Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

October 2008

hpsc EPI-Insight

Volume 9 Issue 10

Disease Surveillance Report of HPSC, Ireland

ISSN: 1393-9548

Contents

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Epidemiology of Influenza in Ireland, 2007/2008 Season

Introduction

The 2007/2008 influenza season was the eighth year of influenza surveillance using sentinel general practices in Ireland. The Health Protection Surveillance Centre (HPSC) is working in collaboration with the National Virus Reference Laboratory (NVRL) and the Irish College of General Practitioners (ICGP) on this project.

Materials and Methods

Clinical data

Fifty-two general practices (located in all HSE areas and representing 4.8% of the national population) were recruited to report electronically, on a weekly basis, the number of patients who consulted with influenza-like illness (ILI). ILI is defined as the sudden onset of symptoms with a temperature of 38°C or higher, with two or more of the following: headache, sore throat, dry cough and myalgia. Cases were those attending for the first time with these symptoms.

Virological data

Sentinel GPs were requested to send a combined nasal and throat swab on at least one ILI patient per week to the NVRL. Swabs were tested for influenza using multiplex realtime one step PCR. The influenza A positive specimens were further characterised by subtyping with primers directed to the HA and subsequent phylogenetic analysis of the nucleotide sequence. The NVRL also tested respiratory specimens (predominantly paediatric), referred mainly from hospitals.

Other indicators of influenza activity

The Departments of Public Health reported an influenza activity index every week to HPSC. The activity index is analogous to that used by the WHO global influenza surveillance system and the European Influenza Surveillance Scheme (EISS).[3,4] Each Department of Public Health established one sentinel hospital in each HSE area, reporting total, emergency, and respiratory admissions data on a weekly basis. Sentinel primary and secondary schools were also located in each HSE area in close proximity to the sentinel GPs, reporting weekly absenteeism data.

The Departments of Public Health notified HPSC weekly of all cases of influenza, all influenza/ILI outbreaks and an enhanced dataset on all hospitalised influenza cases aged between 0 and 14 years of age was also reported to HPSC. From January 2005, HPSC was notified of all registered deaths on a weekly basis from the General Register Office (GRO).

Results

It should be noted that hospital admissions data and enhanced surveillance data for the 2007/2008 season are provisional.

Clinical data

Influenza activity in Ireland peaked slightly earlier in the 2007/2008 season compared to the previous two seasons. Activity was mild, peaking during week 1 2008 at 49.1 per 100,000 population (figure 1). During the peak of activity, the majority of ILI cases reported were in the 15-64 year age group.

Virological data

The NVRL tested 344 sentinel specimens for influenza during the 2007/2008 season. One hundred and fifty (43.9%) sentinel specimens were positive for influenza: 78 influenza A (74 A H1N1, 1 A H3N2 and 3 A unsubtyped) and 72 influenza B. Influenza A (H1N1) was the predominant subtype detected from week 48 2007 to week 7 2008 and influenza B predominated in the latter part of the season. Influenza A (H1N1), accounted for 98.7% of subtyped positive sentinel specimens. The majority of positive influenza sentinel cases were in the 15-64 year age group (87.9%). The NVRL tested 2,207 non-sentinel respiratory specimens, 61 (2.8%) of which were positive: 32 influenza A and 29 influenza B. Four hundred and sixty-three non-sentinel specimens tested positive for respiratory syncytial virus (RSV). The majority of non-sentinel influenza (56.1%) specimens were in the 15-64 year age group, whilst the majority of RSV (93.5%) positive specimens were in the 0-4 year age group.

