Global Influenza Hospital Surveillance Network

GLOBAL INFLUENZA SURVEILLANCE HOSPITAL NETWORK

Annual meeting

17th and 18th October, 2016 - Barcelona, Spain

The GIHSN has covered the following sites this season (2015/2016) – Russia, Czech Republic, France, Canada, Turkey, Spain, India, China, Mexico and Brazil. It is expected that the GIHSN will continue to expand globally. The standardization of data collection is essential in order to get statistical results about the influenza along the years and among all sites.

The 2016 GIHSN Annual Meeting took place on 17th-18th October 2016 in Barcelona, and it had four main objectives:

1. Discuss the different study sites fieldwork experiences and protocols to analyze and derive best methodological practices;
2. Review the data and results generated by each study site and from data pooling;
3. Discuss publications and ways to disseminate the information generated;
4. Review the current framework of this global partnership; evaluate the network's future research prospects and the possibilities for new collaborative partners to join the GIHSN.

The meeting took place in the Hilton Hotel in Barcelona, Spain.

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Main results – Summary by site

- **Russia – St. Petersburg:** Russia – St. Petersburg: Severe influenza epidemic caused by influenza A(H1N1)pdm09 virus antigenically related to A/California/07/09 and genetically belonged to the subgroup 6B.1 was registered in the season 2015-2016. Specific mutations in the internal genes NS, NEP, NP, M1, PA-X of influenza A(H1N1)pdm09 virus were revealed. Influenza B (Victoria lineage) circulation increased towards the end of the season.
- **Russia – Moscow:** Most of the excluded patients were excluded because symptoms started more than 7 days before admission. This season started earlier than the previous one. Influenza A(H1N1)pdm cases predominated until week 09/2016 and influenza B-Victoria predominated from week 10/2016 until the end of the season.
- **Czech Republic:** Patients aged 18 years or more were included in the study. The number of screened patients was around 250 on a residence area that has around 2 million inhabitants. One hospital was included in the study. BMI was found higher for the older patients.
- **France:** Patients aged 18 years or more were included in the study. This last 2015-2016 season started later than the previous one. There was a sharp decrease of patients' enrolment around week 9/2016, possibly due to winter school holidays. Vaccination was found more effective against hospitalized A(H1N1)pdm influenza but not against B (Victoria).
- **Turkey:** The length of stay at hospital was longer for children. There was a high number of exclusions because of the number of hospitalized in the last 30 days. Most of the influenza infections were due to influenza A(H1N1)pdm among 5-17 years old age group. There were a lot of patients with at least one chronic condition.
- **China – Beijing:** There were 5 hospitals in the study. The population of the residence area was around 5 millions. A(H1N)pdm and B/Victoria were predominant this season.
- **India:** Influenza A(H3N2) was the predominant type circulating this season. There were low numbers of people vaccinated and people with influenza confirmed by laboratory. Influenza virus cases reached a peak in February.
- **Valencia:** 2015/2016 season started later than the previous one, with a peak of influenza cases at week 11/2016. Predominant types and subtypes of influenza virus were A(H1N)pdm, followed by B/Victoria. Population of the residence area was around 1 million, distributed in 4 hospitals. There were statistically significant differences by age and occupational socioeconomic class. In addition, statistically significant differences were found in the probability of having influenza for those vaccinated this season and not vaccinated in the two previous seasons, with a lower probability in those vaccinated only in the current season.
- **Mexico:** Four hospitals were included in the study during the 2015/2016 season. They will include one more hospital during the next season. This was a late season with a high number of patients with RSV.
- **Brazil:** Fortaleza stopped the study at the beginning of March due to issues with Ethical Committee, but resumed in the second week of October. Influenza was not detected in Fortaleza during this study period. In Curitiba, the majority of influenza cases were due to A(H1N1)pdm. Influenza vaccination was offered in April for people under 5 years old

and people 60 years or older, but influenza season started in February, with a peak in June-July.

GIHSN pooled results

- Data have been updated just a few days before the Annual Meeting. For the next season, it is planned to finish collecting data before the end of the summer.
- This was a late season in which only 1% of all data was missing.
- It is important to discuss the impact of recruiting only patients with acute respiratory symptoms in the estimation of the burden of disease, as it is usually done in Russia, France, Czech Republic and Mexico. It is worth noting that the probability of having pneumonia in case of having influenza is higher for patients infected with A(H1N1)pdm than for patients with A/not subtyped.
- Pregnancy was found a risk factor of having influenza, A(H1N1)pdm being a predictive factor for severe influenza among pregnant women.
- Overall influenza vaccine effectiveness was around 20%.
- The predominant types and subtypes of influenza this season were A(H1N1)pdm and B/Victoria.
- Comorbidity was related to an increased risk of severe influenza.
- Vaccine effectiveness was high (≈ 65%) in preventing A(H1N1)pdm09 related admissions in the not previously vaccinated.
- Regarding other respiratory viruses, the probability of being positive for each virus was described by epidemiological week and season, and the age and comorbidity related risk was detailed. The next step will be to estimate the burden of disease for respiratory viruses. It should require an earlier start of the study period, as the circulation of respiratory viruses precedes the circulation of influenza in the winter season.
- The eligibility criteria, as well as the collection of data and introduction of patients on datasets, are essential to have a good quality of data. A revision of the Standard Operating Procedures protocol and the list of all variables for the GISHN study have been uploaded on the GIHSN website.
- Patients with a previous hospitalization in the last 30 days were not included in order to exclude nosocomial infections. This is a standard criterion but whether to change it should be discussed. Indeed, the results from the pooled analysis were not too different from Turkey's results, which only excluded patients who had a previous hospitalization in the last 10 days. However, any change in the collected variables would have an impact in comparisons with data obtained in previous seasons.
- The sensitivity of the PCR test is low after 7 days of the onset of symptoms, explains the establishment of the exclusion criteria for those who have swabs taken more than 7 days after the onset of symptoms. After 7 days, the PCR sensitivity decreases by half.
- The ILI criteria should be reviewed if we want to estimate the burden of disease for RSV, as RSV case definition differs slightly and does not include fever. However, the ILI criterion that has been used so far does not include fever as necessary criteria.

