

Healthcare Information Systems to Assess Influenza Outbreaks

An analysis of the 2009 H1N1 Epidemic in Buenos Aires

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Keywords

Health information systems, epidemiology, health care organization

Summary

Objective: To determine whether a private HIS could have detected the influenza epidemic outbreaks earlier through changes in morbidity and mortality patterns.

Methods: Data Source included a health information system (HIS) from an academic tertiary health care center integrating administrative and clinical applications. It used a local interface terminology server which provides support through data autocoding of clinical documentation. Specific data subsets were created to compare the burden of influenza during the epidemiological week (EW) 21 to 26 for years 2007 to 2009 among 150,000 Health Maintenance Organization members in Argentina. The threshold for identifying an epidemic was considered met when the weekly influenza-like illness (ILI) rate exceeded 200 per 100,000 visits. Case fatality rates and mortality rates of severe acute respiratory infection (SARI) from 2007 to 2009 were retrospectively compared. Case fatality rates and mortality rates for A/H1N1 influenza 2009 also were estimated.

Results: The HIS detected the outbreak in EW 23 while the government Ministry of Health (MoH) gave a national epidemic alert during EW 25. The number of visits for ILI increased more than fourfold when comparing 2009 to the period 2007-2008. The SARI mortality rate in 2009 was higher than in 2008 (RR 2.8; 95%CI 1.18-6.63) and similar to that of 2007 (RR 1.05; 95%CI 0.56-1.49). 2009 was the first year with mortalities younger than 65 years attributable to SARI. The estimated A/H1N1 case fatality rate for SARI was 6.2% (95%CI 2.5 to 15.5) and A/H1N1 mortality rate was 6 per 100,000 (95%CI 0 to 11.6).

Conclusion: Our HIS detected the outbreak two weeks before than the MoH gave a national alert. The information system was useful in assessing morbidity and mortality during the 2009 influenza epidemic H1N1 outbreak suggesting that with a private-public integration a more real-time outbreak and disease surveillance system could be implemented.

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Introduction

The surveillance of communicable diseases is important for early outbreak detection to allow prompt response from public health. In order to be effective, such reporting must be timely and accurate, since early detection can potentially help mitigate the mortality, morbidity and costs related to the disease [1].

For the timely detection of epidemic outbreaks, data for reporting early symptoms or changes in known disease patterns is useful. The use of health information systems that integrate information from both clinical and administrative data can play a key role towards this goal [2-4].

Different studies have shown improved timeliness and completeness with electronic reporting of infectious disease surveillance [5, 6]. Countries, like United States, the Netherlands, United Kingdom and Canada, have implemented public health surveillance systems based on a HIS [5, 7-13]. Their experiences have shown that electronic reports contain more complete information on variables common to both conventional and electronic reporting formats [5, 10, 13, 14].

Traditionally, in Argentina, local health departments monitor influenza via legally mandated reporting by physicians and laboratories. However in June 2009, when an outbreak of respiratory illness caused by a new strain of influenza A (H1N1) virus quickly spread throughout Buenos Aires and its surroundings, the national surveillance system fell behind in its obligation to provide timely and accurate alerts to the population.

Based on the clinical and administrative data available from the HIS at an academic tertiary center, we conducted a retrospective study to determine whether a private HIS could have detected the outbreak earlier through changes in morbidity and mortality patterns during the H1N1 epidemic in Buenos Aires, Argentina.

Objective

To determine whether a private HIS could have detected the influenza epidemic outbreaks earlier through changes in morbidity and mortality patterns.

Methods

Design: time series study

The time period analyzed in this study spans epidemiological week (EW) 21 through 26 (May 24th to July 11th) in 2009, and for the same period in 2007 and 2008.

Setting

The study took place within the Health Maintenance Organization (HMO) of Hospital Italiano of Buenos Aires (HIBA). HIBA is a 750-bed tertiary center with high standards in quality of health care and an advanced information system. Its Health Maintenance Organization (HMO) is a health system that functions both as an insurance plan and as a provider of care with approximately 150,000 enrollees, mostly middle income class residents in the city of Buenos Aires and its surrounding suburbs. Primary care is provided in 23 community health centers in the city of Buenos Aires and surrounding areas. Patients who require hospitalization are admitted to the Hospital; laboratory tests are also centralized.

