Clinical features of influenza disease in admitted children during the first postpandemic season and risk factors for hospitalization: a multicentre Spanish experience

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Abstract

The main objectives of this study were to describe the characteristics of children with influenza infection during the postpandemic outbreak, and to compare sociodemographic and clinical data between patients who required hospitalization and those managed on an outpatient basis with a matched case–control study design. This is a multicentre paediatric study in Spain that included patients aged 6 month to 18 years in whom influenza infection was confirmed by real-time reverse transcription–polymerase chain reaction between December 2010 and March 2011. Among the 143 admitted patients, the main reason for admission was respiratory failure (123/143). In 55 there was some previously known disease. The median age was lower in patients without comorbidity (1.8 years: interquartile range 1.0–3.0 versus 5.3 years: interquartile range 1.3–10.7); p <0.01). The lag time from onset of symptoms to starting antiviral treatment was correlated with the length of hospital stay (Rho Spearman = + 0.32; p 0.01). Twenty patients required admission to the paediatric intensive care units, all due to respiratory failure. Children with chest X-ray opacities in more than one quadrant more frequently required admission to intensive care. Having a neurological disease conferred the highest risk of requiring hospitalization (OR 17.18) in a multivariate analysis. This study concludes that influenza in the paediatric population requiring hospitalization during the postpandemic season affected mainly children with neurological or pulmonary comorbidities and children of parents with a lower educational level. Most of the influenza infections caused respiratory symptoms, although neurological manifestations were also observed. Early initiation of oseltamivir was associated with a shorter length of hospital stay.

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Introduction

During 2009 and 2010 the new influenza virus, A(H1N1) pdm09, spread worldwide. Most of the influenza infections during the pandemic season were caused by this novel virus and, typically, the infection caused a mild respiratory disease in children, but severe manifestations and mortality also occurred [1,2]. Although the most common clinical manifestations were similar to those caused by previous circulating influenza viruses [3], severe manifestations were slightly more frequent with the influenza A(H1N1)pdm09 virus [4,5], especially in children with respiratory or neurological comorbidities [2,6].

It is well-known that novel influenza viruses caused morbidity and mortality during previous postpandemic outbreaks [7]. Influenza caused by the novel virus was expected to occur again during the first postpandemic season and to

co-circulate with previous influenza viruses. In autumn 2010, the World Health Organization gave advice on maintaining awareness of changes in the epidemiology and clinical expression of the disease [8].

Recently, Rahamat-Langendoen *et al.* [4] published a study comparing prepandemic, pandemic and postpandemic influenza cases in a single institution including patients of all ages. Poulakou *et al.* [9] have also described the disease in adults and children who required intensive care unit admission during the postpandemic period. As far as we know, there is still not a specific paediatric report that assesses the clinical and epidemiological characteristics of patients with influenza infection after the 2009 pandemics. The main objectives of this study are to describe the epidemiology and clinical characteristics of those patients with influenza infections during the 2010–2011 influenza outbreak, and to compare sociodemographic and clinical data between patients who required hospitalization and those managed on an outpatient basis.

Patients and Methods

This is a multicentre paediatric study in Spain. Hospitalized patients and outpatients were recruited in public Spanish National Health Service centres. We carried out a multicentre study in 17 hospitals from seven Spanish regions (Andalusia, the Basque Country, Castile and Leon, Catalonia, Madrid, Navarre and Valencia Community). Two of these hospitals (Hospital Sant Joan de Déu and Hospital Vall d'Hebrón, both of the province of Barcelona) were paediatric hospitals and the others were general hospitals with paediatric departments. We included patients aged 6 month to 18 years with influenza syndrome in whom influenza infection was confirmed by real-time RT-PCR between December 2010 and March 2011. A prospective matched case–control design was used to compare epidemiological and clinical characteristics between children who required hospital admission (cases) and children who were treated on an outpatient basis (controls). Controls were matched with each case according to age (±3 years), date of hospitalization (±10 days) and province of residence. Patients who could not be matched according to date of hospitalization and province of residence were excluded from the case–control analysis. Sociodemographic and clinical data were gathered using a standard form that was completed by a trained medical interviewer during the hospitalization or at the outpatient clinics. Seasonal and pandemic influenza vaccination and pneumococcal conjugate vaccination status for any of the commercialized vaccines were also recorded. Information on the vaccination status was obtained from hospital medical records or vaccination card; if neither was available, primary healthcare centre registers were consulted. Patients were considered correctly vaccinated if they had received at least two doses of influenza vaccine (including the 2010–2011 influenza virus vaccine strains), the last one >14 days before the onset of influenza symptoms, or only one dose if they were older than 9 years old, according to the recommendations of the American Academy of Pediatrics and the American Advisory Committee on Immunization Practices. Patients were considered correctly vaccinated for pneumococcal conjugated vaccine if they had received the last dose of vaccine at least 14 days before the onset of symptoms and if the number of doses for age was in agreement with the vaccines' factsheets. Parental sociodemographic and health data were also collected.

Descriptive statistics for non-continuous variables are described using absolute frequencies and rates, and data comparisons between cases and controls were performed using McNemar test. Continuous non-normally distributed variables are described as medians and interquartile ranges (IQR, 25–75%) and compared using the paired *t*-test. A multivariate analysis was performed to estimate the adjusted odds ratio of several variables as potential risk factors for hospitalization. The multivariate analysis used a conditional logistic regression model with backward selection of variables with a cut-off point of $p < 0.1$ and 'hospital admission' as the output variable. As a measure of goodness of fit we calculated the Hosmer–Lemeshow test and the predictive accuracy of the model was determined by calculating the area under the curve.

For statistical analysis of the admitted patients, data comparisons were performed using Pearson's chi-square test or Fisher's exact test when the expected count in any category was <5. Continuous non-normally distributed variables were compared using the Mann–Whitney *U* test.

Values of $p < 0.05$ were considered statistically significant. The statistical analysis was made using the SPSS® v19 FOR WINDOWS® package (SPSS Inc., Chicago, IL, USA).

The study was approved by each participating hospital's institutional ethics committee and written informed consent was waived.

Results

During the study, 323 children were recruited (143 hospitalized and 180 outpatients). Of the 143 hospitalized children, 43 (30%) were in paediatric hospitals and the others (100; 70%) were in paediatric departments of general hospitals. Overall, the median age was 2.9 years (IQR: 1.2–6.7). Of the 323 children, 163 (50%) were male and 247 (76%) had no