- Valencia, Turkey, St. Petersburg and Fortaleza provided data for studying respiratory viruses in years 2012-2014. Valencia and St. Petersburg provided the majority of the cases with respiratory viruses in these three seasons, in which the Respiratory Syncytial Virus (RSV) was the predominant respiratory virus along with influenza, with no clear peak of activity in a specific week. Another dominant virus is Rhinovirus/Enterovirus. Significant differences by age groups have been found for RSV, Rhinovirus/Enterovirus and Coronavirus.

Burden of disease

- **Working model from sites (methodology used, issues), a brief introduction:** The GIHSN Coordination Office has estimated the burden of disease for several countries in the 2015/2016 season, following the recommendations issued by WHO, and has presented a poster with the results during a meeting in the WHO in Geneva last July. Valencia has a well-defined denominator, and the burden of disease has been calculated by dividing directly the number of influenza cases included in the study by the population. For St. Petersburg, Moscow and Turkey sites, the denominator was estimated by obtaining the population by age group for the residence area and multiplying the number of subjects in each age-group by the fraction of admissions due to ARI/ILI (in St. Petersburg) or pneumonia (in Moscow) in the participating hospitals over the total of ARI/ILI or pneumonia admissions in the residence area. For other sites, it was not possible to provide residence-area denominators. The heterogeneity of data was high and for the next seasons, it will be necessary to estimate weighted denominators and to explain the heterogeneity inside and across sites.
- **WHO manual for estimating the burden of disease: methodology and implementation:** The WHO manual to calculate the burden of disease includes tools for different scenarios – SARI sentinel sites, hospitals not included as SARI sentinel, ILI surveillance, and theoretical concepts. This manual is completed by practical examples. It appears essential to collect data for the whole influenza season in order to estimate the burden of disease, suggesting that influenza seasons have to be clearly defined. The estimations of the burden of disease can be obtained if the catchment population is known or knowable. In this second case, cases of pneumonia or SARI cases in the residence area and hospitalizations with pneumonia or SARI in the area hospitals must be well-known. Sparse numbers have made not possible the estimation of the burden of disease for the pregnant women or people with chronic medical conditions.

External perspectives and shared experiences

- **Real time influenza surveillance in community:** A study based on the information collected from French pharmacies was developed to assess, for instance, the influenza vaccination coverage. The tool used Vaccination campaign and influenza cases are followed daily with this system.
- **FluNet approaches for estimating burden of disease:** FluNet is a surveillance platform, rather than a system to measure the burden of disease. It is a publicly available database with the possibility to select information from various countries countries. FluNet can be used to estimate the characteristics (or 'metrics') of influenza epidemics (e.g. what is the proportion of influenza B in a season?), construct models, or to do spatio-temporal and modelling analysis.

GIHSN development and perspectives

- **Foundation for influenza epidemiology:** 15 sites will be included in the GIHSN 16/17 study, including 8 new sites. The objectives for the new season will be to increase awareness to expand influenza surveillance and to include more epidemiological information, to identify specific gaps in global influenza surveillance capacity, and to have a better understanding of: risk factors for severe disease, variation of influenza severity from season to season, relationship between virus types or subtypes and severity, and burden of disease related to influenza. Coordination activities and technical support will still be provided by FISABIO.
- **Virological characterization of influenza isolates:** Extensive genetic characterization of influenza viruses by next generation sequencing is now feasible and affordable. New models combining genetic and serological data from viral isolates are needed. Linking influenza genetic information with vaccine effectiveness is possible with extensive datasets (analysis by clade, subclade and significant number of vaccine failures). One objective will be to define a model to predict the evolution of influenza virus by the observation of the trees of the strains.
- **Economic outcomes:** The most expensive health care costs for influenza are those related to hospitalised cases, and these costs are determined heavily by the length of stay. The costs and length of stay of hospitalised cases can often be obtained from the accountancy department of hospitals, and in some countries also from (national or private) insurer databases. Hospitalisation costs are important for the estimation of the cost of illness and the economic burden of disease, which in turn are essential to estimate the cost-effectiveness of interventions such as vaccination. There is a useful recent WHO guide and manual on estimating influenza costs for economic evaluations (see http://apps.who.int/iris/bitstream/10665/250086/1/WHO-IVB-16.05-eng.pdf) .

More information about the Global Influenza Hospital Surveillance Network can be found at www.gihsn.org and in Puig-Barberà et al. (2015) The Global Influenza Hospital

Surveillance Network (GIHSN): a new platform to describe the epidemiology of severe influenza. Influenza and other Respiratory Viruses DOI: 10.1111/irv.12335.
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