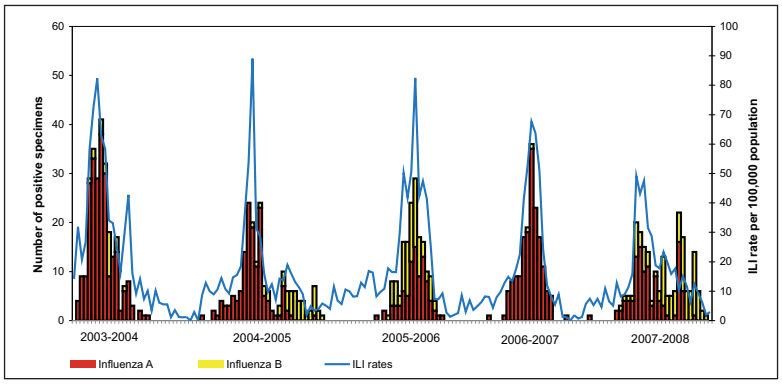

Figure 1. ILI rate per 100,000 population and the number of positive influenza specimens detected by the NVRL during the 2003/2004 – 2007/2008 seasons

Based on antigenic or genetic characterisation of 70 influenza viruses, 59 were A/Solomon Island/3/2006 (H1N1)-like, seven were A/Wisconsin/67/2005 (H3N2)-like and four were B/Florida/4/2006-like (B/Yamagata/16/88 lineage).

Oseltamivir Resistance in Ireland

Results from the NVRL on antiviral drug susceptibility among seasonal influenza viruses circulating in Ireland during the 2007/2008 season revealed that some of the A (H1N1) viruses in circulation were resistant to the antiviral drug, oseltamivir (brand name Tamiflu). The NVRL conducted nucleotide sequencing on specimens taken by sentinel GPs

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Rotavirus in Ireland, 2007

Introduction

Rotavirus causes a sporadic, seasonal, often severe infective gastroenteritis of infants and young children. It is the most common cause of acute gastroenteritis in children worldwide and a frequent cause of diarrhoea-associated deaths in developing countries.[1] The World Health Organization estimates that every child will be infected by rotavirus by the age of five. In developed countries, mortality due to rotavirus is low; however, the morbidity and economic costs associated with infection are significant.[2]

Illness is characterised by sudden onset of diarrhoea and vomiting, often with mild fever. Occasionally there is blood in the stools. Symptoms usually last for only a few days but in severe cases hospitalisation may be required due to dehydration. The incubation period is about two days. Transmission is usually from person to person, mainly via the faeco-oral route. Children less than two years of age are most susceptible to infection, although cases are often seen in elderly and immunocompromised adults, particularly in institutional settings. Spread can be extensive and rapid, through direct contact, airborne droplet spread, or contact with contaminated fomites such as toys.

Methods

Acute infectious gastroenteritis (AIG) became a statutorily notifiable disease for the first time in January 2004 under the Infectious Disease Amendment (No 3) Regulations 2003 (S.I. 707 of 2003)[3].

In this category, cases of rotavirus, *Clostridium difficile* and 'gastroenteritis, unspecified' are notifiable. Prior to 2004, laboratory-based data on rotavirus was captured within the disease category of 'Gastroenteritis in children less than two years of age'. Data on all cases of AIG due to rotavirus notified between 1/1/04 and 31/12/07 were extracted from the CIDR system on the 10th September 2008 and analysed using standardised methods.

Results

Incidence

There were 2520 notifications of AIG in 2007. Rotavirus was the causative organism identified in 2326 (92%) of these, giving a crude incidence rate (CIR) of 54.9 cases per 100,000 population (Table 1). This is the highest rate recorded since rotavirus became notifiable with an increase from a CIR of 50.0 cases per 100,000 in 2006 to 54.9. Over the period 2004-2007, 8289 cases of rotavirus were reported giving an annual average of 2072 cases per annum.

As in previous years, regional variation was observed in the number of cases reported. Figure 1 compares the CIR for each region for both 2006 and 2007. Most notably increases are seen in HSE-M, where the CIR increased by 22.3% HSE-SE, where the CIR increased by 28.6%, and, HSE-W, where the CIR increased by 36.9%

Seasonal distribution

Rotaviral infection has a well documented seasonal pattern in Ireland with peaks in cases occurring each year in early spring[4]. However in 2007, there was a change to this pattern. The usual upsurge did not appear until week 12, a full four weeks later than is usual, and the plateau continued for a month longer than usual. This delay was seen in other countries including the US and Germany.

Analysis of the data by week of notification from 2004 to 2007 is shown in Figure 2. (There is a 'false' second peak seen in 2005 during week 33, 2005 which is attributable to bulk uploading of notifications for the HSE-W region).

