

# Impact of influenza during the post-pandemic season: epidemiological picture from syndromic and virological surveillance

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## Key words

Influenza • Pandemia • Syndromic surveillance

## Summary

**Introduction.** Following the observation that 1 or 2 pandemic peak due to the circulation of AH1N1v had occurred in most countries and in most World Health Organization (WHO) Regions, WHO declared on August 10<sup>th</sup>, 2010 that the world was moving into the post-pandemic period, whose surveillance presents considerable interest both from epidemiological and clinical point of view. We described the epidemiological picture emerged from syndromic and virological surveillance during the post-pandemic season in Liguria, Italy.

**Materials and methods.** An Emergency Department Syndrome surveillance system, based on data collected at "San Martino" and IRCCS "G. Gaslini" Liguria Regional Reference University Hospitals for adults and children is active since July 2007. Monitored syndromes include "Influenza-Like Illness" (ILI) and "Low Respiratory Tract Infections" (LRTI). The Ligurian Regional Reference laboratory for Influenza virological surveillance and diagnosis offers rapid detection of influenza viruses by real-time

and block RT-PCR, viral culture and genetic characterization by entire sequence analysis of haemagglutinin- and neuraminidase-coding regions in accordance with the international standards established by the global laboratory network.

**Results and discussion.** The integration of syndromic surveillance system and laboratory surveillance for rapid detection and characterization of the disease responsible agent represented a specific and sensitive tool for influenza surveillance.

The post-pandemic season was characterized by early onset and by the heaviest impacts for ILI and LRTI among the recent epidemic seasons. In contrast to the picture observed during the pandemic season, the 2010/11 winter was characterized by the intensive circulation of pandemic AH1N1v coupled with sustained activity due to influenza B and Respiratory Syncytial Virus (RSV). Antigenic and molecular characterization of influenza strains confirmed the good matching between circulating and 2010/11 vaccine viruses.

## Introduction

The post-pandemic influenza season has many features of considerable interest both from epidemiological and clinical point of view. Firstly, the incidence and the mortality of influenza during the first season after the appearance of pandemic virus can be higher than that observed in the previous year. For example, both monthly pneumonia and influenza and all-cause mortality rates during the 1969-70 season were higher than rates observed during 1968-69 peak, when the pandemic A/Hong Kong/1968 spread in adults aged between 45 and 64 years and between 65 and 69 years [1, 2]. Secondly, the impact of influenza may be affected by a number of unpredictable virological factors: host adaptation phenomena, changes in virulence or pathogenicity due to the appearance of new determinants, change in antigenic pattern of pandemic virus and vaccine escape mutant or wide circulation of other-than-pandemic type and subtype may characterized the post-pandemic season. For these reasons, the implementation of surveillance systems is strongly recommended by World Health Organi-

zation (WHO) and European Centre for Disease Prevention and Control [3].

In order to early detect disease outbreaks, to minimize the spread of etiologic agents, to increase of the communication and information capacity among different alert systems, notably the clinical-epidemiological sentinel-based surveillance system and the Hospital Information System (HIS), and to reduce the burden of diseases in the community, a syndromic surveillance system based on the real-time analysis of emergency room acceptance data from the regional reference hospitals for children and adults was designed, organized and validated since 2007 [4, 5]. The main objectives of syndromic surveillance system are: (i) to rapidly detect outbreaks of "Influenza-Like Illness" (ILI), "Low Respiratory Tract Infections" (LRTI), "fever-with-maculo-papular or vesicular rash", "non-hemorrhagic gastroenteritis", "hepatitis" syndromes; (ii) to determine their size, spread and time; (iii) to quickly activate the epidemiological investigation; (iv) to allow a better public health response; and (v) to monitor disease trends. Part of the project is the integration with laboratory surveillance that, with regard to surveillance of ILI

and LRTI, includes detection and characterization of the main respiratory viruses and bacteria from patients hospitalized in Liguria Administrative Region.

The aim of study is to describe the epidemiological picture emerged from syndromic and virological surveillance during the following season at the appearance of AH1N1v in April 2009 and its spread during the 2009/10 autumn and winter.

