

2009 Pandemic Influenza H1N1: Paediatric Perspectives

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Abstract

Children, especially those younger than 5 years of age and those with chronic medical conditions, such as respiratory diseases, neurological diseases, immunosuppression, receiving long-term aspirin therapy, obesity or co-infection with bacteria, are at an increased risk of pandemic H1N1 infection-related complications. This paper reviews the underlying medical conditions associated with death or complications of pandemic H1N1 infection in children.

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Introduction

The pandemic H1N1 influenza virus, containing genes from avian, human and swine influenza viruses, emerged in North America, and caused illness in more than 190 countries and resulted in more than 4500 deaths worldwide.¹⁻⁴ According to Taiwan Centres for Disease Control (Taiwan CDC) data, among 2,089 typed influenza isolates from June 1 to October 10 in 2009, 1,805 (87%) were pandemic H1N1.⁵ Transmissibility of pandemic H1N1 infection is substantially higher than that of seasonal flu, less than that seen in the 1918 influenza pandemic, and comparable with that seen in the 1957 pandemic.⁶

Between April 15 and May 5 2009, a total of 642 confirmed cases of pandemic H1N1 infection were identified in 41 states in the United States of America (USA).⁷ The finding that 60% of patients were 18 years of age or younger suggests that children and young adults may be more susceptible to pandemic H1N1 infection than are older persons.^{7,8} Clinical attack rates in children were also found twice that in adults (<15 years of age: 61%; ≥15 years: 29%).⁶ Likely, among 175 severe cases with pandemic H1N1 infection in Taiwan up to September 11 in 2009, 82 patients (47%) were ≤18 years.⁵ Therefore, USA, Finland and Mexico recommended pandemic H1N1 vaccination for children.^{9,10}

Because sensitivities of rapid influenza-diagnostic tests are low, it is important to analyse risk factors of pandemic H1N1 infection to remind us of giving suspected patients, who had these risk factors, antiviral medication and critical care as soon as possible.^{11,12}

As of 8 August 2009, Centre for Disease Control and Prevention in the USA (US CDC) had received reports of 477 deaths associated with pandemic H1N1.¹³ Of 36 children who died, 7 (19%) were aged less than 5 years, and 24 (67%) had one or more of the high-risk medical conditions.¹³ Twenty-two (92%) of the 24 children with high-risk medical conditions had neurodevelopmental conditions.¹³ Of the 122 hospitalised paediatric patients who were infected with pandemic H1N1 in the USA (from April to June), 60% of children had an underlying medical condition.¹⁴ Critically ill children in 4 United Kingdom (UK) intensive-care units with 2009 pandemic H1N1 infection were summarised, and most cases have occurred with known co-morbidities, including chronic lung disorders and immunodeficiency.¹⁵ As of 29 December 2009, 30 patients with pandemic H1N1 infection expired in Taiwan. Six (20%) were paediatric patients, including 3 with seizure or cerebral palsy, 2 with pneumonia and 1 with obesity.⁵ We compared the paediatric patients with complicated pandemic H1N1 infections in Taiwan with those in USA, UK, Australia, Mexico and elsewhere, and reviewed the literature on risk factors for complications in children (Table 1).

Children Aged Younger than 5 Years

Seven (19%) of 36 children who died in the USA in 2009 were aged less than 5 years.¹³ Similarly, 32 (18%) of 175 severe cases with pandemic H1N1 infection in Taiwan were younger than 6 years old. The risk of influenza-associated hospitalisations in healthy children younger than 2 years

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Table 1. Comparison of Paediatric Patients with Different Risk Factors who had Complicated Pandemic H1N1 Infection in the USA, UK and Taiwan.^{5,13-15}

Risk factor	USA (death, n = 36)	USA (hospitalised, n = 122)	UK (critically ill, n = 13)	Taiwan (death, n = 6)
Neurological diseases	22 (61.1%) developmental delay or cerebral palsy	40 (33%) neurocognitive disorder (14), neuromuscular disorder (13), seizure disorder (13)	5 (38.5%) cerebral palsy (3), epilepsy (2)	3 (50.0%) seizure (1), developmental delay (1), cerebral palsy (1)
Respiratory diseases	10 (27.8%) chronic pulmonary conditions	35 (29%) asthma	12 (92.3%) lung disorders	2 (33.3%) pneumonia
Obesity	Not described	Not described	Not described	1 (16.7%)

old is found equal to or greater than the risk of other high-risk groups.¹⁶ In the USA, the hospitalisation rate for laboratory-confirmed pandemic H1N1 infection among children younger than 2 years old was 2.5 times higher than the rate for children aged 2 to 4 years old, which had slightly (20%) higher rates of hospitalisation compared with children aged 5 to 17 years old.¹⁶ In studies of seasonal influenza, the risk for hospitalisation was also highest for infants, with the risk decreasing as age increased.¹⁶

Neurological Diseases

Of 36 children with pandemic H1N1 infection who died in the USA, 22 (61.1%) had neurodevelopmental conditions, such as developmental delay or cerebral palsy.¹³ From data of 122 hospitalised paediatric patients in the USA, 14 (11%) had neurocognitive disorders, 13 (11%) had neuromuscular disorders and 13 (11%) had seizure disorder.¹⁴ According to data of 13 critically ill children in the UK with pandemic H1N1 infection, 5 had neural disease, including cerebral palsy (3) and epilepsy (2), and 3 of them died among a total of 4 mortal children.¹⁵

In Taiwan, 3 mortalities were recorded.⁵ One 10-year-old girl with chronic seizure since 5 months old was infected by pandemic H1N1. She presented with fever and seizure and it resulted in death within a day because of cardiopulmonary failure. One 8-year-old girl had cerebral palsy. Another 10-year-old boy had a pre-existing multiple developmental delay which was complicated with pneumonia.