Surveillance system

The HMO is paperless with medical and administrative electronic records [15, 16]. The HMO electronic information system requires clinical entries of drug prescriptions, physical examinations and provides reports of laboratory results. The data entries are linked to a specific medical problem coded using the Spanish version of SNOMED CT [17-19]. As a medical problem, influenza like illnesses and pneumonia diagnoses are entered, reported and aggregated with a local thesaurus on a terminology server.

Case definitions, according to the Ministry of Health (MoH), were obtained with automated extraction of routinely generated coded data:

- **Influenza Like Illness (ILI):** Sudden onset of fever of >38 °C and cough or sore throat in the absence of other diagnoses.

- **Severe acute respiratory illness (SARI):** Meets ILI case definition AND shortness of breath or difficulty breathing AND requiring hospital admission [20].
- **Suspected Case of Influenza H1N1:** The MoH's definition changed during the epidemic: in May, only ILI patients that had been in Mexico and the USA were considered possible cases. By June, ILI patients who had been in contact with a confirmed case were included, and by July, any person having flu-like symptoms was included. Suspected cases were required to be reported to the national authorities [21-23].
- **Confirmed H1N1 patients:** A real-time PCR test was used to confirm the diagnosis. Virological specimens derived from nasopharyngeal swabs were collected in suspected cases until Epidemiology Week (EW) 24. After that week, only SARI cases were swabbed [21-23].

Organizational changes adopted by our institution are explained elsewhere [25, 26].

Analysis

The analysis plan was based on the recommendation given by the World Health Organization (WHO) on July 16th, 2009 suggesting the assessment of the impact of the A/H₁N₁ pandemic on the health care system, trend of cases, intensity of A/H1N1 and the geographical spread.

Measurement

Impact on the health care system

The number of unscheduled medical visits for any cause and for ILI during the study period was described for 2007 to 2009. The relative increase in the number of visits between 2008 and 2009 was expressed as a percentage and 95% confidence intervals (95%CI) were calculated.

The rate of outpatient visits for ILI was described by EW (21 to 26) from 2007 to 2009. An epidemic was considered present when the rate of visits for ILI exceeded 200 per 100,000 per week [26, 27].

Trend of cases

The tendency of adult and pediatric visits was analyzed throughout time. The daily number of visits for ILI, in those both older and younger than 15 years old, was plotted to define the onset date of the epidemic in each age stratum.

The weekly ILI + pneumonia rate per 100,000 and the number of suspected cases reported according to the health national authority's definition was shown by EW.

Intensity of disease

SARI rates and SARI mortality rates for the period under study were reported per 100,000 health plan members and their 95%CI for 2007, 2008 and 2009. Paired wise comparison were done using chi² test. The risk of death for SARI during 2009 was compared to 2008 and 2007 computing rate ratios and 95% CIs.

Case fatality rates for SARI per 100 with their 95%CI by age strata (under and over 65 years old) are given for 2009 and 2008 and compared using chi² test.

Finally, the mortality rate due to A/H1N1 among our health plan members for 2009 and the case fatality rate among confirmed A/H1N1 cases were also described.

The electronic medical records from deceased SARI patients during EW 21 to 26 for year 2009 were manually checked to validate the SARI definition and diagnosis, including the nasopharyngeal swab indication for the detection of respiratory viruses. All-cause mortality rates were calculated from the HMO mortality registry.

Geographical spread

Patients with ILI that visited the emergency department during EW 21 and the first ten positive A/H1N1 cases of the same week were georeferenced using the HIBA Geographic Information System (GIS) [24].

Results

A total population of 148.741 persons was affiliated with the HMO on May 31st 2009 with a mean age of 45 years (SD 25) and with 58% being female.

Impact on the health care system

From May 24th 2009 (EW 21) to July 11th 2009 (EW 26), a total of 19,095 persons (13%) sought care for at least one unscheduled medical visits for any cause: 48% (9,127 patients) asked for home visits, 55% (10,582) for unscheduled outpatient visits and 5.3% (1,020) for emergency visits.