## Materials and methods

In July 2007 a pilot Emergency Department Syndrome surveillance system, based on data collected at “San Martino” and IRCCS “G. Gaslini” Liguria Regional Reference University Hospitals for adults and children, began. “San Martino” and “G. Gaslini” Hospitals are situated in Genova, a city of 650,000 inhabitants, capital of Liguria, an administrative Region in Northern Italy. They were selected as a pilot sites because it represents the largest hospitals with the largest catchment area in Genova, covering approximately 55% and 100% of all urban area Emergency Department visits for adults and children, respectively.

Syndrome coding, data capture, transmission and processing, statistical analysis to assess indicators of disease activity and alert thresholds, and signal response were operatively described in Ansaldi et al. [5].

Based on these case definitions, each syndrome was identified by a combination of keywords that must appear in specific fields (anamnesis, case history, objective examination and comments) of the Emergency Department registration and triage software. The keywords identification has been done in collaboration with Emergency Department, HIS and “Clinical governance” Unit staff of the two Hospitals and it was followed by an evaluation phase of different combinations in order to optimize the case capture in terms of sensitivity and specificity.

The text strings identified during the assessment phase and which have been used during the surveillance phase, are for ILI (influenza) or (fever or hyperpyrexia) and (pharyngitis or pharyngodinia or cough or dyspnea or sore throat or airway inflammation) and for LRTI (pneumonia) or (bronchiolitis) or (bronchitis) or (bronchopneumonia). An informatics system was developed in order to scan the chief complaint (anamnesis and case history), the objective examination and the comment fields for the word strings assigned to the single syndrome. The system provides for an automatic review of Emergency Department acceptance data folders, identifying suspected cases. Medical records captured by the system included information about the time and date of admission, date of birth, gender, home zip-code, triage categories, and hospital identification number. The medical records for the final, filtered set of encounters were reviewed manually by 2 of the investigators who accepted or rejected the cases in accordance with the operative case definitions and extracted more precise information regarding patient illness. In order to define indicators of activity and the alert thresholds value for ILI and LRTI, a ret-

rospective analysis of the Emergency Department access database was performed on data collected between November 1, 2006 and July 1, 2008. Day-of-the-week adjustments are made by estimating and removing day-of-the-week means, using historical time series as previously described by Duniak et al. [6]. An indicator and a threshold value that can achieve optimum sensitivity and specificity in predicting relevant epidemiological events were established using the ROC curve approach.

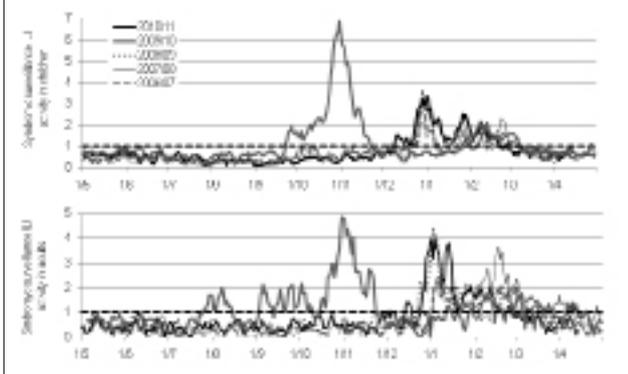
In Liguria the Regional Reference laboratory for Influenza virological surveillance and diagnosis offers rapid detection of influenza viruses by real-time and block RT-PCR, viral culture and genetic characterization by entire sequence analysis of haemagglutinin- and neuraminidase- coding regions in accordance with the international standards established by the global laboratory network. Furthermore, collected respiratory samples are routinely tested by multiplex PCR for detection of the main respiratory bacteria and viruses. The detection of *Streptococcus pn*, *Legionella pn*, *Chlamidia pn*, *Haemophilus influenzae*, *Mycoplasma pn*, *Bordetella pertussis* and by type A and B Influenza Virus, Respiratory Syncytial Virus (RSV), Parainfluenza virus, Adenovirus, Coronavirus, Metapneumovirus, Rhinovirus is performed using multiplex molecular amplification assays [Seeplex PneumoBacter ACE (Seegene) and Seeplex RV12 ACE (Seegene)].

