

## **Editorial**

### **H1N1 2009 in Karachi: A situational analysis**

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The novel H1N1 influenza A, also known as Swine Flu, first emerged in Mexico in March 2009, when the Government of Mexico reported increasing cases of Influenza-Like Illness (ILI).<sup>1,2</sup> By April, more than 854 cases of pneumonia with 59 deaths were recorded. On the 24th of April 2009, the United States Government reported seven human cases of what was thought to be Swine Influenza in California. Twelve of the 18 laboratory confirmed Mexican cases were found to be genetically identical to this virus,<sup>1</sup> which emerged as a consequence of a series of viral coinfections in pigs leading to gene reassortment between human, avian and two strains of swine influenza A viruses.<sup>3</sup> As opposed to the seasonal H1N1, this novel influenza virus was unique not only in the continent of origin (North America, not Asia), the season of origin (spring, not late fall), but also the cohort at risk for infection and death (children and young adults, not infants and the elderly).<sup>4</sup> Moreover, this virus had not been previously detected in animals or humans and the geographical spread of multiple community outbreaks along with the somewhat unusual age groups affected, all portended a pandemic. As the infection spread, however, it became apparent that the virus was in actuality a new strain of the human influenza virus and not a swine influenza virus and the name was changed to 2009 Pandemic influenza A H1N1 virus or simply 2009 H1N1 Influenza virus.<sup>5</sup>

As predicted, the number of cases and the number of countries affected rose sharply and by July 2009, the WHO officially declared that the world was in the midst of a novel H1N1 influenza pandemic. Since then there have been more than 622482 cases as of November 2009 and 13554 deaths as of January 2010. However, as a number of regions have stopped reporting the number of cases and deaths, the actual numbers are likely to far exceed these estimates. In countries where outbreaks have occurred, obesity and pregnancy<sup>6,7</sup> have been reported as risk factors for admission to an intensive care unit (ICU). Diarrhoea has been documented in up to 20% and fever in up to 85% of inpatients. However, fever was absent in

as many as 50% of outpatients and nearly three quarters of the patients had one or more underlying medical conditions.<sup>6</sup>

Karachi saw its first four confirmed cases of novel H1N1 in June 2009. All four were young individuals in their teens and had a history of recent travel to the US, where they developed ILI. The symptoms were mild and they recovered without antiviral treatment. Between June and November, there was only one more case of laboratory confirmed novel H1N1 influenza A. Similar to the prior cases, this 63 year old gentleman, who had presented in August, also had a history of recent travel (this time to Singapore). He made a full recovery after 5 days of Oseltamivir. In early October and November, the number of ILI cases rose suddenly. The symptoms of myalgia, sore throat, non-productive cough, fever, chills, headache and fatigue were non-specific and clinically indistinguishable from the ongoing seasonal Dengue fever outbreak, which was one reason for delays in diagnosis. Similarly, as reported from other affected countries,<sup>8</sup> as opposed to the seasonal influenza, vomiting and diarrhoea was also noted to be a common feature in our patients. Other signs of increased influenza activity in the community were also present including an increase in the number of Emergency Room visits with respiratory complaints as well as an increase in the number of admissions due to severe respiratory disease. Most of these patients were not tested for the novel H1N1, however, in a cluster of individuals (total number in excess of 50) 12 could be tested and 6 were confirmed positive with H1N1. Following this, in December, the number of cases reported by the laboratory at the Aga Khan University Hospital increased dramatically. Interestingly, this occurred almost immediately after the lay press reported that H1N1 cases were on the rise in Karachi. Hence this increase may actually represent better case detection due to increased awareness, as opposed to an actual rise in the number of individuals infected in the city. Nonetheless, the numbers of ILI cases have continued to increase and by the end of January, 2010 those which have tested positive for H1N1

stand in excess of 80 in Karachi alone.

It is important to note that laboratory diagnosis depends on nucleic acid amplification of H1N1 virus through real time reverse transcriptase polymerase chain reaction (rRT-PCR)<sup>9</sup> which is available at two centers in the country: NIH Islamabad and the Aga Khan University Hospital, Karachi. However, most patients with clinical illness consistent with uncomplicated influenza who reside in an area where influenza viruses are circulating do not require diagnostic influenza testing for clinical management. Only patients who are hospitalized with suspected H1N1 infection or in whom a diagnosis of influenza will modify decisions regarding clinical care (for example in individuals at risk of developing severe disease such as pregnant women, children less than 2 years or those with chronic medical problems) need to be tested.<sup>9</sup> Therefore, the number of patients infected with H1N1 flu reported by the press is subject to a severe selection bias as most cases are mild and go undetected.

