Valladolid National Influenza Centre

Annual Report of the Influenza Activity in Castile and Leon, Spain

2019-2020 season

REPORT: Influenza activity during the 2019-2020 influenza season

Valladolid National Influenza Centre

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Valladolid, Castile and León, Spain

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1. Summary

- The virological surveillance of influenza in Castile and Leon (Spain) during the 2019-2020 influenza season was characterized by the mixed circulation of both A(H1N1)pdm09 & influenza B viruses, being predominantly the A(H1) pdm09. Only a few percentages of A(H3N2) subtype was detected during this period.

- The first case of influenza infection was identified in week 43/2020, and corresponded to one hospitalized child (female; 4 years old) infected by Influenza B type virus. The first case in the Sentinel Network was identified in week 48/2019 in a child (male; 11 years old) infected also by an influenza B type virus.

- The epidemic started the week 2/2020 with an incidence rate of 101.6 cases/100,000 inhabitants. The epidemic cut-off in Castile and Leon is fixed in 50 cases/100,000 inhabitants.

- The influenza epidemic peaked in Castile and Leon the week 5/2020 with an incidence rate of 303.0 cases/100,000 inhabitants, corresponding to a medium activity of influenza virus circulation.

- The predominant virus in Hospitalized was the A(H1N1)pdm09 virus, and in the Sentinel Network the influenza B virus was the most commonly detected.

- The A(H1N1)pdm09 subtype was more frequently detected in hospitalized than in those patients from the Sentinel Network. The 53.4% of viruses identified in hospitalized patients were A(H1)pdm09 viruses and 39.3% were influenza B. The 43.8% of viruses identified in Sentinel Network patients were A(H1N1)pdm09 and 45.0% were influenza B. Some co-detections of A(H1N1)pdm09 and A(H3N2) subtypes were observed in both hospitalized and sentinel patients.

- The most affected age groups in hospitalized patients were the elderly people (50.9%), and the children (5-14 years) (30.2%) in the Sentinel Network.

- Co-infections o influenza and other respiratory viruses were more frequently detected in hospitalized (17.6%) than in sentinel patients (19.3%), being the A(H1N1)pdm09 subtype the most frequently detected in co-infection in hospitalized (9.8%) and influenza B in sentinels (12.7%).

2. Influenza Surveillance System in Castile and Leon

The surveillance of influenza in Castile and Leon (Spain) has been carried out since the year 1976 through the National Influenza Center of Valladolid (Valladolid NIC), and in collaboration with the Sentinel Network of Castile and Leon (SNCyL) since 1989. The system is designed to monitor influenza activity in the community and at the hospital level. The SNCyL has a number of sentinel doctors and pediatricians (general practitioners) distributed according to population criteria throughout the territory of Castile and Leon. These physicians collect pharyngeal swabs from patients who come to their primary health care centers with ILI symptoms. The collection of these samples is supervised by the technical coordinator of the SNCyL, Dr. Tomas Vega. This surveillance is also nourished by samples from hospitalized patients collected in the hospitals of the different cities of Castile and Leon.

The collected data are sent weekly to the Health Department of the Government of Castile and Leon, which produces a report on the characteristics of the circulating flu and the affected population. This report can be viewed in Spanish through the following web link:

https://www.saludcastillayleon.es/ciudadanos/es/enfermedades-problemas-salud/gripe/informacion-semanal-gripe

3. Influenza activity in Castile and Leon during the 2019-2020 influenza season

The influenza season during 2019-2020 has been affected by the SARS-CoV-2 pandemic. The first case of influenza in Castile and Leon during the 2019-2020 season was detected in week 43/2018, and correspond to a hospitalized female child of 4 years old, in Valladolid. The epidemic threshold has been overpassed in the week 2/2020 (101.6 cases/100.000 inhabitants), and the epidemic peaked in the week 5/2020 with an incidence rate of 303.0 cases per 100,000 inhabitants (Figure 1). The maximum intensity level of influenza circulation during this epidemic peak was medium. The epidemic lasted eight consecutive weeks and finalized in week 10th.

