Epidemiological and clinical characteristics of influenza A(H1N1)v infection in children: The first 45 cases in Cyprus, June – August 2009

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Following the first imported case in a tourist in Cyprus on 2 June 2009, the influenza A(H1N1)v virus has spread on the island affecting mainly young adults and children. We describe here the first 45 cases in children. Fever, cough, rhinorrhoea and sore throat were the most common symptoms of infection. Half of the children had fever for one day or only for a few hours. Five children were hospitalised, and overall their symptoms were mild. Adherence to oseltamivir treatment was very high, with low frequency of gastrointestinal side effects such as nausea and vomiting. Camping places and summer schools played a significant role in spreading the infection among children of school age.

Introduction

Despite the rapid spread of the pandemic influenza A(H1N1)v virus [1,2], most cases did not have a serious course of disease. About 2-5% of people with laboratory-confirmed infection needed hospitalisation in the United States (US) and Canada [3]. Between half and two thirds of hospitalised cases had co-morbidities such as asthma, other chronic pulmonary disease, diabetes, and autoimmune disorders [3,4]. Fatalities due to pandemic H1N1 influenza have also occurred [5].

Based on seasonal influenza data, children under the age of five years and especially those under the age of two years, as well as those with underlying chronic conditions are at substantially higher risk of hospitalisation compared to older or otherwise healthy children. Pulmonary complications such as bronchitis or pneumonia, neurological complications (e.g. encephalitis or encephalopathy) or a sepsis-like syndrome in neonates have been reported even in previously healthy children [6]. Recent data support the development of neurological complications in children in association with the influenza A(H1N1)v infection in the US [7]. These data as well as the uncertainties about the severity of the evolving epidemic among children resulted in an Emergency Use Authorization decision of the US Food and Drug Administration supporting the use of the neuraminidase inhibitor oseltamivir during the current epidemic even for children under the age of one year [8].

On 2 June 2009, the first confirmed case of pandemic H1N1 influenza was reported in Cyprus. Here we describe the epidemiological and clinical characteristics of the first 45 cases of influenza A(H1N1)v virus infection among children under the age of 16 years, seen at the Archbishop Makarios Hospital in Nicosia.

Methods

Definitions of suspected, probable and confirmed cases were issued by the Department of Medical and Public Health Services at the Ministry of Health (MOH) in accordance with those issued by international organisations. All cases under 16 years of age seen from 4 July to 6 August 2009 at the Archbishop Makarios Hospital (AMH) in Nicosia are described. The AMH is the only referral hospital for mother and child care in Cyprus. For each child examined or admitted to the AMH, a questionnaire was obtained with information on age, residence, possible epidemiological link to A(H1N1)v influenza cases, symptoms, underlying risk factors for severe disease, treatment with oseltamivir and follow-up. Diagnosis was confirmed by testing respiratory samples (nasopharyngeal and pharyngeal swabs) with RT-PCR with specific primers for influenza A(H1N1)v virus. Cases were reported to the Department of Medical and Public Health Services with demographic information as well as clinical details.

Results

The first paediatric case was a 15 year-old boy who developed symptoms on 2 July 2009. He was a household contact of his older sister who had developed influenza-like illness after spending her holidays at a tourist resort in Cyprus. A few days later the third sibling also fell ill with similar symptoms. Two of the children tested positive for influenza A(H1N1)v virus in their respiratory secretions. By 6 August, a total of 45 laboratory-confirmed cases, all 15 years-old or younger, had been detected (Figure 1).

The confirmed cases were between 40 days and 15 years-old with a median age of nine years (Figure 2). Ten of these cases were five years-old or younger and four of them were under the age of one year.