Age

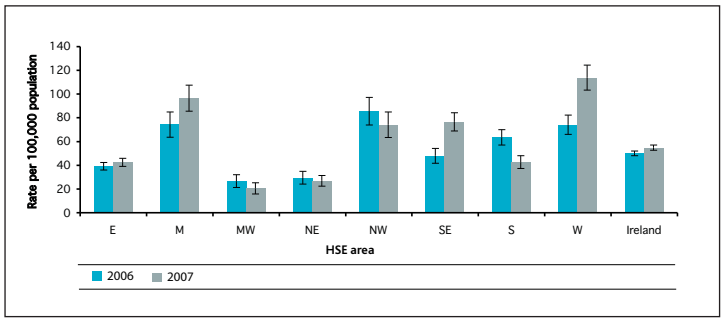

Figure 1: Crude incidence rate by region for human rotavirus notifications in Ireland by HSE area, 2006 and 2007.

Table 1. Number of cases, CIR of rotavirus notifications in Ireland by HSE area, 2007, and total number with crude incidence rate for 2004-2007.

HSE Area	No. of cases	*CIR incl. 95% C.I.	*ASIR incl. 95% C.I.
E	637	42.5 [39.2 - 45.8]	43.5 [40.1 - 46.9]
M	243	96.6 [84.4 - 108.7]	88.3 [77.2 - 99.3]
MW	74	20.5 [15.8 - 25.2]	20.6 [15.9 - 25.3]
NE	106	26.9 [21.8 - 32.0]	23.4 [18.9 - 27.9]
NW	176	74.2 [63.3 - 85.2]	73.2 [62.4 - 83.9]
SE	353	76.6 [68.6 - 84.6]	74.5 [66.7 - 82.2]
S	265	42.7 [37.5 - 47.8]	44.5 [39.1 - 49.8]
W	472	113.9 [103.7 - 124.2]	117.7 [107.1- 128.3]
Total 2007	**2326**	***54.9 [52.6 - 57.1]**	
Total 2006	**2112**	***50.0 [48.0 - 52.0]**	
Total 2005	**2251**	***53.1 [50.9 – 55.3]**	
Total 2004	**1600**	***37.8 [35.9 – 39.6]**	

* Rates calculated using 2006 census data and may differ from previously published rates

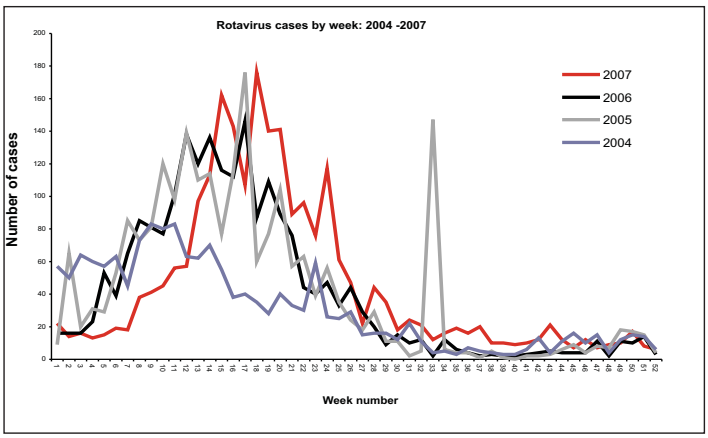

Figure 2: Seasonal distribution of rotavirus events by week, 2004-2007 (CIDR)

Table 2: Age specific incidence rates for rotavirus in Ireland, 2007

Age Group (Years)	Number of cases	Age specific incidence rate
0-4	2255	746.1
5-9	45	15.6
10-14	7	2.6
15-19	0	0.0
20-24	0	0.0
25-34	1	0.1
35-44	1	0.2
45-54	0	0.0
55-64	1	0.2
65+	7	1.5
Unknown	9	
Total	**2326**	**54.6**