Comparing the number of total unscheduled visits between June 2008 and June 2009, there were 4230 per 100,000 more unscheduled visits: 24,113 visits per 100,000 in 2008 vs. 28,343 visits per 100,000 in 2009; 17.5% (95%CI 17.06 to 18.02) more unscheduled visits for any cause in 2009 than 2008.

Thirty four percent (6566 patients) of the total of the patients that had sought care for any cause during EW 21 to 26 for year 2009 had done it due to ILI. The number of ILI visits increased more than fourfold comparing the same period for 2009 to 2007-2008 (►Fig. 1).

Trend of cases

The outbreak started among children with a quick onset on June 5th. The adult onset was later, on June 12th, and broader than that of pediatric patients. (►Fig. 1) The number of pediatric visits due to ILI on June 6th was 63 for year 2009 while the average number of visits in previous years on the same date was 1.33.

Weekly total ILI visit rates per 100,000 members increased from EW 21, reached epidemiological threshold on week 23, remained high until EW 26 and then started to drop below peak observed levels. However, the weekly number of suspected cases requiring national notification did not increase similarly to the increase observed in the ILI rates (►Fig. 2).

One hundred and eight patients were A/H1N1 laboratory-confirmed: 100% of suspected cases in EW 21, 22 and 23 and lower than 50% of those suspected cases after that week.

Intensity of disease

The SARI rates during EW 21 to 26 were similar for 2007, 2008 and 2009: 84.5 (95%CI 70.4 to 111.5), 82.9 (95%CI 69.1 to 99.5) and 97.4 (95%CI 82.6 to 115) per 100,000 respectively. There were no statistically significant difference between SARI rates when comparing 2009 to 2008 ($p = 0.297$) and between 2009 and 2007 ($p = 0.334$) (►Fig. 3).

The SARI mortality rate (13.4; 95%CI 8.67 to 20.84) during EW 21 to 26 for 2009, was higher when compared to 2008 (4.79; 95%CI 2.28 to 10.06) (RR 2.8; 95%CI 1.18 to 6.63; $p = 0.031$) and similar to that of 2007 (12.7; 95%CI 8.05 to 20.29) (RR 1.05; 95%CI 0.56 to 1.49; $p = 0.969$) (►Fig. 3).

Comparable proportions of SARI cases that required ICU care were found in the three years (2009: 22%; 2008: 21% and 2007: 21%). However, the case fatality rate for SARI was 14% (95%CI 8.57 to 20.36) (20 cases) in 2009 compared to 6% (95%CI 2.35 to 11.55) in 2008 ($p = 0.031$). Case fatality rate was highest in 2009 in both age groups (younger and older than 65 years old) (►Fig. 4).

Twenty nine laboratory-confirmed A/H1N1 patients were admitted to the Hospital, and five of them died in 2009. All five laboratories of confirmed enrollees who died had at least one comorbidity (obesity/overweight, congestive heart failure, diabetes, asthma, hypertension, human immunodeficiency virus infection, chronic kidney disease and/or cancer).

Mortality among these laboratory-confirmed inpatient A/H1N1 cases was 17% (4/23) for adults and one out of six for pediatric cases. However, in a manual check of the electronic medical records of the 20 dead patients who had contracted SARI during the study period in 2009, only 10 had been swabbed. The ten non-swabbed mortalities met clinical criteria to had undergone swabbing; six of them were admitted before the national swab requirement for people that had not been in Mexico. Applying the Ministry of Health weekly reported percentage of A/H1N1 to our non-swabbed deceased patients, 4 of them could have been unregistered positive deceased A/H1N1 patients.

After adding confirmed and estimated unregistered positive dead A/H1N1 patients, the A/H1N1 case fatality rate for severe acute respiratory ill patient was estimated as 6.2% (95%CI 2.5 to 15.5). The A/H1N1 mortality rate between May 24th and July 11th among middle income Argentinian HMO members was estimated as 6 per 100,000 (95%CI 0 to 11.6).

Geographical spread

The distribution of people that sought care due to flu like symptoms during the earlier weeks (EW 21) was geographically plotted and had spread throughout the city of Buenos Aires by this time (►Fig. 5).