Most cases of ILI in Karachi (proven to be H1N1 or otherwise) have been mild and self limiting. While a total of 7 deaths (personal communication, Sindh focal person for swine flu) have been reported from Karachi alone, in the absence of an accurate denominator (i.e. the total number of infected), estimating mortality rates is impossible. According to a press release<sup>10</sup> the official figure of confirmed H1N1 cases for Pakistan stands at 168 out of total 650 suspected cases, which were tested at National Institute of Health (NIH) Islamabad with 14 deaths. This figure does not take into account 80 confirmed cases and 7 deaths from Karachi.

Under the current circumstances, mortality data, not only from Pakistan but also from other parts of the world should be viewed with caution. When testing confirms H1N1 infection in patients with underlying medical conditions, many doctors record these deaths as due to the medical condition, and not to the pandemic virus. These cases are also missed in official statistics. Moreover, in Pakistan and also in a large number of other developing countries, most deaths are neither investigated nor certified in terms of the cause.<sup>11</sup> Finally, accurate test results will also depend on availability, cost and how and when samples were taken. These factors coupled with the lack of a national Flu surveillance system makes it unlikely that accurate figures regarding the burden of H1N1 and the mortality rate from H1N1 in Pakistan will be forthcoming. When we look at other countries, the overall estimated case fatality rate in the UK has been 26 (range 11-66) per 100 000<sup>12</sup> and in the US, 20 per 100 000.<sup>13</sup>

The antiviral agents which are effective against the current H1N1 pandemic strain such as Oseltamivir and Zanamivir may be partly responsible for these low rates. However, viewed statistically, mortality in this pandemic compares favourably with 20th century influenza pandemics

and for the most part the infection seems to be mild.<sup>6</sup> Treatment for most cases is therefore not recommended and is limited only to those with severe disease or those who are at risk of developing severe disease (see above). When a decision is made to use antiviral treatment for influenza, however, it should be initiated as soon as possible and without waiting for test results as antiviral treatment is most effective when administered within 48 hours of onset of symptoms.<sup>14</sup> However, studies have shown that hospitalized patients still benefit when treatment is started with Oseltamivir more than 48 hours after the onset of illness.<sup>15</sup> These recommendations have recently been questioned. A team of Cochrane reviewers surveyed the literature on efficacy of Oseltamivir and Zanamivir and from 8 acceptable prophylaxis trials and 12 acceptable treatment trials found that for pre- or postexposure prophylaxis against influenza, both drugs were mildly effective. For treatment, both drugs shortened duration of symptomatic influenza by 12 to 24 hours if taken early in infection. The reviewers reported difficulty in evaluating the data supporting Oseltamivir's claimed ability to prevent complications of influenza.<sup>16</sup>

Globally, questions have been raised about how severe the pandemic would be and whether hospitals would have sufficient surge capacity. This is an important consideration for hospitals in Pakistan, since we are in the middle of an outbreak and no one should be complacent about an unpredictable virus which is capable of killing children and young adults in their prime.<sup>4</sup> A lower population impact than previous pandemics, however, is not a justification for public health inaction. With the influenza H1N1 2009 pandemic finally here, the only reliable means of preventing infection is the vaccine. This unfortunately remains in short supply and is not expected to become available in Pakistan before the end of January 2010 (or later). Once this arrives, priority should be given to high risk groups only (i.e. health care workers, pregnant women, immunocompromised individuals, and young children. Adherence to Infection Control practices in the hospital is paramount and depends heavily on respiratory etiquette, hand hygiene, and avoiding close contact with sick people. People with ILI should be instructed to keep their hands clean and stay at home for at least 24 hours after resolution of fever and should stay away from people at high risk for severe infection, e.g. pregnant women, young children, those with chronic medical conditions and suppressed immunity.

As clinicians, the onus therefore falls on us to help our patients comprehend the often sensationalized news in the lay press regarding H1N1 by emphasizing the relatively mild nature of the disease in most individuals and the limited need for testing and treatment. As always, simple precautions both in the hospital and home will suffice in preventing this infection from spreading further.

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