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Characterisation of nosocomial and community-acquired influenza in a large university hospital during two consecutive influenza seasons

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ABSTRACT

Background: Nosocomial influenza is increasingly recognized as an important public health threat causing considerable morbidity and mortality each year. However, data on nosocomial influenza is usually collected during outbreaks only and clinical information of nosocomial influenza is sparsely available.
Objectives: To systematically analyse the distribution of nosocomial and community-acquired influenza and epidemiological characteristics in a tertiary care unit in two consecutive seasons.
Study design: A retrospective observational study was conducted to identify and characterise cases of nosocomial and community-acquired influenza at Freiburg University hospital from 1 January 2013 to 30 April 2014. A validated multiplex RT-PCR to detect influenza virus and other respiratory pathogens was used throughout. Clinical information was retrieved from the hospital-based information system.
Results: Overall, 218 patients with laboratory-confirmed influenza were included (179 in the first, 39 patients in the second season). A rate of 20% of nosocomial influenza was observed throughout. A fatal outcome was recorded for 9% of nosocomial cases, which were mainly associated with influenza virus A(H1N1)pdm09. Nosocomial influenza occurred in all age groups, but fatalities were only observed in patients ≥18 years. Patients with nosocomial influenza were significantly older, underwent therapy for blood malignancies and immunosuppressive regimens more frequently, and received solid organ transplantation more often compared to community-acquired patients.
Conclusions: Despite the different distribution of virus subtypes and epidemiological properties between both influenza seasons, the rate of nosocomial cases remained similar. Systematic detection and targeted prevention measures seem mandatory to minimize nosocomial influenza.

1. Background

Nosocomial influenza is increasingly recognized as an important health threat not only in the acute-care hospital setting [1]. Outbreaks of influenza or influenza-like illness (ILI) in hospitals usually occur during the annual peak of community influenza activity. Of note, hospitalized patients are often vulnerable to infections, e.g. due to underlying medical problems or immunosuppressive therapies. Transmission of influenza within hospitals is facilitated by its short incubation time, transmission via respiratory droplets, and crowded places. The origin of nosocomial infections often remains unknown, but patients, health-care workers (HCW) and visitors are the most common sources of infection.

Knowledge on nosocomial influenza is essential to understand the burden and impact of the disease and to develop strategies for its prevention. However, in most countries there is no systematic surveillance warranting the early detection of nosocomial influenza, and studies are usually triggered by nosocomial outbreaks or the appearance of novel influenza viruses [1]. In addition, data on the clinical characteristics and baseline epidemiological data are only sparsely available for nosocomial influenza. This finding gives rise to the suspicion that a considerable proportion of cases remain undetected. Novel multiplex PCR assays facilitate the rapid detection of various respiratory pathogens including influenza virus.

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2. Objectives

In order to compare the distribution and epidemiological characteristics of nosocomial and community-acquired influenza, we systematically analysed all patients with laboratory-confirmed influenza in a large tertiary care hospital from 2013 to 2014.

3. Study design

3.1. Study population

We conducted a retrospective observational study on all patients with laboratory-confirmed influenza admitted to the Freiburg University Medical Center, from 1 January 2013 to 30 April 2014. A case-patient was defined as a person with influenza-like illness (ILI) and influenza virus detected by real-time PCR (RT-PCR). The criteria for ILI included sudden onset of symptoms, at least one of four systemic symptoms (fever, malaise, headache, myalgia), and at least one respiratory symptom (cough, sore throat, shortness of breath) [2]. Severe influenza was defined by admission of a case-patient to an intensive care unit (ICU) or in-hospital death. Influenza-associated death was defined as death due to influenza as primary or contributing cause. Nosocomial influenza was defined as a case-patient with symptom onset ≥72 h after admission to hospital and admission not related to respiratory symptoms. Testing of patients for influenza was performed upon request of the treating physician. We extracted the positive influenza results from our laboratory information system and clinical information was retrieved from the hospital-based information system. Influenza vaccination history was collected by the local public health authorities or obtained from the patient's general practitioner. Routine conventional bacteriology was not uniformly performed for all patients and is not reported in this study. Informed consent was obtained and documented by contract between patients and Freiburg University Medical Center.