Discussion

Main finding of this study

In 150,000 middle income Argentinian HMO members the A/H1N1 epidemic sharply spread over a 6 week period.

The HIBA⁷ HIS detected an epidemic increase in the ILI consultation rate two weeks before the MoH issued a national alert. The consultation rate surpassed during week 23 the epidemic threshold. The MoH policy of containment at that stage called for restricted swab testing only in those people who had been in contact with another confirmed case. However, the few nasopharyngeal swabs obtained from suspected cases at our hospital prior to EW 23 reflected a high H1N1 viral circulation.

When comparing this seasonal period to previous years the impact on the health care system was primarily in ambulatory care; there was a marginal increase in admissions.

Morbidity from respiratory diseases between May 24th and July 11th 2009 was similar to the same period in the previous year. Mortality from SARI was three fold higher for year 2009 compared to the 2008 period and similar to 2007, a year when Influenza A also reached an epidemic threshold. However, a new pattern of SARI mortalities was observed in 2009: no cases had been registered in enrollees under 65 years old in previous years while the case fatality rate for elderly was highest.

Rate comparisons to other national populations are not available as we were unable to find standardized SARI morbidity and mortality rates for the same period of time. However in Mexico during a four week period (March 24th to April 29th, 2009), a 5% case fatality rate for severe pneumonia was found while we experienced 14% (95%CI 8.57 to 20.36) during six weeks (from May 24th to July 11th, 2009) for severe acute respiratory diseases. The age specific case fatality rate for the Mexican population younger than 65 was 4.9% and for older 28%, compared to our rates of 6.2% (95%IC 2.53 to 14.64) and 23% (95%IC 14.12 to 38.87) respectively. Thus, this might reflect that the disease's affect was constant across Buenos Aires and Mexico, the difference in the age distribution between the two populations might be what is driving the higher total rate in Buenos Aires [28].

Our HIS can contribute to accomplish the World Health Organization recommendation for influenza surveillance in Argentina. In other countries weekly influenza reports were developed based on data collected routinely. In the US, information on patient visits to health care providers for influenza-like illness is collected through the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet). ILINet consists of more than 3,000 healthcare providers in all 50 states allowing for comparing weekly influenza rates. Also rapid tracking of influenza-associated deaths is done through vital statistics [27].

By other hand, the Real-time Outbreak and Disease Surveillance (RODS) system, also detected outbreaks but based on data collected routinely for other purposes than health. Examples of such data include absenteeism data, sales of over-the-counter health care products, etc [8].

A national integration of all kind of information systems could be one strategy to face a future epidemic.

What this study adds

New policies to address outbreaks are now feasible thanks to the development and integration of health information systems. This includes strengthening surveillance and integrating private and public health information systems, building up networks, and improving private-public communication.

Limitations of this study

The time period covered by this study was during the main epidemic wave but incompletely describes the winter season.

We are not able to describe the impact in Buenos Aires city as a whole due to the dearth of low income enrollees in our HMO population.

In retrospect, our national surveillance system failed to provide us with expeditious, qualitative alerts. An indicator of such failure was the non-implementation of full-scale swab testing to patients with symptoms of SARI from the very start of the outbreak. Thus, we emphasize that public health surveillance systems should adopt new methods for detecting outbreaks of infectious disease that integrate data from the private healthcare system.

Conclusions

The health information system of a private academic hospital in Buenos Aires was useful in assessing the morbidity and mortality attributable to the 2009 flu epidemic H1N1 outbreak. This suggests that, with integration of public and private data sources, a more real-time outbreak and disease surveillance system could be implemented. The impact on the health care system was mainly in ambulatory care. SARI mortalities for 2009 were 3 fold higher than in 2008 and in a younger age strata.

Implications of results for practitioners

An early warning information system, using daily automated extraction of routinely generated coded data daily, should allow for planning increases of the ambulatory visit response in an efficient cost-effective manner. Such planning would include making additional human resources available, such as doctors, nurses and administrative staff, as well as ad hoc consulting rooms. This emerging information technology is useful for planning an efficient healthcare delivery.

Conflict of interest

The authors have no real or potential conflict of interest with any financial or contractual organization that would influence objective methods of analyzing and reporting the results.

