Journal of Hospital Infection 82 (2012) 94–100

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Nosocomial vs community-acquired pandemic influenza A (H1N1) 2009: a nested case–control study

G. Khandaker [a], H. Rashid [a,*], Y. Zurynski [b], P.C. Richmond [c], J. Buttery [d], H. Marshall [e,f], M. Gold [f], T. Walls [g], B. Whitehead [h], E.J. Elliott [b,i], R. Booy [a]

[a] National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, The Children's Hospital at Westmead and The University of Sydney, Sydney, New South Wales, Australia
[b] Discipline of Paediatrics and Child Health, Sydney Medical School, The University of Sydney, Sydney, and the Australian Paediatric Surveillance Unit, New South Wales, Australia
[c] School of Paediatrics and Child Health, University of Western Australia, Perth, Western Australia, Australia
[d] Murdoch Children's Research Institute, Royal Children's Hospital, Department of Paediatrics, Monash University, Melbourne, Victoria, Australia
[e] Vaccinology and Immunology Research Trials Unit, Women's and Children's Hospital, Women's and Children's Health Network, South Australia, Australia
[f] Discipline of Paediatrics, School of Reproductive Medicine and Paediatrics, University of Adelaide, South Australia, Australia
[g] Paediatric Infectious Diseases, Sydney Children's Hospital, Randwick, New South Wales, Australia
[h] Respiratory Medicine, John Hunter Children's Hospital, New South Wales, Australia
[i] The Children's Hospital at Westmead, Westmead, New South Wales, Australia

ARTICLE INFO

Article history:
Received 10 February 2012
Accepted 2 July 2012
Available online 1 September 2012

Keywords:
Australia
Children
Community-acquired influenza
Nosocomial influenza
Pandemic influenza

SUMMARY

Background: The characteristics of nosocomial influenza in children are not well described.

Aim: To compare the characteristics of nosocomial and community-acquired pandemic influenza A (H1N1) 2009 (pH1N1) in Australian children.

Methods: In a nested case–control study, the clinical and epidemiological features of nosocomial vs community-acquired pH1N1 were compared among hospitalized children aged <15 years in six paediatric hospitals in Australia between 1 June and 30 September 2009.

Findings: Of 506 hospitalized children with pH1N1, 47 (9.3%) were of nosocomial origin. These 47 cases were compared with 141 gender- and age-matched controls. Cases had a significantly higher proportion of underlying medical conditions compared with controls (81% vs 42%, $P < 0.001$), and were more likely to be exposed to household smokers (36% vs 20%, $P = 0.02$). Fewer children with nosocomial influenza presented with classical symptoms of influenza, including subjective fever and lethargy. A higher proportion of children with nosocomial influenza received treatment with oseltamivir (77% vs 43%, $P < 0.001$), and they required a longer stay in hospital following the onset of influenza (mean 8.5 days vs 4.5 days, $P = 0.006$). Three children (2%) in the community-acquired group died of pH1N1, but there were no deaths in the nosocomial group.

* Corresponding author. Address: National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, The Children's Hospital at Westmead, Cnr Hawkesbury Rd and Hainsworth St, Locked Bag 4001, Westmead, NSW 2145, Australia. Tel.: +61 2 9845 1489; fax: +61 2 9845 1418.
E-mail address: harunor.rashid@health.nsw.gov.au (H. Rashid).

0195-6701/$ – see front matter
http://dx.doi.org/10.1016/j.jhin.2012.07.006

Conclusion: This study shows that children with pre-existing diseases and those who are exposed to household smokers are more susceptible to nosocomial pH1N1. They may have 'occult presentation' of influenza, but their course of illness is not markedly different from that of children with community-acquired influenza.

Introduction

Nosocomial or healthcare-associated influenza is documented in the medical literature,[1–7] but to the authors' knowledge, there are no studies reporting comparative data on clinical and epidemiological features of nosocomial vs community-acquired influenza. Paediatric nosocomial influenza leads to extended hospital stay, excess morbidity and mortality, and economic loss.[1] The latter has been estimated conservatively to be approximately US $7500 per patient for each additional stay in hospital.[8] In epidemic/pandemic situations, this can strain an already overburdened healthcare system.

