LETTER TO THE EDITOR

Influenza A(H1N1) pandemic: 2 years after

M.F. ALLAM, K.M. ABD ELAZIZ*
Department of Preventive Medicine and Public Health, Faculty of Medicine, University of Cordoba, Spain; * Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Key words

Influenza A • H1N1 • Swine Flu • Pandemic

Dear Sir,

In 2009, the emergence of the new H1N1 influenza virus saw the world brace itself for the first influenza pandemic since 1968. Two years after, it is time to evaluate the situation of that Influenza A(H1N1) pandemic and its combat measures.

First, alert level was raised rapidly from level 3 to level 6 in 6 weeks. On 25 April 2009, the WHO declared a level 3 Influenza Pandemic Alert. Three days after, level 4 alert was declared due to international spread of clusters of human-to-human transmission. The continuous confirmation of new cases in various countries required the WHO to raise the pandemic alert to level 5, less than 1 week after declaring level 3. The maximum alert response was declared on the 11th of June, meanwhile most human infections appeared to be mild [1]. Recent study analysed the records of past influenza outbreaks to determine a definition for pandemics. The authors concluded that defining an influenza pandemic on the early observations may be adequate to declare an alerting response but doesn't assure worldwide spread or excess mortality [2].

Second, the WHO reported an estimate of 22-33% of secondary attack rate among contacts of H1N1 influenza, however chemoprophylaxis was given to contacts without previous studies regarding its effectiveness in outbreaks or epidemics. Contacts received antivirals for 10 days, meanwhile patients with mild and moderate symptoms of influenza received antivirals for only 5 days [3]. A study published in 2009 proved that secondary attack rate among house hold contacts of cases of H1N1 was only 7.6%, which was much lower than the reported figures by the WHO. This study also proved that rates of infection did not differ significantly in those receiving chemoprophylaxis compared to household contacts that didn't receive chemoprophylaxis [4].

Third, use of masks by the general population and in airports proved to be inefficient and unnecessary. It rather gave a sensation of panic and insecurity. A study was done in France to evaluate the use of protective measures in prevention of acute respiratory symptoms for French participating in Hajj of 2009. This study showed that although 79% of the subjects used facemask this didn't significantly reduced the acute respiratory symptoms among them [5]. A recent systemic review evaluated the effectiveness of facemasks in prevention of H1N1 infection and concluded that wearing face masks for infected people could protect others but there are fewer data to support the use of face masks for prevention of H1N1 infection. This review recommended more research on the natural infections in the community to define the effectiveness of facemasks for prevention of influenza virus transmission [6].

Fourth, controls for body temperature in airports did not show to be effective to control the spread of the virus and alerted people more. A study was done to retrospectively assess the feasibility of detecting influenza cases upon relying solely on fever screening. The findings proved that the sensitivity of fever for detecting H1N1-2009 cases upon arrival was estimated to be 22.2% among confirmed H1N1-2009 cases, and 55.6% of the H1N1-2009 cases were under antipyretic medications upon arrival to a Japanese airport [7].

Fifth, the compulsory vaccination campaign for healthcare workers (HCWs) was inefficient and created negative attitude towards the vaccine. Vaccine coverage was very low between HCWs. A recent Italian online survey demonstrated that Influenza A(H1N1) pandemic modified the behaviour of HCWs, however a high percentage did not realize that vaccination is a fundamental means of prevention and how important it was that they get vaccinated [8].

Sixth, in many cases antiviral oseltamivir was used massively to treat cases with mild symptoms of influenza. Many European countries recommended antiviral drugs for treating all patients, even those with mild symptoms. This medically unsupported recommendation alarmed the general population and opened up a debate about the availability of these drugs for the population worldwide if there were to be a sustained influenza A (H1N1) pandemic. Moreover, almost all the strains of H1N1 that circulated in 2008-2009 were resistant to oseltamivir. The incidence rate of resistance among patients varied from 3.6 to 27.6%. This resistance was associated with the development of pneumonia with a statistically significant relative risk of 4.16 in a recent systematic review [9]. The consequences of antiviral resistance could lead to person-to-person transmission with oseltamivir resistant strains of H1N1 influenza virus. This transmission was documented in a recent study in a haematology unit in