Ethical considerations

The ethical principles that pertain to this study comply with the Helsinki Declaration [29].

Every patient signed consent for using his/her medical data for research purposes and without personal identification when entering the HMO.

The institutional review board (IRB) of the Hospital Italiano approved the Spanish-language version of the protocol (internal number 1224).

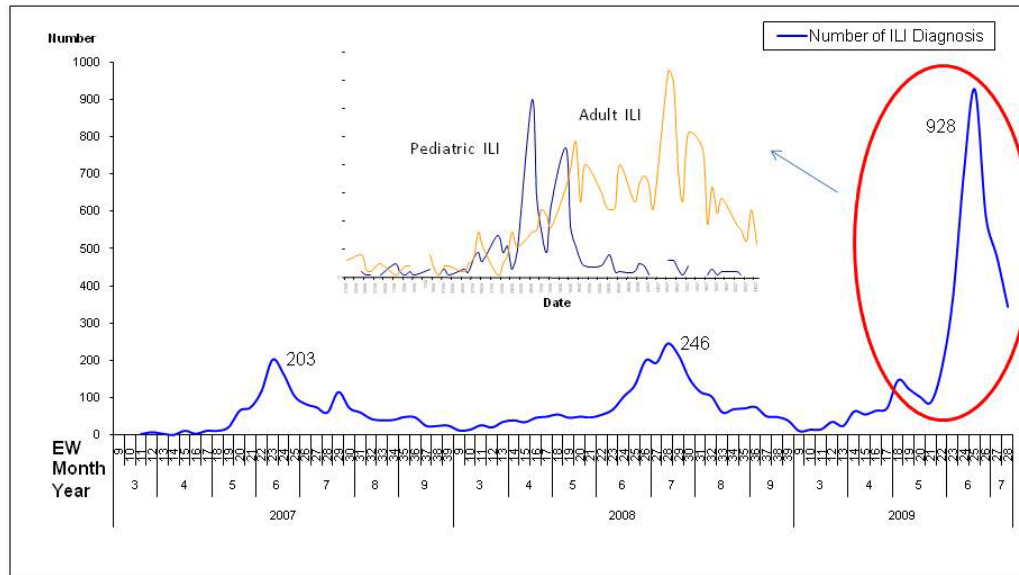


Fig. 1 Number of Influenza Like Illness visits to the Hospital Italiano’s HMO from year 2007 to the epidemiological week number 28 of year 2009.

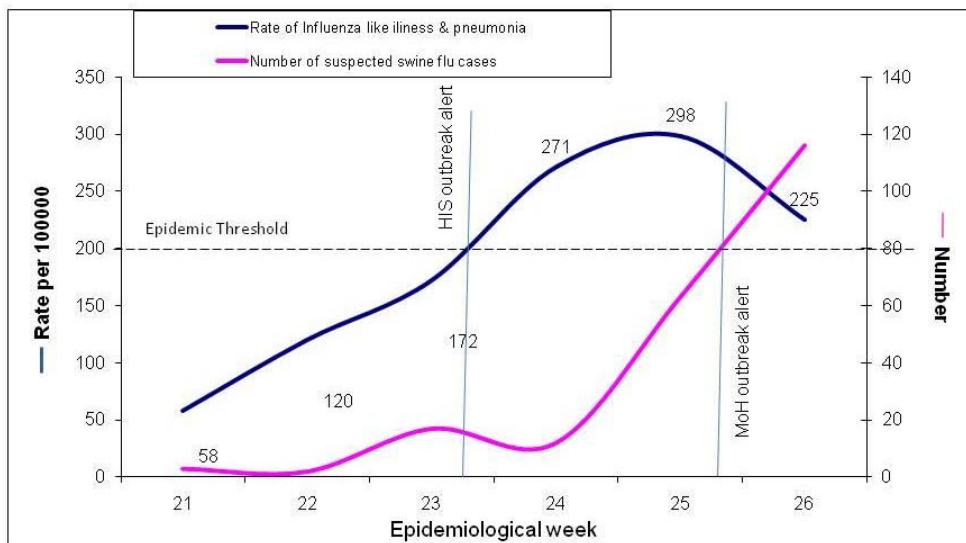


Fig. 2 Outbreak alert defined by HIS weekly Influenza-like illness + Pneumonia rate vs. the number of suspected cases defined by the Ministry of Health, from May 24th 2009 to July 11th 2009.