## Results and discussion

Syndromic surveillance system for ILI and LRTI did not reported alert signals during the spring and summer 2010 and no circulation of influenza viruses were detected by Regional Influenza laboratory since the last influenza isolation during week 7/2010 (Fig. 1). The ILI activity indicator exceeded the threshold value on December 1<sup>st</sup>, 2010 in adults and on December 9<sup>th</sup>, 2010 in children. Contemporary, LRTI threshold break-through was observed between December 5<sup>th</sup>, 2010 and December 9<sup>th</sup>, 2010 and virological surveillance system detected circulation of influenza B virus in children and adults and RSV in infants and toddler during weeks 48-51/2010. The epidemic threshold breakthrough was earlier than that seen in previous seasons: in children, during the 2006/07, 2007/08 and 2008/09 seasons the syndromic surveillance system reported epidemic threshold breakthrough between December 21<sup>st</sup> and December 23<sup>rd</sup>, according the season, two weeks later than that has been observed during the post-pandemic season. In adults, during the previous epidemic seasons, activity indicator exceeded the threshold value 3-4 weeks later respect with that observed during the post-pandemic winter. (Fig. 1)

The ILI epidemic threshold breakthrough observed by syndromic surveillance system at the beginning of December could be considered specific signals able to anticipate the first breakthrough by sentinel-based surveillance system of 23 and 14 days in adults and children, respectively. The ability of syndromic surveillance system to anticipate the alarm signal respect with sentinel-based surveillance system had emerged also during pre-

**Fig. 1.** Syndromic surveillance indicator of ILI activity in children and adults from 2006 to 2011.



vious epidemic seasons and pandemic waves (data not shown).

The first detection of influenza viruses was followed by an increase of Emergency Department accesses for ILI and LRTI and of influenza positive samples. Between December 9<sup>th</sup>, 2010 and February 20<sup>th</sup>, 2011 and between December 25<sup>th</sup>, 2010 and February 26<sup>th</sup>, 2011 the ILI syndrome surveillance epidemic cut-off was permanently exceeded in children and adults, respectively. Similarly, LRTI epidemic cut-off was continuously gone beyond between December 21<sup>th</sup>, 2010 and February 20<sup>th</sup>, 2011. ILI activity peaks during the Christmas holiday (December 31<sup>th</sup>, 2010 and January 3<sup>rd</sup>, 2011 in children and adults, respectively), reaching values 3- and 4-fold higher than epidemic cut-off in children and adults, respectively. A second peak of comparable size was observed at mid-January in adults. Conversely, the profile of Emergency Department accesses for LRTI showed a long-lasting plateau (activity average +23% than epidemic cut-off) from the end of December to the end of February.

The impacts of ILI and LRTI during the post-pandemic season were the heaviest among the epidemic seasons. Emergency Department accesses for ILI were on average 18% and 10% higher, in children and adults, respectively, than that observed during the 2006/07, 2007/08 and 2008/09 seasons and LRTI activity observed during

the 2010/11 winter was twice higher than that observed during the 2008/09 seasons.

The 2010/11 season was characterized by intensive circulation of pandemic AH1N1v (67% out of influenza virus) and sustained activity due to influenza B (24% out of influenza virus) and RSV. Antigenic and molecular characterization of influenza strains confirmed the good matching between circulating and 2010/11 vaccine viruses [7]. Influenza A virus and *Streptococcus pn* were frequently detected in patients with severe cases of ILI and LRTI and with ARDS. Molecular characterization of influenza viruses and of *Streptococcus pn* detected in more severe cases is currently ongoing to assess molecular determinant of pathogenicity or serotype more strictly correlated with severe disease.

In conclusion, the integration of syndromic surveillance system and laboratory surveillance for rapid detection and characterization of the disease responsible agent could be an effective answer to the need for major enhancements to the public health infrastructure to rapidly detect events with a potentially high burden on the community and health system, for which current surveillance capabilities are not adequate. The syndrome surveillance system represented a specific and sensitive tool for influenza surveillance.

The post-pandemic season was characterized by early onset and by the heaviest impacts for ILI and LRTI among the recent epidemic seasons. In adults, emergency Department accesses for ILI during the 2010/11 winter were lower but not far from that observed during the pandemic peak, which was more pointed, while in children the circulation of AH1N1v during the autumn 2009 determined an higher (+27%) impact than that observed during the post-pandemic season. LRTI activity observed during the 2010/11 winter was twice higher than that observed during the 2008/09 seasons and during the 2009 autumn. In contrast to the picture observed during the pandemic season, the 2010/11 winter was characterized by the intensive circulation of pandemic A H1N1v coupled by sustained activity due to influenza B virus and RSV. The good matching between circulating and 2010/11 vaccine strains has provided an optimal vaccine efficacy.

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