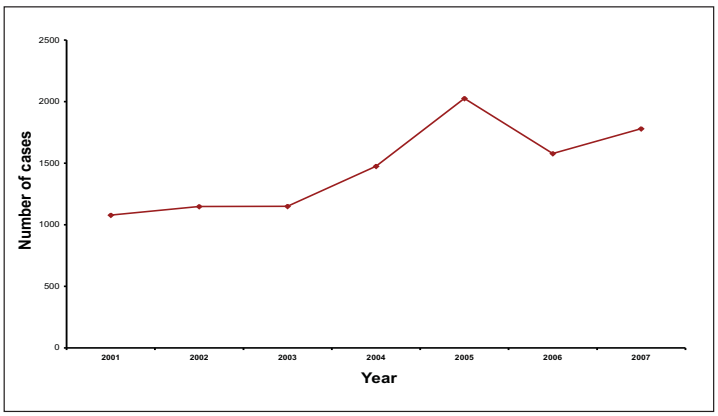

Figure 3: Number of cases of rotavirus in children aged less than two years of age by year, 2001 to 2007

Rotavirus is primarily a paediatric illness, with children generally affected in the first 2-3 years of life. Table 2 shows number and age specific incidence rates for rotavirus in 2007. As is usual, the peak incidence of clinical disease occurred in the 6-24 month age group. The majority of infections (n=1780) occurred in children less the two years of age. There has been a progressive increase in the notifications of cases in this age group over recent years (see Figure 3). The CIR increased from 676.6 per 100,000 cases in 2006 to 746.1 per 100,000 cases in 2007.

Sex distribution

In 2007 males accounted for 1,186 cases (51%); females 1,116 (48%), with 1% of cases unknown. This represented a ratio of males: females of 1.06:1. This was similar to previous years.

Outbreak data

In 2007, there were seven rotavirus outbreaks and one mixed norovirus/rotavirus outbreak notified on CIDR (see Table 3). In total, 47 cases of illness resulted from these eight outbreaks. The mixed outbreak occurred in a crèche and was the largest reported resulting in seventeen people ill. Transmission was from person to person. The second largest outbreak occurring within a hospital; 10 patients were affected and spread was again from person to person. No additional information such as age or gender was reported on CIDR.

There were five outbreaks of rotaviral illness reported in the period 2004 to 2006. These outbreaks resulted in 33 cases of illness.

Discussion

Given the universal distribution in the environment of rotavirus and its ready transmissibility, the numbers of cases of illness notified will be an underestimate of the true burden of illness. Rates of notification are most probably reflective of cultural and other patterns of health seeking behaviour, habits of clinical investigation and notification practices.

Although rotavirus notifications fell in 2006, there was a rebound in 2007, resulting in a continuation of the increasing trend noted since 2001. This increasing trend could , in part, be explained by increased awareness amongst reporting clinicians.

The crude incidence rate (CIR) of rotavirus increased to 54.9 cases per 100,000 in 2007 (50.0 cases per 100,000 in 2006) and is comparable with the CIR reported in 2005 of 53.1 cases per 1000,000. Regional increases were seen in the HSE-E and more notably in HSE-M, HSE-SE and the HSE-W. These differences are likely to reflect variations in testing patterns and reporting habits in different HSE areas

The national crude incidence rate of infection in the Republic of Ireland is still considerably higher than that in Northern Ireland (20.6/100,000)[5]. The CIR in England and Scotland for 2007 was not available at time of writing. Comparison however with data from Northern Ireland is complicated by the fact that rotavirus illness is not statutorily notifiable in the UK although there is a well established voluntary laboratory reporting system for rotavirus. The CIR in Northern Ireland given in this report is derived from laboratory reports only.

Of interest was that the Irish rotavirus season came a month later than usual in 2007 (see Figure 2). This pattern was repeated in a number of other countries.[6] US observers link this observation with the increasing use of rotavirus vaccine in the US. Given the fact that this delay was seen in countries that have no extensive rotavirus vaccine use, other factors such as environmental climatic conditions may have played a part.

Rotavirus Vaccines

In 1998, a tetravalent rotavirus vaccine, Rotashield® was recommended for routine vaccination of US infants with 3 doses at ages 2, 4, and 6 months. The vaccine had a greater than 80% efficacy, but significant evidence of association with intussusception appeared within 12 months of introduction and it was withdrawn. Since then, two vaccines, RotaRix® (live oral vaccine from a strain isolated from a case of infantile gastroenteritis) and RotaTeq® (five reassortant rotaviruses developed from human and bovine parent strains) have undergone trials.[7] A number of countries are examining their need for rotavirus vaccination.