the United Kingdom and showed that 50% of the patients inside the unit were infected by direct transmission by the resistant strains of H1N1 Influenza 2009 virus [10].
Lastly, according to the available data on the mortality of cases of Influenza A(H1N1) pandemic it was noticed that the mortality rate in general was very low 1.62% [11]. Mortality rate was quite lower (0.9 per 100.000 inhabitants) among confirmed Argentinean cases aged above 60 years old [12]. These reports confirm that the mistaken perception of virulence was perpetuated which in turn, created irrational fears for both the illness and unfair, uninformed expectations for its remedies.
Lessons from Influenza A(H1N1) pandemic 2009 could help in the development of new protocols and guidelines to control future pandemics.

References

[1] *Global influenza surveillance network: laboratory surveillance and response to pandemic H1N1 2009*. Wkly Epidemiol Report 2009;84(36):361-5.

[2] Potter CW, Jennings R. *A definition for influenza pandemics based on historical records*. J Infect (2011), doi:10.1016/j.jinf.2011.04.013

[3] CDC. *Updated interim recommendations for the use of antiviral medications in the treatment and prevention of influenza for the 2009-2010 season*. Available at: http://www.cdc.gov/h1n1flu/recommendations.htm (Accessed 15 July 2011).

[4] Odaira F, Takahashi H, Toyokawa T, et al. *Assessment of secondary attack rate and effectiveness of antiviral prophylaxis among household contacts in an influenza A(H1N1)v outbreak in Kobe, Japan, May-June 2009*. Euro Surveill 2009;14(35). pii: 19320.

[5] Gautret P, Vu Hai V, Sani S, et al. *Protective measures against acute respiratory symptoms in French pilgrims participating in the Hajj of 2009*. J Travel Med 2011;18:53-5.

[6] Cowling BJ, Zhou Y, Ip DK, et al. *Face masks to prevent transmission of influenza virus: a systematic review*. Epidemiol Infect 2010;138:449-56.

[7] Nishiura H, Kamiya K. *Fever screening during the influenza (H1N1-2009) pandemic at Narita International Airport, Japan*. BMC Infect Dis 2011;11:111.

[8] La Torre G, Di Thiene D, Cadeddu C, et al. *Behaviours regarding preventive measures against pandemic H1N1 influenza among Italian healthcare workers, October 2009*. Euro Surveill 2009;14(49), pii: 19432.

[9] Thorlund K, Awad T, Boivin G, et al. *Systematic review of influenza resistance to the neuraminidase inhibitors*. BMC Infect Dis 2011;11:134.

[10] Moore C, Galiano M, Lackenby A, et al. *Evidence of person-to-person transmission of oseltamivir-resistant pandemic influenza A(H1N1) 2009 virus in a hematology unit*. J Infect Dis 2011;203:18-24.

[11] Swine Flu Count. *Worldwide Statistics of the H1N1 Influenza A pandemic*. Available at: http://www.flucount.org/ (Accessed 15 July 2011).

[12] Roriz-Cruz M, Rosset I, Montero-Odasso M. *Lower mortality from H1N1 influenza in older Argentineans: men more affected*. J Am Geriatr Soc 2010;58:1813-5.

■ Received on September 12, 2011. Accepted on February 1, 2012.

■ Correspondence: Mohamed Farouk Allam, Department of Preventive Medicine and Public Health, Faculty of Medicine, University of Cordoba, avda. Menéndez Pidal, s/n Cordoba 14004, Spain - Tel. +34 957 218 278 - Fax +34 957 218 573 - E-mail: fm2faahm@uco.es