3.2. Laboratory methods

Pharyngeal swabs or broncho-alveolar lavage fluids were collected from patients and processed immediately. Total nucleic acid was extracted from samples using the QIAmp MinElute Virus kit (Qiagen, Hilden, Germany) on an automated QIAcube (Qiagen) according to the recommendations of the manufacturer. Detection of respiratory pathogens was done using the FTD respiratory pathogens 21 kit (Fast track diagnostics, Junglingster, Luxemburg). The assay is able to detect influenza A and B viruses, and also enables detection on a subtype level for A(H1N1) pdm09. In addition, the assay is capable to detect coronaviruses 229E, NL63, OC43, HKU1, enterovirus/parechovirus, parainfluenza viruses 1–4, human metapneumovirus A/B, human bocavirus, rhinovirus, respiratory syncytial virus A/B, and adenovirus. Of note, all samples positive in the general influenza A assay were classified as A(H3N2) without further typing. This was based on the finding that only influenza virus A(H1N1) pdm09 and A(H3N2) had circulated in Germany from 2010 on according to national surveillance data [3]. Thermal cycling was done using an ABI 7500 machine (Applied Biosystems, Wiesbaden, Germany) as recommended. The FTD respiratory pathogens 21 kit was supplemented with three in-house real-time PCR assays for the detection of *Bordetella pertussis*, *Legionella pneumophila*, and *Chlamydia pneumonia* as described elsewhere [4].

3.3. Statistical analysis

Continuous variables (age) were analysed using Student's *t*-test and categorical variables using Fisher's exact test. Frequencies of patient characteristics, case severity, and virus subtypes were compared between the first and the second influenza season and between nosocomial and non-nosocomial influenza cases. *P*-values ≤0.05 were considered as statistically significant. Data analysis was carried our using IBM SPSS Statistics 22 software.

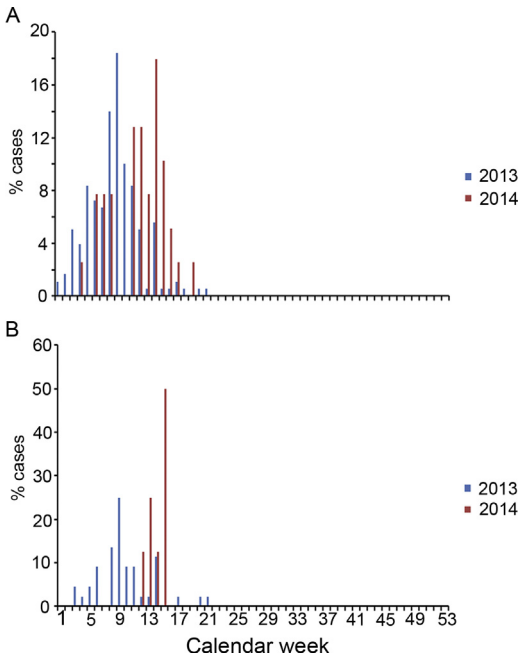

Fig. 1. Distribution of influenza cases (A) and nosocomial influenza cases (B) from January 2013 until April 2014.

4. Results

4.1. Patient characteristics

A total of 218 case-patients with laboratory-confirmed influenza were included, 179 in the influenza season 2012/13, and only 39 patients in 2013/14 (Table 1). The clinical characteristics are shown in Table 1. A total of 8/88 (9%) immunosuppressed patients were vaccinated, compared to only 3/116 (2.6%) of immunocompetent individuals (vaccination data was missing for 14 patients).

4.2. Descriptive epidemiology

In the 2012/13 season, the overall detection of influenza among admitted patients gradually increased from January 2013 on and peaked around week 9 with a steady decline (Fig. 1). In the 2013/14 season, two peaks were observed around week 9 and 14 of 2014, respectively (Fig. 1). The distribution of influenza virus subtypes in each season is shown in Table 1 and Supplemental Fig. 1. In 2013, A(H1N1) pdm09 was most frequently detected across all age groups, whereas in 2014 A(H3N2) dominated (Fig. 2).

In addition to influenza virus, another respiratory virus (i.e. the co-detection of influenza virus and another non-influenza virus in the same sample) was identified in 11/179 (6%) of patients in 2012/13 and 2/39 (5%) in 2013/14, respectively. Co-detection of non-influenza virus occurred with RSV ($n=5$), coronavirus ($n=5$), bocavirus ($n=1$), rhinovirus ($n=1$), and parainfluenza virus ($n=1$). None of the atypical bacteria included in the multiplex assays were detected among the 218 patients.