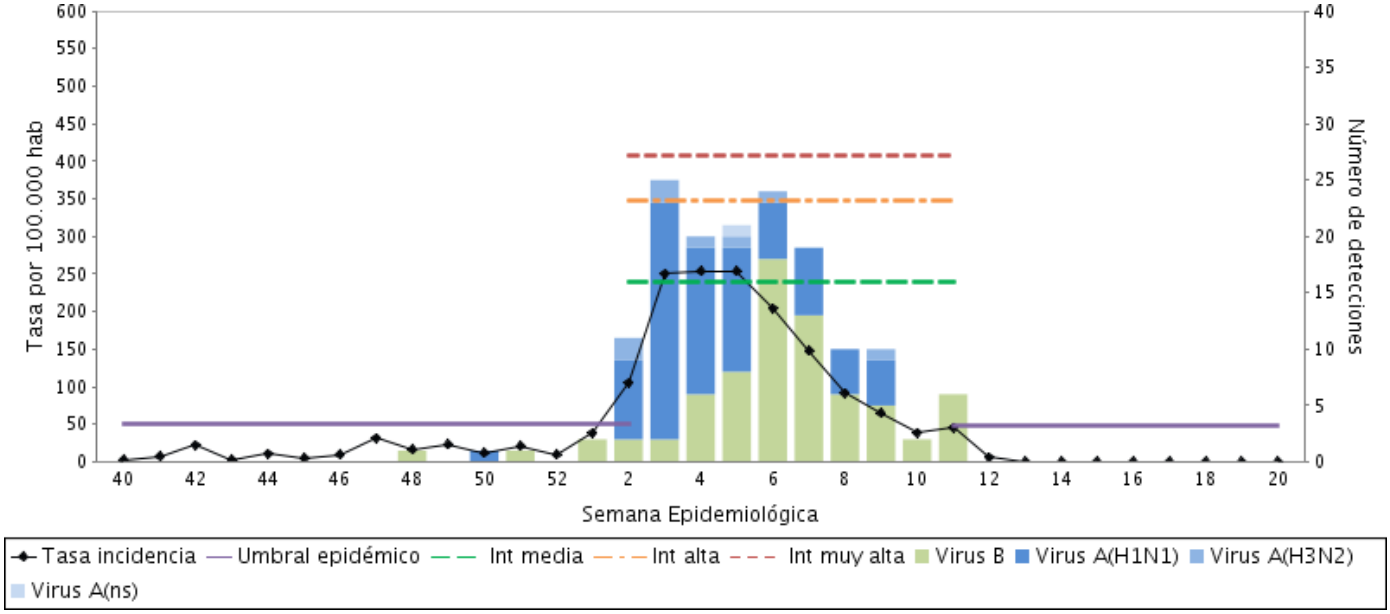

Figure 1. Incidence rate (cases/100,000 inhabitants) and number of influenza detections per week between weeks 40/2019 and 20/2020 in Castile and Leon (Spain). Source: https://www.saludcastillayleon.es/ciudadanos/es/enfermedades-problemas-salud/gripe/informacion-semanal-gripe

The cumulative rate of influenza per 100,000 inhabitants up to week 20/2019 was high, especially in the children (0-4 years and 5-14 years) with a sharp different profile between the elderly and young people (Figure 2).

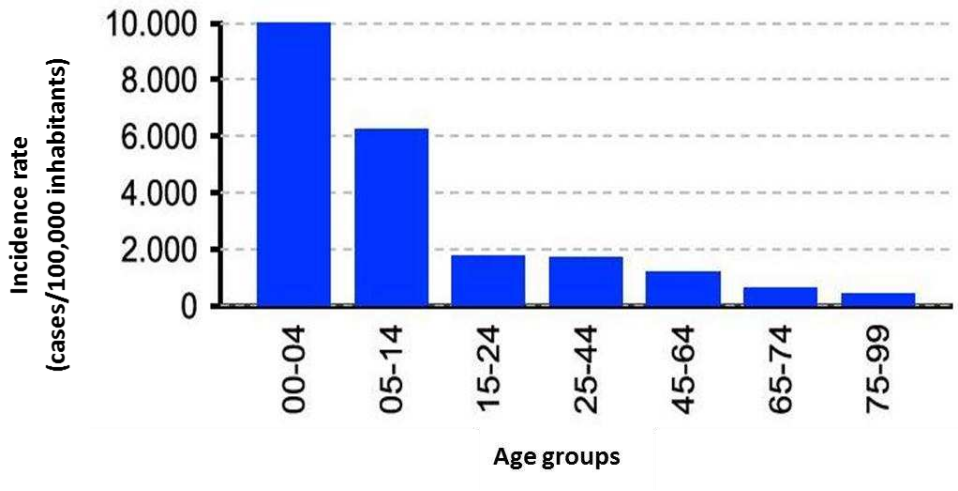

Figure 2. Cumulative flu rate per 100,000 inhabitants in the different age groups until week 20/2019. Source: https://www.saludcastillayleon.es/ciudadanos/es/enfermedades-problemas-salud/gripe/informacion-semanal-gripe