Pneumonia and Chronic Respiratory Diseases

Lister et al¹⁵ reported of 13 critically ill children in the UK with pandemic H1N1 infection where 12 progressed with lung disorders, including increased infiltrates and dyspnoea. From 24 March to 29 April in Mexico, a total of 2155 cases of severe pneumonia, involving 821 hospitalisations and 100 deaths, were reported. Much higher rates of death (87%) and severe pneumonia (71%) were found in pandemic H1N1

influenza-infected patients between the ages of 5 and 59 years old, as compared with average rates of 17% and 32%, respectively, in that age group during the referent periods of influenza seasons from 2006 through 2008.¹⁷ Perez-Padilla et al¹⁸ reported that among 18 patients with pneumonia and pandemic H1N1 influenza infection complicated by respiratory failure in Mexico, there were only 2 children: one was 5 years old and the other 15 years old but both of them expired. Data from the US CDC indicated that 10 (28%) had chronic pulmonary conditions.¹¹ According to the data of 30 hospitalised patients with pandemic H1N1 infection in California from April to May, 11 patients (37%) had chronic lung disease, such as asthma and chronic obstructive pulmonary disease.¹⁹ Jain et al¹² reported that among 122 hospitalised paediatric patients with pandemic H1N1 infection in the USA, 35 (29%) had asthma. Of the 249 patients who underwent chest radiography on admission, 100 (40%) had findings consistent with pneumonia.¹² The rapidly progressing course of pandemic H1N1 infection and respiratory distress were targeted for early inpatient-based treatment with antiviral drugs and carefully followed-up in Australia.²⁰ In Taiwan, a 6-year-old girl and a 10-year-old boy with pandemic H1N1 infection were complicated with pneumonia and ended up with death.⁵

Immunosuppression

This group includes those caused by medications or by HIV. Data from the US CDC indicated that among 36 children who died, 2 (6%) had immunosuppression.¹³ From the data of 122 hospitalised paediatric patients who were infected by pandemic H1N1 in the USA, 11 (9%) had immunosuppression.¹²

Obesity

The US CDC reported that among 10 critically ill intensive-care patients with severe pandemic H1N1 infection in Michigan, 9 were obese (body mass index [BMI]

≥ 30), including 7 who were extremely obese ($\text{BMI} \geq 40$).²¹ From the data of 601 critically ill intensive-care patients with severe pandemic H1N1 infection in Australia and New Zealand, 172 patients were obese ($[\text{BMI}] \geq 35$).²² These results suggest that morbidly obese people (BMI equal to or greater than 40) and obese people (BMI 30 to 39) may be at an increased risk of hospitalisation and death if they were infected with pandemic H1N1. Obese patients often have underlying conditions that put them at an increased risk for complications of pandemic H1N1 infection, such as chronic respiratory illness, diabetes or liver disease. In Taiwan, among 50 paediatric patients with severe pandemic H1N1 infection between 2 July and 29 August 2009, 8 (16%) were obese and 1 of them had mortality.⁵

Other High-risk Medical Conditions

Other co-morbidities, such as cardiovascular, renal, hepatic, haematological or metabolic disorders were also mentioned. According to data from the US CDC, among 36 children who died, 3 (8%) had congenital heart disease and 2 (6%) had metabolic or endocrine conditions.¹³ Among 13 critically ill children in the UK, 1 child had acute myeloid leukaemia, 1 had severe ketoacidosis due to the newly diagnosed diabetes mellitus, 1 had sickle cell crisis due to pre-existing sickle-cell disease.¹⁵ Among 122 hospitalised paediatric patients with pandemic H1N1 in the USA, 5 (4%) had chronic cardiovascular disease, 7 (6%) had chronic renal disease and 3 (2%) had diabetes.¹⁴ In Taiwan, chronic kidney disease was found more frequently in patients with respiratory failure than those without ($P = 0.04$).⁵

Co-infection with Bacteria

Of the 23 children with culture or pathology results reported from the US CDC, 10 (43%) had a laboratory-confirmed bacterial co-infection, including *Staphylococcus aureus* (5, including 3 methicillin-resistant *S. aureus*), *Streptococcus pneumoniae* (3), *Streptococcus pyogenes* (1) and *Streptococcus constellatus* (1).¹³ Among 689 critically ill intensive-care patients with severe pandemic H1N1 infection in Australia and New Zealand, 140 (20.3%) had secondary bacterial pneumonia.²² Clinicians also should be aware of the potential risk of severe bacterial co-infections among children with influenza and treat them with empirical antibiotics accordingly.

Conclusion

Early empiric treatment with oseltamivir or zanamivir and hospitalisation should be considered for children with suspected or confirmed pandemic H1N1 infection if they have a higher risk for complications, including younger age, chronic respiratory diseases, chronic neurological diseases, immunosuppression, receiving long-term aspirin therapy and obesity. If the clinical course is complicated

with pneumonia, seizure or bacterial co-infection, given a higher mortality rate, intensive care for these children is necessary.

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