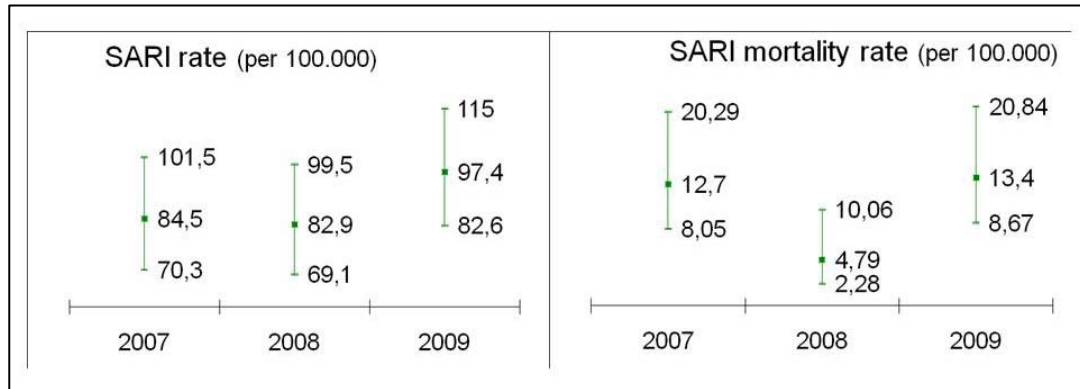


Fig. 3 Severe Acute Respiratory Illness (SARI) and SARI mortality rate from epidemiological week 21 to 26 for 2007, 2008 and 2009 at the Hospital Italiano's HMO. Error bars represent the 98% confidence interval.

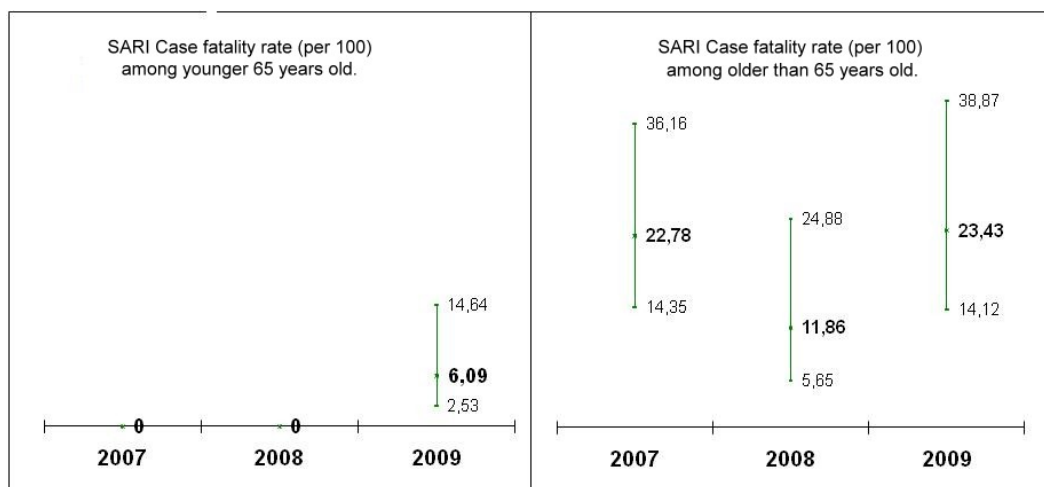


Fig. 4 Case fatality rates for Severe Acute Respiratory Illness (SARI) by age strata (under and over 65 years old) from epidemiological week 21 to 26 for 2007, 2008 and 2009 at the Hospital Italiano's HMO. Error bars represent the 95% confidence interval.