Table

Clinical findings in children with laboratory confirmed influenza A(H1N1)v virus infection

Symptom	Number of children / all children for whom this information was available	(%)
Fever	44/45	98
Cough	43/45	96
Rhinorrhoea	34/43	79
Vomiting	8/39	21
Diarrhoea	7/40	18
Conjunctivitis	3/45	7
Sore Throat*	25/34	73
Malaise*	21/31	68
Headache*	17/30	57
Arthralgia*	8/34	24

* assessed in children over the age of five years (n=35)

Figure 1

Cases of laboratory-confirmed influenza A(H1N1)v in children, by day of symptom onset, Cyprus, 2 July – 6 August 2009 (n=45)

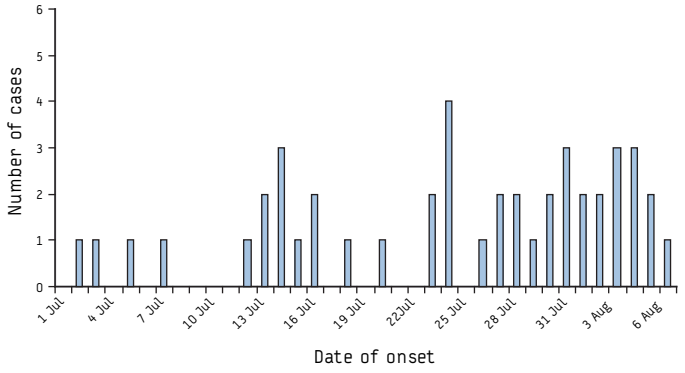
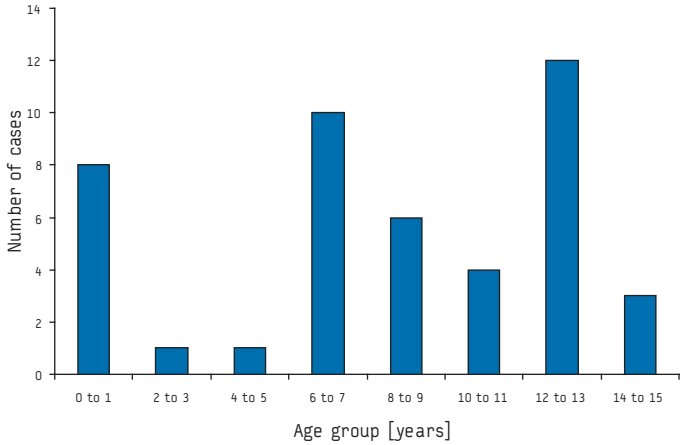


Figure 2

Cases of laboratory-confirmed influenza A(H1N1)v in children, by age group, Cyprus, 2 July-6 August 2009 (n=45)



As of 20 August 2009, no influenza-related fatalities have occurred in Cyprus. Five of the children were hospitalised, one due to very young age (40 days-old), one because of mild complicating pneumonia, and the remaining three children because of concurrent problems not necessarily related to influenza. Mean duration of hospitalisation was 3.4 days (range 1-7 days). Only two of the hospitalised children required treatment with oseltamivir. None of the hospitalised children had underlying chronic diseases.

Only three of the children diagnosed with influenza A(H1N1) v virus infection had underlying risk factors for severe influenza infection, all of them chronic asthma. One of them was additionally obese. All three received oseltamivir and made a quick recovery.

Cases generally presented with symptoms typical of influenza infection as described in the Table. Subjective symptoms such as headache or sore throat were only assessed in over five year-olds. Half of the 34 children with complete fever information had fever for only one day, in nine children the fever lasted for two days, and in eight cases it lasted for three or more days. The median duration of fever in laboratory-confirmed cases was one day.

Fourteen confirmed cases were linked to an index case though their household or a close friend, two of them were travel-related and the remaining 26 cases were linked to six different clusters. For three cases no epidemiological link could be identified. The six clusters were related to camping places (three clusters), summer schools (two clusters) and a handball team that had visited Italy (4 cases). In seven out of 10 cases in children under five years, the transmission was related to household members. For the remaining three, one was associated with family travel, one with a summer school cluster, while the transmission link for the last was unknown.

Policy for the management of cases and contacts

During the first few weeks of the outbreak, oseltamivir treatment was given to all suspected, possible and confirmed cases until confirmatory laboratory results were available. Contacts were traced and offered antiviral prophylaxis. Suspected, probable and confirmed cases were requested to stay at home and avoid contact with other people for at least seven days. Following new guidance from the Ministry of Health on 22 July 2009, treatment with oseltamivir was not offered to every paediatric case but only given to children who had severe symptoms or were up to five years old, and to those with an underlying risk factor that could contribute to severe disease. Furthermore, since no prophylaxis was given to the contacts, contact tracing for index cases was abandoned and only household members and close friends were advised to seek medical advice in case of fever or respiratory symptoms.

