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Unexpected severity of cases of influenza B infection in patients that required hospitalization during the first postpandemic wave

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Summary *Objectives:* After the last pandemic the knowledge regarding influenza A infection has improved however, the outcomes of influenza B infection remain poorly studied. The aim of this study was to compare the features of influenza B versus influenza A(H1N1)pdm09 infections during the 2010—2011 epidemic-season.
Methods: A prospective, observational-cohort of adults with laboratory-confirmed influenza infection during the 2010—2011 epidemic-season was studied
Results: Fifty cases of influenza B and 80 of influenza A(H1N1)pdm09 infection were enrolled. Among patients with influenza B, the median age was 34 years-old (23—64), 30% pregnant, 24% obese, 34% transplant recipients and 14% with bacterial co-infection. Twenty-eight percent of patients had pneumonia with alveolar localized pattern and five (10%) died. Pneumonia was associated with delayed antiviral therapy, older age, higher Charlson score, invasive mechanical ventilation and bacterial co-infection. Obesity and pregnancy were not associated with complicated influenza B infection. The proportion of pneumonia, admission to the ICU and mortality did not differ between cases of influenza A(H1N1)pdm09 and influenza B infection.
Conclusions: Influenza B infection causes severe infection and it is associated with pneumonia or death, similar to influenza A(H1N1)pdm09 infection. Rapid diagnosis and early antiviral therapy are necessary for managing influenza pneumonia during epidemic periods.

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Introduction

Influenza B virus has been classically considered less pathogenic than influenza A virus in adults and mostly responsible for mild respiratory infections, while severe illness and poor prognosis have been associated with bacterial co-infection.[1,2]

Until the pandemic by the new influenza A (H1N1) pdm09, the diagnostic methods to detect influenza virus in respiratory samples were infrequently used due to the low sensitivity of the available antigenic detection methods. Currently, the most rapid, accurate and sensitive test for diagnosing influenza virus infections is based on real-time PCR (rt-PCR) assay[3] which is currently generalized for diagnosis of clinical suspicion of severe infections such as pneumonia, during the yearly epidemic season, permitting the early detection to prescribe antiviral therapy. The rt-PCR is available for both influenza A and B viruses, but has been mostly used for the detection of influenza A infection.

Recent studies have shown that influenza B infection causes similar rates of hospitalization, pneumonia and deaths than influenza A in children.[4,5] However, the disease burden of influenza B virus in adults has been scarcely described and based on a few cases reports.[6]

In our centre, after the 2009 pandemic, we included the rt-PCR assay for diagnosing influenza A and B viruses for cases of hospitalized community-acquired pneumonia and cases of influenza attended in the hospital during the influenza season associated with severe disease, pregnancy, or transplantation. The aim of this study was to describe the frequency of the influenza B virus in the 2010—2011 season and to compare the features, severity and outcome of cases of influenza B and influenza A (H1N1) pdm09 infections, as well as to assess whether the risk factors associated with pneumonia and mortality described during the 2009 pandemic by influenza A (H1N1)pdm09 infection,[1—4] such as obesity, pregnancy, co-infection or treatment delay, were associated with severity in the cases of influenza B infection.

Materials and methods

Study design and study population

A prospective, observational cohort study was conducted from December 1, 2010 to March 31, 2011 at the University Hospital Virgen del Rocío, in Seville, Spain. All patients, older than 14 years with confirmed influenza infection were included, if admitted because of influenza severe disease or attended as outpatient if pregnancy or solid organ transplantation.

Cases were identified on a daily basis by evaluating all positive rt-PCR tests at the Microbiology Service and all patients admitted to the hospital due to respiratory symptoms (influenza-like syndrome, dyspnea, pneumonia, acute exacerbation of chronic obstructive pulmonary disease) and/or fever with unknown cause. Cases were evaluated by an Infectious Diseases physician and a nasopharyngeal swabs (NPS) were collected within the first 24 h of hospitalization and processed immediately, if required. Additionally, all pregnant or transplant recipients consulting as outpatients during the same period with influenza-like symptoms were tested for influenza infection by rt-PCR in NPS, after evaluation by an Infectious Diseases physician. A confirmed case was defined in the presence of influenza like-illness with positive rt-PCR for influenza A or B viruses.

Microbiological studies

The samples were tested for influenza infection using rt-PCR assays. For influenza A(H1N1)pdm09 was used the Inf A/H1N1 Detection system (Roche, Mannheim, Germany), for influenza A(H3N2) the RNA Virus Master ref. 05619416001 and Sondas TaqMan for H3N2 ref. 011101253 TIB MOLBIOL (Roche, Mannheim, Germany), and for influenza B the Detection Light cycler 2.0 (Roche, Mannheim, Germany). In patients admitted by pneumonia, a standard hospital etiologic study was performed including blood and sputum cultures, and urine *Streptococcus pneumoniae* antigen; bronchial aspirates, bronchoalveolar lavage, and protected specimen brush, were carried out in selected cases if clinically required. Sputum samples were processed if they contained more than 25 polymorphonuclear cells and less than 10 epithelial cells per high-power field.

Clinical assessment and follow up

Clinical data were recorded using a standardized protocol. Hospitalized patients were followed up until discharge or death. For outpatients, follow up visits were scheduled at 7, 14 and 28 days after diagnosis.

The following variables were recorded: demographics, medical comorbidities, Charlson Comorbidity Index.[7] smoking habit,[8] pregnancy, obesity (BMI $\geq$30, weight in kilograms divided by the square of the height in meters), transplant recipient, seasonal 2010—2011 influenza vaccination, first symptom, pneumonia and severity assessed by the CURB-65 index,[9] chest X-ray findings, concomitant bacterial respiratory infection, antiviral therapy, time from onset of influenza symptoms to antiviral therapy, and outcome. Severe cases were considered those that required hospitalization, developed pneumonia, severe sepsis, organ dysfunction and/or died during hospitalization.

All patients received oseltamivir as treatment for influenza; early antiviral therapy was considered when administrated within 48 h from the onset of symptoms.[10]

Statistical analysis

Categorical variables are expressed as frequencies and percentages, and compared using the chi-square or Fisher's exact tests. Continuous variables are expressed as median and interquartile range and comparisons were performed using the *t* test or the Mann—Whitney test as required. Normality was tested with Kolmogorov—Smirnov or Shapiro—Wilk tests depending on whether the groups had more or less than 50 individuals, respectively. Statistical analysis was performed using SPSS v.18. (SPSS Inc., Chicago, Illinois, USA) and a p-value <0.05 was considered significant.