Co-Editor Reply

The 2009/10 pandemic constituted a major test of our understanding of how to utilise the most modern means of prevention of a widespread infectious disease. The pandemic plan drawn up by the World Health Organization was tested in the field, and displayed both merits and limitations.
Basically, the plan aimed to slow down the spread of the pandemic and mitigate its consequences. The first aim was pursued by implementing measures already tested during the SARS outbreak, in order to throw up a sanitary cordon. The limited efficacy of using masks, both as personal protection devices and as a means of protecting others, however, had been known for some time.
A further attempt to prevent the disease from crossing national boundaries was made by measuring the body temperature of travellers at border check-points. Nevertheless, it was well known that the only truly efficacious means would have been to implement protection with a ring prophylaxis using antivirals [1].
For what concerns drugs, it is well known that the virus is able to become resistant, as has been amply demonstrated in the case of the amantadanes [2]. By contrast, with regard to neuroaninidase inhibitors, up until the H1N1v pandemic only sporadic cases of resistance to Oseltamivir had been observed, while Zanamivir, not least on account of its mode of administration, did not seem to give rise to large-scale phenomena of resistance [3]. Clearly, the weakness of the therapy and prevention of influenza is linked to protocols which utilise a single drug.
With regard to vaccination, several logistical problems had to be tackled. These can be summed up as the need to promptly deploy an abundant supply of efficacious

vaccine. In this perspective, the pharmaceutical companies had been preparing themselves since 1997, when a virus lethal to man, namely the H5N1 avian virus, made its appearance on the epidemiological scene [4].
The WHO plan had envisaged since phase 4 that the pharmaceutical companies should initiate production of the vaccine [5]. It is interesting to note that the manufacturers were able to produce a large quantity of suitable vaccine within the required time.
In phase 4, however, it was not possible to predict the true gravity of the H1N1v pandemic, even though cases already appeared to be relatively mild during the "Mexican" pandemic. Indeed, the pandemic of 1918 was characterised in the spring of that year by a first wave with mild clinical symptoms and a benign course, so much so that it was called a 3-day fever. It was the second wave, which began at the end of August and peaked in October-November, that would become the "killer wave".
Thus, in April-May 2009, the lethal potential of the H1N1v virus could not yet be established, as, with the benefit of hindsight, it later was. Starting from the principle that the wisest strategy is to prepare for the worst, a large-scale vaccination campaign was prepared by the developed nations, Italy among them. If any problem did arise, it was caused by the lack of a precise, well-established plan; attempts to adopt a flexible approach ended up by generating disorientation and confusion not only among the public but also, and in the first place, among doctors and other healthcare workers.
First of all, adequate training was not provided for doctors, particularly paediatricians. No less serious was the fact that doctors and other healthcare workers failed to promote vaccination. In addition, the information campaign promoted by the Ministry of Health proved ineffective, as it was principally aimed at avoiding panic in the population. Indeed, the campaign displayed serious lack of truth with regard to the potential risks linked to the spread of the H1N1v virus. Finally, the campaign undertaken by the CODACONS (Consumers' Association) against the purchase of the vaccine by the Ministry of Health was also inappropriate; indeed if the virus had had such mutations as to render it "lethal", as happened in 1918, the purchase of the vaccine would been a very wise decision.
In short, if the vaccine had been used properly, large savings could have been made, in that many cases of disease would have been avoided. Although not severe, these cases have constituted a considerable cost for Italian society [6].

Roberto Gasparini
Co-Editor

References

[1] Lee VJ, Yap J, Cook AR, et al. *Oseltamivir ring prophylaxis for containment of 2009 H1N1 influenza outbreaks*. N Engl J Med 2010;362:2166-74.

[2] WHO. *Points to Consider:Antiviral Drug Resistance*. Available at: http://www.who.int/immunization/sage/Penn_Points_to_consider_on_antiviral_drug_resistance.pdf. Accessed on February 1st 2012.

[3] WHO. *Summary of influenza antiviral susceptibility surveillance findings, September 2010 - March 2011*. Available at: http://www.who.int/influenza/gisrs_laboratory/updates/antiviral_susceptibility/en/. Accessed on February 1st 2012.

[4] Subbarao K, Klimov A, Katz J, et al. *Characterization of an avian influenza A (H5N1) virus isolated from a child with a fatal respiratory illness*. Science 1998;279:393-6.

[5] WHO.*WHO global influenza preparedness plan. The role of WHO and recommendations for national measures before and during pandemics*. World Health Organization 2005. Available at: http://www.who.int/csr/resources/publications/influenza/en/WHO_CDS_CSR_GIP_2005_5.pdf. Accessed on February 1st 2012.

[6] Lai PL, Panatto D, Ansaldi F, et al. *Burden of the 1999-2008 seasonal influenza epidemics in Italy: comparison with the H1N1v (A/California/07/09) pandemic*. Hum Vaccin 2011;7:217-25.