Treatment with oseltamivir, compliance and side effects

Nineteen of the confirmed cases were treated with oseltamivir. Seven children received oseltamivir because of the initial 'treatment for all' policy before 22 July 2009, three because of underlying chronic asthma, four because of persistent fever more than five days or because of complicating pneumonia, and five children because of their very young age (under two years-old). Compliance was assessed by telephone interviews during the follow up assessment of confirmed cases. Fifteen of 17 contacted parents reported that their child had taken the full course of treatment as prescribed. Only two of those who received the medication presented with side effects. Both of them developed gastrointestinal symptoms such as vomiting and nausea. In one of those cases vomiting was so severe that the antiviral treatment was discontinued. No children developed stomach pain or neuropsychiatric side effects.

Discussion

The H1N1 influenza pandemic started late in Cyprus as the first case was detected on 2 June. After the first case however, the disease spread quickly, initially among younger people who visited tourist resorts and entertainment clubs or school-aged children who stayed at camping places or summer schools. Most children of preschool age as well as infants and toddlers, who represent 22% of our cases, acquired the infection mainly through household contacts. Similar rates of household transmission were noted in the first descriptions of the outbreak in the United Kingdom (UK), although the UK rates were not based only on infants and toddlers [9].

The incidence rate of gastrointestinal symptoms such as diarrhoea among confirmed cases in children was found to be 17%. It is difficult to compare with similar series in other countries as no other paediatric series has been published as yet. In series not differentiating children, the frequency of diarrhoea ranged from 3% in Germany to 28% in the UK [9,10].

As observed elsewhere [11,12], the course of disease in our patients appeared to be mild, as half of them had fever for a maximum of one day. Despite the fact that five of the children in our series were hospitalised, only one of them had mild pneumonia as a complication related to influenza. The other children were mostly admitted for monitoring.

Compliance with oseltamivir treatment in our study was high with over 80%. Furthermore, the rate of side effects, two of 19 cases, was low. The only side effects seen in the children were nausea and vomiting, the most common side effects reported in the literature [13,14]. In a recent study on school-age children in the UK, who received oseltamivir for influenza prophylaxis, the rate of adverse effects was much higher, since 40% of the students developed gastrointestinal symptoms, and 18% had mild neuropsychiatric side effects such as poor concentration, sleeping problems, bad dreams and strange behaviour [15]. No patient in our series presented with any kind of neuropsychiatric side effects as described in that report.

Our study's limitations include the possibility that paediatric cases in the Nicosia district might have been underdiagnosed, since many children with viral upper respiratory illness and strong epidemiological link to influenza cases, including children who became ill in summer camps, did not visit the hospital for assessment, but preferred to visit their private family paediatricians. In addition, patients were only considered suspected cases and were tested for the influenza A(H1N1)v virus if they fulfilled the strict definition of suspected case and therefore fever was a necessary prerequisite. All but one case of confirmed influenza infection in our series (98%) had fever, whereas in various reports from other countries, fever was present in 90 to 95% of cases [4,9]. Finally, the number of patients with pandemic H1N1 influenza in Cyprus is relatively small in comparison to the number of cases reported in other countries. Therefore, our conclusions regarding the severity of the illness may change as the number of cases increases.

Conclusion

Influenza A(H1N1)v virus infection has spread rapidly in Cyprus. Symptoms among children were classic and the majority of paediatric cases had a mild clinical course. Treatment with antivirals appears to have not had any major adverse effects. Despite the summer season and the schools being closed, places such as summer schools and camps contributed significantly to the spread of the disease among children. Regardless of the above, we need to focus on the coming influenza season and apply different methods including the coming influenza A(H1N1)v vaccine in order to avoid severe cases, which may inevitably occur due to the low level of immunity to the pandemic virus strain or affect vulnerable segments of the population.

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