Both vaccines appear to be safe and efficacious. They are, however expensive. The European Centre for Disease Prevention and Control is currently reviewing these vaccines from the standpoints of efficacy and safety, cost benefit and public health. They will issue their evaluation to Member States later in the year.

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Table 3: Rotavirus Outbreaks notified on CIDR, 2007.

Rotavirus Outbreaks 2007		
Date	**Location**	**Number People Ill**
April	Hospital	10
April	Private House	2
April	Creche	4
December	Private House	2
July	Community	2
June	Private House	2
June	Creche	8
Mixed Rotavirus Outbreaks 2007		
Date	**Location**	**Number People Ill**
May	Creche	17

Acknowledgements

We wish to thank all who have provided data for this report, including specialists in public health medicine, senior/area medical officers, surveillance scientists, clinical microbiologists, medical scientists, infection control nurses, principal/ environmental health officers.

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between November 2007 and February 2008. Seven of 63 specimens (11.1%) tested were resistant to oseltamivir. These viruses retain sensitivity to zanamivir, amantadine and rimantadine.

Vaccination status
Of the 150 positive influenza virus detections from sentinel specimens, 131 (87.3%) were unvaccinated, 5 (3.3%) were vaccinated and vaccination status was unknown in 14 (9.3%) cases. Of the five vaccinated cases, influenza A (H1N1) was detected in two cases and influenza B in three cases.

Regional influenza activity
Regional influenza activity peaked during week 1 2008, with HSE NE, MW and SE all reporting localised influenza activity. Overall, influenza activity was most intense in HSE E during the 2007/2008 season.

Outbreaks
Two ILI/influenza outbreaks were reported to HPSC this season, both from HSE E, one during week 12 2008 in a long term care facility associated with influenza A (H3N2) and one during week 16 2008 on a coach tour from Dublin to Clare associated with influenza B.

Sentinel hospitals and sentinel schools
Hospital respiratory admissions (as a proportion of total hospital admissions) in sentinel hospitals peaked during week 52 2007 (figure 2), one week prior to the peak in sentinel GP ILI consultation rates. Absenteeism in several sentinel schools was also at elevated levels during peaks in ILI consultation rates.

Enhanced influenza surveillance (for hospitalised 0-14 year olds)
A total of 299 influenza notifications were reported on CIDR during the 2007/2008 influenza season. Fifty-five of these notifications were patients aged between 0 to 14 years and six were hospitalised. Enhanced data were completed for all six cases. During the previous season, 29 influenza cases aged 0-14 years were hospitalised. During the 2007/2008 season, one case was hospitalised in December 2007, four in January 2008 and one in March 2008. One enhanced case was in the 5-14 year age group and five were in the 0-4 year age group (all five were under one year of age). Four cases were notified from HSE E and two from HSE M. Three enhanced cases were positive for influenza A and three were positive for influenza B. Symptoms included fever (5/6), cough (6/6), gastrointestinal manifestations (2/6) and fatigue (2/6). Complications included bronchitis, croup and other respiratory complications. The mean number of days in hospital was 13.6 (ranging from 5-30). One case was in an at risk category for influenza. No cases were vaccinated. Outcome was recorded in all cases; four recovered and outcome was unknown in two cases.

Mortality data
During the 2007/2008 influenza season, two deaths attributed to influenza have been registered with the GRO. These deaths were both in adults over 65 years of age, one in HSE NW registered in week 8 2008 and one in HSE S registered in week 14 2008. It should be noted that the death registered in HSE-S was not a laboratory confirmed case of influenza.

Influenza activity in Europe
In Europe, influenza activity first increased above baseline levels towards the end of 2007 and the first countries where clinical influenza activity peaked were Ireland, England and Spain. Clinical consultation rates were lower than during the previous season for the majority of countries. Influenza A (H1N1) was the predominant subtype circulating in Europe from week 1 2008 and influenza B was predominant from week 9 2008.

