness was reported in children and suggested planning responses in intensive care units with swine derived H1N1 virus [8]. The story of the 2009 H1N1 influenza has been tracked since the beginning and the experience of the previous pandemics was the key to afford on time screening procedures and to promote specific vaccine programs all over the world [9,10]. The current concepts on the emergence of influenza A viruses are reported in many review articles [11,12]. Persons who were born before 1957 had a reduced risk of infection [13]. Furthermore cross-reactive antibody responses were measured in people vaccinated with 1976 swine influenza vaccines [14]. Therefore, a good portion of older adults had pre-existing cross reaction antibodies to the 2009 pandemic H1N1 influenza virus [15].

This is similar to what happened with the recent strains of 1957 Asian flu (A2) for which it was demonstrated the presence of antibodies in older segment of that population. In Asian influence there were obviously strains with dominant characters, other than those that had characterized the previous years, but similar to those of the strains widespread much before (1889-90 pandemic). This is consistent with Burnet theory on the origin of new epidemic strains. Most old people have antibodies directed towards the antigens from the strains with which they were in contact. As age progresses the immunity spectrum broaden reflecting the ample repertoire of polyvalent antibodies generated following the contact with many primary and secondary antigens present in viral strains encountered during the years. But each contact with a flu virus of type A involves not only specific antibodies, but also an increase in those directed towards the strain responsible for the first flu infection of the subject (phenomenon of Davenport or doctrine of original sin). In this way, the immunization to a particular strain increases in a certain period, limiting further distribution of the virus and creating a selective advantage, for some viral variants , to multiply and spread. The new strains will be in conditions of growing in

hosts, regardless of whether they have or not an immunologic experience with the previous strains. As a result, shortly after the appearance of a new type, the old forms will disappear and the new family will become dominant for a period that usually covers 10-20 years, in which there is, for the emergence of minor antigenic variation, the subdivision in various subtypes.

The outcome of a new epidemic strain may, therefore, be regarded as a developmental process involving both the characteristics of the strain and the susceptibility of the population. For a viral strain to reach a wide distribution, its antigenic characteristics must ensure that it escapes the neutralization of the host antibodies and of the surrounding population. So the outbreaks will happen with those strains that have dominant antigens that fit the deficiency, or better, the absence of the antibody in the population. It seems, in conclusion, that the flu virus shows ability and an aptitude for survival owing to the emergence of new models that allow the virus to affect populations still partly immune to previous antigenic forms. According to this view, the changes in the influenza A can be designed in a single meaning, in the context of a principle and of an evolutionary progress, from Burnet said immunological drift. Here, we report the data on the H1N1 influenza in the Italian region Campania, which resulted the most affected by the S-OIV and the one with more lethal cases. We discuss the possible causes of these high incidence and mortality rates as well as their implications on the public opinion and the prevention campaign.

Results

Among the Italian regions that were most affected by the S-OIV, Campania was leading for incidence of the infection, with a rising number of flu-related fatalities in its main town, Naples. This obviously generated some panic among the population. The Virology Laboratory of Cotugno Hospital in Naples is the sole center for the surveillance on the virus approved by the Italian Ministry of Health for Campania region. This allows us to make a wide comparison of cases, helping to correlate all the different diagnosis. 5706 diagnostic tests were performed at the Virology Laboratory of Cotugno Hospital in Naples starting on April 28, 2009 (3 days after the WHO alert) until December 31, 2009. The method used for the detection of S-OIV was a real-time reverse-transcriptase-polymerase chain reaction assay [2]. Of these 5706 tests, 40,80% (2329) resulted to be positive. In May, 2 out of 25 tests were found to be positive for the H1N1 virus and corresponded to the first two positive patients in Campania. Only few tests were performed in April, May and June (3, 25 and 11 respectively). Whereas during and after the summer the number of tests performed increased, peaking in November: 222 in July (48,64% positive), 127 in August (52,76% positive), 396 in September (30,30% positive), 999 in October (53,65% positive), 3103 in November (45,47% positive), 820 in December (10,36% positive). In Campania the peak of influenza occurred during the 44th week of 2009 and preceded of about two weeks the incidence peak at national level.

Of the 2329 patients who were positive for H1N1 infection, 1284 (55,10%) were males and 1045 (44,90%) females; similar percentages were found for negative patients (56,40% males versus 43,60% females) suggesting that gender does not seem to affect the incidence rates.

Most patients who reached the Virology Laboratory of Cotugno Hospital were from the main town Naples (4290 patients, 77,0% of which were positive). Whereas 1416 were from the other Campania provinces Salerno (824 patients, 12,62% of which were positive), Caserta (382 patients, 6,35% of which were positive), Avellino (161 patients, 3,13% of which were positive), Benevento (49 patients, 0,90% of which were positive). The number of tests performed reflects the number of inhabitants belonging to each Campania province. In fact, according to data from the National Institute of Statistics (http://demo.istat.it/) in 2009 Naples was the most populated province followed by Salerno, Caserta, Avellino and Benevento. However, the percentage of patients who resulted positive for H1N1 infection was much higher in Naples compared to the other Campania provinces. This is probably due to the higher population density in the main town Naples, which favors the infection spreading.