During the first wave of the pandemic influenza A (H1N1) 2009 (pH1N1), the rate of all-cause nosocomial infections doubled in some countries (e.g. Mexico) compared with previous years.[9] Subsequently, there have been several case reports, case series and outbreak investigations on nosocomial pandemic influenza in children.[10–13] A recent surveillance report from the UK described 15 cases of paediatric nosocomial influenza; to the authors' knowledge, this is the largest published report of nosocomial pH1N1 to date.[14]

The literature suggests a variable presentation and outcome of hospital-acquired pH1N1 influenza. Most case series or outbreak investigations reported that paediatric nosocomial pH1N1 was generally mild, rarely needed aggressive medical care and had very low mortality.[10–13] However, the recent UK surveillance report indicated that the course and outcome of hospital-acquired pH1N1 can be severe both in terms of mortality and the need for escalated medical care.[14] The report suggested that more than half of the children needed intensive medical care, and one-fifth of all children with nosocomial pH1N1 died. In order to compare the clinical and epidemiological features, risk factors and outcomes of nosocomial and community-acquired pH1N1 in children, a nested case–control study was conducted at six major paediatric hospitals in Australia. A nested case–control design was chosen for this study in order to achieve a statistically efficient analysis with matching for potential confounders.

Methods

Setting

This study is part of an active hospital-based surveillance system called 'PAEDS' (Paediatric Active Enhanced Disease Surveillance), which is a collaborative project between the Australian Paediatric Surveillance Unit (APSU) and the National Centre for Immunisation Research and Surveillance (NCIRS) that involves six tertiary paediatric referral centres in Australia (Children's Hospital at Westmead in Western Sydney, Sydney Children's Hospital in Eastern Sydney, John Hunter Children's Hospital in Newcastle, Royal Children's Hospital in Melbourne, Women's and Children's Hospital in Adelaide and Princes Margaret Hospital in Perth). In 2009, the New South Wales Department of Health approved immediate commencement of the study in the three New South Wales hospitals without prior ethics approval, under provisions of the Health Records and Information Privacy Act 2002 (http://www.lawlink.nsw.gov.au). Subsequently, approval was also obtained from the human research ethics committee at each of the participating hospitals.

Participants

Some aspects of the baseline data from the surveillance work have been published elsewhere with methodological details.[15] Briefly, all admitted children aged <15 years who had laboratory-confirmed influenza in the participating hospitals between 1 June and 30 September 2009 were included. Nurses employed by PAEDS proactively identified children presenting at participating hospitals with signs and symptoms of influenza. Laboratory confirmation required a positive nasopharyngeal aspirate or combined nasopharyngeal and throat swabs for immunofluorescence; many children also had a rapid antigen test for influenza (A and B). Specimens positive for influenza A were referred for further typing by polymerase chain reaction (PCR) to state reference laboratories. A positive diagnosis was made when PCR was positive for pH1N1 influenza. Nosocomial influenza was considered if clinical signs and symptoms of influenza developed after 72 h of hospital admission for another reason. In case of transfer from other hospitals, a diagnosis of nosocomial influenza was made if the patient developed symptoms and signs of influenza after 72 h of admission in the referring hospital.

Data on age, gender, symptoms and signs of the illness, pre-existing chronic medical conditions and vaccination history, diagnostic test results, clinical course, complications and history of contact with a suspected case of pH1N1 were collected from relevant sources: guardians, patients' hospital records and the Australian Childhood Immunization Register. Chronic medical conditions were defined as those illnesses that are recognized to increase the risk of influenza complications as listed in the *Australian Immunisation Handbook* (9th edition).[16] Bacterial co-infections were defined as isolation of a bacterial pathogen from blood.

A nested case–control comparison was performed: children with nosocomial pH1N1 influenza were defined as 'cases', and children with community-acquired pH1N1 who were hospitalized during the study period were defined as 'controls'. For every case with nosocomial pH1N1 infection, three controls were selected that were matched by gender and age. The controls were not necessarily from the same hospital as the case patient.

Statistical analysis

Data analysis was performed using Statistical Package for the Social Sciences Version 19 (IBM Corporation, New York, NY,