

EDITORIAL

Influenza A / H1N1 Pandemic: The Scare of 2009

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Introduction

The world was taken by surprise with the announcement of a major influenza outbreak resulting in significant mortality in Mexico in late April 2009. The intense world media attention rapidly escalated the efforts of all countries around the world to activate their own respective influenza pandemic preparedness plans. The identification of a new 're-assorted' influenza virus as the source of this rapidly spreading infection fuelled fears that this was the next major influenza pandemic that the world had been warned about. The World Health Organisation (WHO) promptly raised the influenza alert level from 4 to 5 on April 29th, 2009 and finally to the highest level of 6 on June 10th, 2009.

On the local front, much discussion has taken place (in both print and electronic media) on the measures taken by the various agencies on the front line of this outbreak. While there are some who feel that too much is being done, so much so that everyday activities are being hampered, there is probably an equally sizeable group in our population who feel that the measures taken have been insufficient. During an outbreak, especially one of global magnitude, many forces influence our reactions to the perceived threat. The operative word here is perceived, and perception is a heterogeneous entity that is governed by myriad factors. Hence, it is imperative that our reactions be as evidence-based as possible. Our responses should therefore always be based on sound science. At the same time, they must be guided by common sense and a clear understanding of local realities, both of our strengths and our limitations.

Influenza A / H1N1 2009: The Science

Infectiousness And Severity

Within the first weeks of the outbreak, it was clear that this novel influenza A/H1N1 virus is extremely infectious. It has a secondary attack rate of 22 to 33%, which is significantly higher than that of seasonal flu, which is estimated at 5 to 15%. This is likely due to the lack of immunity in

humankind to this novel virus. The initial reports of 'high' mortality from Mexico have not been reported in other countries. The reasons for this are likely multiple, but they may include complex heterogeneity in the degree of immunity in local populations to circulating influenza strains, as well as transmission factors such as geographic conditions, social mixing and local seasonal changes, etc. The global case fatality rate as of July 15th, 2009 stands at 0.45% (with varying rates in different countries; e.g., Argentina 1.7%, Mexico 1.1%, USA 0.5% and Canada 0.31%).

Clinical Manifestations

The clinical characteristics of this novel influenza virus appear to be similar to those of seasonal strains with some minor differences. From the early patient cohorts in Mexico, the United States of America and the United Kingdom, it became apparent that 25–30% of patients with influenza A/H1N1 had diarrhoea and/or vomiting as one of their main symptoms. However, this has not been seen universally. In Malaysia, less than 5% of all patients admitted to the Sungai Buloh Hospital had these symptoms. Most patients had mild self-limiting symptoms. Common presenting symptoms include fever (94%), cough (92%), sore throat (66%), headaches (38–81%), rhinorrhoea (27%), arthralgia (56%), diarrhoea (25%) and vomiting (25%) (1,2,3). Nonetheless, patients with certain risk factors or co-morbidities were more likely to experience influenza-associated complications, the most frequent of which was pneumonia (either primary viral pneumonia or secondary bacterial pneumonia). The other noted complications include myocarditis, encephalitis, persistent diarrhoea and shock. Patients who are at risk for severe complications of influenza A H1N1 infection include but may not be limited to the following groups: children under the age of 5 years; adults 65 years of age or older; persons of any age with an underlying chronic medical condition such as chronic respiratory disease (asthma, chronic obstructive pulmonary disease, obstructive sleep apnoea, etc.), chronic renal disease, diabetes mellitus, an immunosuppressed condition (e.g.,

those with HIV infection) or malignancy; those on chemotherapy or long-term steroid treatment; and pregnant women.

In a cohort analysis of 642 influenza A/H1N1-infected patients in the US (1) from April 15th to May 5th, 2009 the Novel Swine-Origin Influenza A (H1N1) virus Investigation Team reported that only 9% of these patients required hospitalisation, and 54% of those admitted had co-morbidities that conferred an increased risk. There were eight intensive care admissions with two deaths. None of the patients, however, were 65 years of age or older.

Modes Of Transmission

The modes of transmission of this novel virus in humans are thought to be mainly through the dissemination of large droplets and possibly small-particle droplet nuclei expelled when an infected person coughs. There is also potential for transmission through contact with fomites that are contaminated with respiratory or gastrointestinal material. Since many patients with influenza A H1N1 infection have had diarrhoea, the potential for faecal viral shedding and subsequent faecal-oral transmission should also be considered.