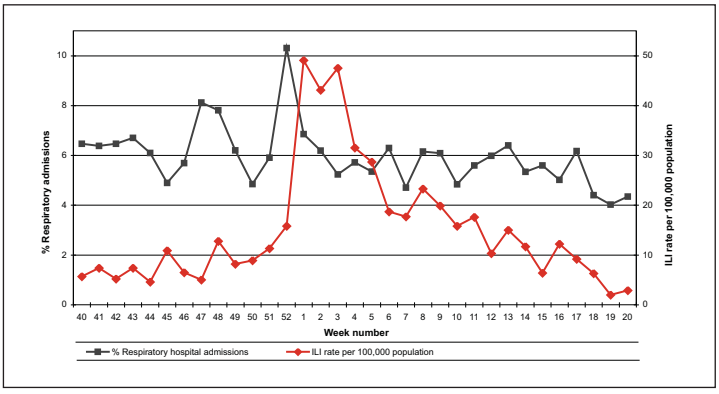

Figure 2. Respiratory admissions as a percentage of total hospital admissions in sentinel hospitals and ILI rates per 100,000 population by week for the 2007/2008 influenza season

Discussion

Influenza activity was mild and peaked early in Ireland during the 2007/2008 influenza season. Influenza A (H1N1) predominated for the first part of the season, followed by influenza B in the latter part. The A (H1N1) and B strains circulating matched the strains contained in this season's vaccine. Influenza activity was also mild to moderate in most of Europe, Canada and the US.

The mild levels of influenza activity during the 2007/2008 season were reflected by the decrease in the number of hospitalised 0-14 year olds notified to HPSC compared to the previous season. Nonetheless, these enhanced surveillance data highlighted the significant morbidity associated with influenza in children. None of the children hospitalised this season were vaccinated and one was in an at risk group, reiterating the need for health care professionals to promote influenza vaccine uptake in these groups.

During the 2007/2008 season the NVRL developed two new techniques which resulted in the timely characterisation of circulating influenza A strains and also the detection of antiviral resistance. These new techniques proved very beneficial in providing timely data during the investigation of an outbreak in a long stay institute in HSE E.

Oseltamivir resistant viruses were detected in 19 European countries (including Ireland), the USA, Canada, Australia and Hong Kong during the 2007/2008 season. The proportion of resistant A/H1N1 viruses varied across Europe, with the highest detected in Norway (67%). A/H1N1 (H274Y) viruses are the first human influenza viruses resistant to oseltamivir found transmitting in the community anywhere in the world. Similar viruses have been observed before but usually following treatment and those viruses have not been able to transmit and infect and have rapidly disappeared. There is no evidence that the appearance of these new viruses is related to the use of oseltamivir which is currently thought not to be widely prescribed in Europe. Experts from ECDC, the European Commission, EISS and WHO are currently assessing the significance of this development. At this stage it is difficult to comment on the significance of these findings. Current Irish national guidance on the use of antivirals for treatment and prophylaxis of influenza remain in place though they are being kept under review.

For the forthcoming season, a number of additional measures have been put in place in Ireland to improve surveillance of ILI/influenza. The NVRL will further develop work on genetic characteristion to include influenza B strains. They will also continue monitoring oseltamivir resistance. Work is in progress to increase the number of sentinel GPs, thereby improving geographical and population representation. Sentinel GPs are also currently monitoring ILI on a year round basis. Other activities include monthly surveillance of influenza vaccine uptake in those aged 50 years and older. Baseline threshold levels for influenza activity will be used for the first time in Ireland during the 2008/2009 season. Case based reporting of avian influenza is now operational on CIDR and an interim MS Access database for contacts of avian influenza cases is in the final stages of development. Data from these projects will in turn inform continuing national progress on pandemic preparedness and will be vital in the event of an influenza pandemic for planning and control measures.

Further information on influenza is available on the HPSC website at http://www.ndsc.ie/DiseaseTopicsA-Z/InfluenzaFlu/

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Acknowledgements
We would like to thank the sentinel GPs, the NVRL, departments of public health, sentinel schools and hospitals that provide data throughout the influenza season.

References on request