In Campania the age group from 7 months to 10 years, including 634 patients, showed the highest percentage of incidence for H1N1 infection (28,85%), (Table 1). This is consistent to what observed at the National level, in fact, in Italy the age group from 0 to 14 years resulted the most affected, as reported by INFLUNET the surveillance network for influenza coordinated by the Italian Ministry of Health.

2179 Total	A (0-6 months)	B1 (7 months 10 years)	B2 (11-17 years)	C1 (18-27 years)	C2 (28-35 years)	C3 (36-49 years)	D (over 50 years)
	51	634	321	406	200	292	293
% on total positive	2,36%	28,85%	14,61%	18,47%	9,10%	13,29%	13,33%
F--%F on total for group of age	21-41,2%	267-42,10%	154-48,00%	180-44,30%	92-46,00%	131-44,85%	131-44,70%
M--%M on total for group of age	30-58,8%	367-57,90%	167-52,00%	226-55,70%	108-54,00%	161-55,15%	162-55,30%

Table 1: Positive Patients Classified According to the Age Group.

Discussion and Conclusions

Although the number of victims caused by H1N1 influenza is decidedly inferior to other pandemics [6,15] a potential risk of a panic syndrome existed because of a bad information or a scarce knowledge of the phenomenon. . The virus, that was first detected in Mexico, reached other parts of the world as happens for all the types of influence virus [14]. While for the SARS a direct contact was necessary, through the so-called droplets of Pflugge, this swine-derived influence spreads to more distance through the air and is very contagious. Among the Italian regions that were most affected by the S-OIV, Campania was leading for incidence of the infection and flu-related fatalities. This can be in part due to the fact that Campania is the most densely populated Italian region, which obviously favors the spreading of the infection. In fact, also at the regional level, the main town Naples, which is the most

densely populated Campania province, had the higher percentage of flu incidence compared with the other provinces. Consistent with the incidence data relative to the whole Italian population the most affected group resulted to be the younger population. This is probably owed to both the higher population density due to the scholarization and to the more promiscuous behaviors. As for the high mortality rates, in our opinion, the data about Campania may appear to be higher than other areas in Italy because Cotugno hospital in Campania has medical specialists qualified to make detailed diagnoses to determine if H1N1 is the main or a co-factor in mortality cases. Similar centers, which are able to compare cases to see if H1N1 is the main or a co-factor of mortality are not so readily available throughout other regions. This means that data from other regions (especially from the South) might not be as accurate as Campania's data. It's also reasonable to suppose that given a lack of capability in many cases to determine a precise diagnosis for the H1N1 virus, it may not always be possible to know when the virus is a main factor or a co-factor in the mortality of a patient [16]. Also, for what it may concern the increased deaths observed in Naples and/or in Campania during the peak of the novel influenza A (H1N1), we can remember the Will Rogers phenomenon because the element being moved (S-OIV infected samples) to the Virology laboratories of the Cotugno Hospital was above the current average of the set it was entering. By definition, adding it to the new set will raise the incidence of H1N1 virus infection and then the mortality average. The analysis of the factors that contribute to higher flu incidence is important not only to address the panic issues among the population but has also implications on the prevention campaign.

The massive campaign for vaccination across Italy helped to stop the spread of the virus, which while not very aggressive, is very contagious. From the first symptoms through convalescence, an episode of H1N1 flu lasts about 10 days. The epidemic itself, however, could possibly last for months, since several human variants of the flu may merge with H1N1 to create a new and possibly more dangerous and harmful viral variant [11,12]. The vaccination against the influence is the most effective method to prevent the illness. From the moment of the isolation of a new flu virus, one must wait for the preparation of a new specific vaccine to be ready for the next influence season in Autumn [17]. The vaccine against the virus prevents the flu in 70-80% of cases. It takes about two to three weeks after the injection to develop antibodies for the virus [18].

Vaccines are free and can be administered by family doctors or pediatricians for children. It is recommended, but not obligatory, for children between 6 months and 2 years of age. The Ministry of Health also provides vaccinations to all hospital- based doctors and medics, blood donors and chronically ill patients up to age 65. The last group of patients who will be vaccinated include healthy people between 6 months and 27 years. The prototype vaccine did not cause any particular collateral damages [19] and only a single dose is necessary for protection [20].

Analysing the risk of Flu for understanding a better prevention

A particularly bad flu is sweeping Italy killing many children so far this season and nearly doubling the hospitalization rate among people over 65 in the past month of February 2015 [21]. The main reason is that the predominant strain of the flu this year is H3N2, a variety that has shown itself in prior years to be more virulent than other kinds. In addition, the vaccine that is supposed to protect against the flu is missing its mark because two-thirds of the H3N2 strains that experts are seeing were not included in this year's flu shot. The vaccine used contains the strain A/Texas/50/2012 that is not the virus now wide spreading in almost the entire country [22]. Flu typically infects 5 to 15 per cent of the population. It can be dangerous for those with weak immune systems, including the elderly and children. In Italy hit by the more virulent flu strain the hospitalization rates among people over 65 are rising sharply going to over 100 for every 100.000 people. The last H3N2 season was in 2012-2013 and the cumulative hospitalization rate among the elderly that season was almost 200 for every 100.000 people. It is a good advice for doctors to give antiviral drugs to patients if they get sick. Of course next flu vaccine will be completed with the H3N2 strain now circulating among people [23].

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