The incubation period appears to range from two to seven days. On the basis of data regarding viral shedding from seasonal influenza, most patients with influenza A/H1N1 infections are likely to shed virus starting from one day before the onset of symptoms through five to seven days after the onset of symptoms or until symptoms resolve; in young children and in immunocompromised or severely ill patients, the infectious period might be longer. The potential for persons with asymptomatic infection to be the source of infection to others is still uncertain; nonetheless, as for other influenza viruses, viral shedding is frequently highest during the period of fever and acute respiratory symptoms.

Antiviral Therapy

During the 2008–2009 influenza season, almost all circulating human (H1N1) viruses (seasonal influenza) in the United States were resistant to oseltamivir. However, genetic and phenotypic analyses indicate that the novel influenza A H1N1 2009 virus is susceptible to oseltamivir and zanamivir but resistant to the adamantanes. However, this should be taken in the context of the announcement from WHO of oseltamivir resistance in three patients from Denmark, Japan and Hong Kong on July 8th. In light of this latest report, prudence should be applied in our use of these antivirals. As of July 8th, 2009 the Ministry of Health in Malaysia has

recommended that given the severity of illness observed among some patients with influenza A H1N1 infection, therapy with neuraminidase inhibitors should be prioritised for hospitalised patients (i.e., those with moderate to severe illness) with suspected or confirmed infections.

Mitigating The Influenza A / H1N1 2009 Pandemic

While the initial endeavours from the Malaysian Ministry of Health (the lead agency in our nation's response) was centred around containment, it is also spelt out in the National Influenza Pandemic Preparedness Plan (NIPPP) that as the number of cases increases, mitigation strategies may have to be applied. Containment as defined by many international agencies is merely an attempt to delay the initial spread of the virus in the local population. Its goal is to dampen the sharp rise in cases and prevent a sustained overwhelming demand on the healthcare system. A rapid upsurge of cases in any given community could also negatively impact essential services and the economy.

Mitigation is a collective term recommended by WHO for actions taken in countries in phases 5 and 6 of pandemic alert to reduce the impact of the pandemic (4)

The mitigation measures taken by the Malaysian Ministry of Health are centred around the following objectives:

- reducing transmission
- ensuring healthcare for those who may be infected
- maximizing care for those with disease
- protecting the most vulnerable
- ensuring the continuance of essential services and minimizing the pandemic's impact on the country's socio-economic development

Preventing the introduction of infected visitors through vigorous case-finding, as well as active contact tracing, can be a legitimate initial measure by which countries can delay the introduction of the virus into the local population. However, to be effective, this strategy needs to be comprehensively implemented, and it must target incoming travellers from all areas of sustained community transmission. To sustain these intensive efforts over any prolonged period of time would require huge amounts of resources; both in personnel and finances. Such efforts have to be made in conjunction with surveillance for local transmission, especially of those infections that cannot be linked to another case.

In Malaysia, the first case, which was a Malaysian student returning from the US, was detected on May 15th, 2009. This was followed by a constant flow of imported cases from various countries with contained local transmission until June 16th, 2009 when we reported our first case involving local transmission. This was soon followed by multiple clusters in schools, which all involved cases returning from abroad with the infection. As of July 14th, 2009 the Ministry of Health has confirmed 804 cases, with 555 (69%) imported cases and 249 (31%) involving local transmission. It is expected that the number of cases involving local transmission will continue to rise substantially. It was evident by early July that local transmission was already established in this country, and this triggered our move towards mitigation.

Moving away from a containment strategy toward a mitigation strategy mainly involves giving up public health measures actively targeting incoming travellers from affected areas and not actively pursuing case-finding outside of groups at higher risk of experiencing severe disease. Such scaling down of the delaying strategy could be phased in over a certain period (4). A mitigation strategy would focus on the following strategies:

- Providing the public, including incoming travelers, with relevant information
- Promoting self isolation of symptomatic persons and treatment according to national protocols, with special consideration given to non-nationals visiting the country (enforced quarantine and contact tracing are no longer routine procedures)
- Ensuring early treatment of all those in a country developing illness according to national policies. In Malaysia, H1N1 screening, hospitalization and antiviral therapy is recommended for those with moderate to severe illness
- Improving public hygiene and infection control in health institutions

The next phase of the pandemic will involve the much-awaited influenza A/H1N1 vaccine, which is expected in the last quarter of 2009. How the world will coordinate this enormous undertaking will be a test of its resolve to keep public health principles, ethics and humanitarian values above politics and business. We live in interesting times and there can be little doubt that we still have a lot to learn about this virus and about ourselves from this pandemic.

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