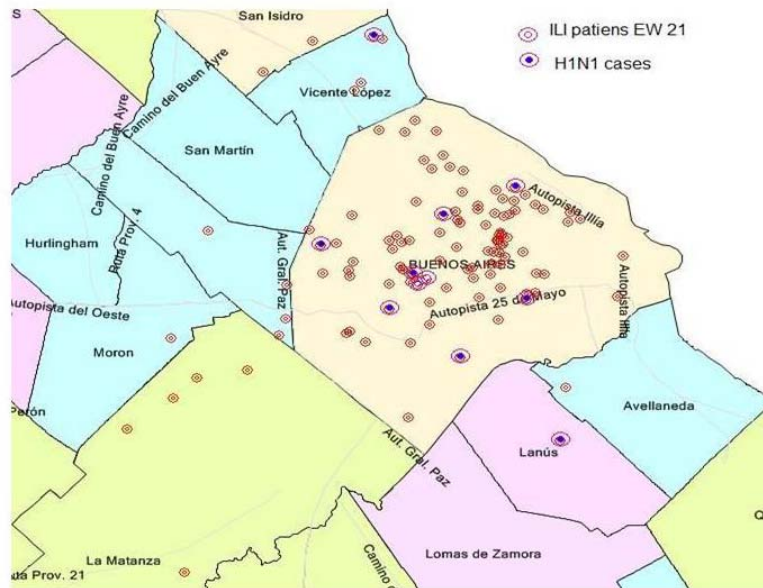


Fig. 5 Georeferency of ILI patients from May 24th to June 6th and the first ten confirmed H1N1 cases from the Hospital Italiano's HMO.

References

1. German RR, Lee LM, Horan JM, Milstein RL, Pertowski CA, Waller MN. Updated guidelines for evaluating public health surveillance systems: recommendations from the Guidelines Working Group. *MMWR Recomm Rep* 2001; 50 (RR-13): 1-35; quiz CE1-7.
2. Pina J, Turner A, Kwan-Gett T, Duchin J. Task analysis in action: the role of information systems in communicable disease reporting. *AMIA Annu Symp Proc* 2009; 2009: 531-535.
3. Haux R. Health information systems – past, present, future. *Int J Med Inform*. 2006; 75(3-4): 268-281. doi:10.1016/j.ijmedinf.2005.08.002 PMID:16169771
4. Koo D, O'Carroll P, LaVenture M. Public health 101 for informaticians. *J Am Med Inform Assoc* 2001; 8(6): 585-597. PMID:11687565 PMCID:130068
5. Ward M, Brandsema P, van Straten E, Bosman A. Electronic reporting improves timeliness and completeness of infectious disease notification, The Netherlands, 2003. *Euro Surveill* 2005; 10(1): 27-30. PMID:15701937
6. Emergency department chief complaint syndromic surveillance system pilot project: technical evaluation. In: Care OMoHaL-T, editor.; 2006.
7. National Electronic Disease Surveillance System (NEDSS): a standards-based approach to connect public health and clinical medicine. *J Public Health Manag Pract* 2001; 7(6): 43-50. PMID:11713753
8. Espino JU, Wagner M, Szczepaniak C, Tsui FC, Su H, Olszewski R, et al. Removing a barrier to computer-based outbreak and disease surveillance – the RODS Open Source Project. *MMWR Morb Mortal Wkly Rep* 2004; 53 (Suppl.): 32-39. PMID:15714624
9. Espino JU, Wagner MM, Tsui FC, Su HD, Olszewski RT, Lie Z, et al. The RODS Open Source Project: removing a barrier to syndromic surveillance. *Stud Health Technol Inform* 2004; 107(Pt 2): 1192-1196. PMID:15361001
10. Panackal AA, M'likanatha N M, Tsui FC, McMahon J, Wagner MM, Dixon BW, et al. Automatic electronic laboratory-based reporting of notifiable infectious diseases at a large health system. *Emerg Infect Dis* 2002; 8(7): 685-691. PMID:12095435 PMCID:2730325
11. Moore KM, Edgar BL, McGuinness D. Implementation of an automated, real-time public health surveillance system linking emergency departments and health units: rationale and methodology. *Cjem* 2008; 10(2): 114-119. PMID:10165364
12. Parsons DF, Garnerin P, Flahault A, Gotham IJ. Status of electronic reporting of notifiable conditions in the United States and Europe. *Telemed J* 1996 Winter; 2(4): 273-284.
13. Grant AD, Eke B. Application of information technology to the laboratory reporting of communicable disease in England and Wales. *Commun Dis Rep CDR Rev* 1993; 3(6): R75-R78. PMID:18172157 PMCID:2376898
14. Overhage JM, Grannis S, McDonald CJ. A comparison of the completeness and timeliness of automated electronic laboratory reporting and spontaneous reporting of notifiable conditions. *Am J Public Health* 2008; 98(2): 344-350. doi:10.2105/AJPH.2006.092700
15. Luna D, et al. Implementación de una Historia Clínica Electrónica Ambulatoria. Buenos Aires, Argentina. http://www.frcu.utn.edu.ar/deptos/depto_3/32JAIO/sis/SIS_08.pdf. 6to Simposio de Informática en Salud – 32 JAIO. Buenos Aires – Argentina 2003.
16. Luna D, et al. Informatización de la capa clínica de un sistema de salud metropolitana: el proyecto itálica. *Tecnologías en Información en salud*; 2006; Chile; 2006.
17. Quiros FG. SNOMED CT and ICPC-2E cross mapping: coding to facilitate the access to information. 2004. p. 17th World Conference of Family Doctors. Orlando, FL. 168, PMID:17911820
18. Osornio AL, Luna D, Gambarte ML, Gomez A, Reynoso G, de Quiros FG. Creation of a local interface terminology to SNOMED CT. *Stud Health Technol Inform* 2007; 129(Pt 1): 765-769. PMID:17911791
19. Gambarte ML, Osornio AL, Martinez M, Reynoso G, Luna D, de Quiros FG. A practical approach to advanced terminology services in health information systems. *Stud Health Technol Inform* 2007; 129(Pt 1): 621-625. PMID:14708275
20. Human infection with pandemic (H1N1) 2009 virus: updated interim WHO guidance on global surveillance. http://www.who.int/csr/disease/swineflu/WHO_case_definition_swine_flu_2009_04_29.pdf. In: Organization WH, editor.; 2009.
21. Situación de la Influenza A (H1N1). Parte diario N° 3. Fecha: 01/05/09, Ministerio de Salud de la Nación. Ministerio de Salud de la Nación.
22. Situación de la Influenza A (H1N1). Parte periódico N° 62. Fecha: 09/07/09. Ministerio de Salud de la Nación.
23. Alerta por el Cambio de Fase 4 a Fase 5 para Pandemia de Influenza Actualización de la Situación Mundial sobre Brotes de Nuevo virus de Influenza Alerta J10-J18 6.2009. 2009, Ministerio de Salud de la Nación.
24. Campos AG F, Martínez M, Mauro A, Luna D, Soriano E. Quiros FGBd. Georeferenciamiento en un Sistema de Información en Salud [geore-fer_aaim_com_ar_orales_77_pdf.pdf](http://www.frcu.utn.edu.ar/deptos/depto_3/32JAIO/sis/SIS_08.pdf). INFOLAC2008 – AAIM © 2008

25. Matejic P MM, Vázquez R, Gil N, Tejerizo JC. Nueva gripe A. [Internet]. Como enfrentó la crisis el Hospital XXX de Buenos Aires. Rev. Hosp. B.Aires http://www.hospitalxxx.org.ar/docencia/nexo/index.php?contenido=ver_actualidad.php&id_actualidad.
26. Goddard NL, Kyncl J, Watson JM. Appropriateness of thresholds currently used to describe influenza activity in England. *Commun Dis Public Health* 2003; 6(3): 238-245. PMID:19564633
27. Overview of Influenza Surveillance in the United States. <http://www.cdc.gov/flu/weekly/pdf/overview.pdf>; 2007.
28. Chowell G, Bertozzi SM, Colchero MA, Lopez-Gatell H, Alpuche-Aranda C, Hernandez M, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. *N Engl J Med* 2009; 361(7): 674-679. doi:10.1056/NEJMoa0904023 PMID:18371248
29. Rickham PP. Human Experimentation. Code of Ethics of the World Medical Association. Declaration of Helsinki. *Br Med J* 1964; 2(5402): 177. PMID:14150898 PMCID:1816102