Globally in Spain, influenza epidemic started in week 2/2020 and peaked in week 5/2020, similar to Castile and Leon, with an incidence rate of 271.4 cases per 100,000 inhabitants and a medium intensity level. The epidemic in Spain lasted for 9 weeks (Figure 3).

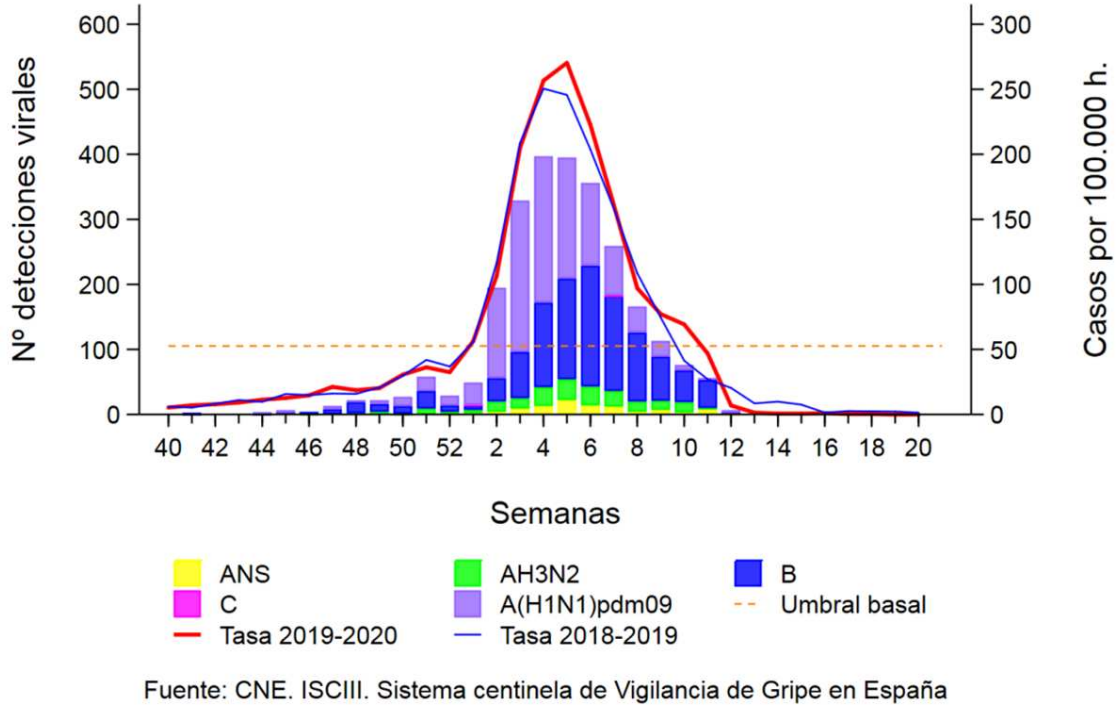

Figure 3. Incidence rate and number of flu detections per week between weeks 40/2019 and 20/2020 in Spain. Source: CNE. Sistema centinela de vigilancia de la gripe en España; http://vgripe.isciii.es/inicio.do.

4. Virological surveillance

The SNCyL sends pharyngeal swabs of ILI-cases to Valladolid NIC during the surveillance period. Furthermore, hospitals in Castile and Leon send different respiratory samples from ILI-cases for the diagnostic of influenza and other respiratory viruses. Influenza virus infection and other respiratory viruses are detected in the laboratory by different diagnostic methods based on PCR and cell culture. Influenza virus isolation is carried out by culturing in MDCK and MDCK/Siat1 cells, as well as in embryonated chicken eggs for subsequent antigenic and genetic characterization. Antiviral resistance evaluation is carried out by molecular methods searching for mutations in the NA-H275Y of A(H1N1)pdm09 subtype, and others phenotypic and genetic methods.

General data

Since the week 40/2019 till week 20/2020, a total of 621 influenza viruses have been diagnosed and confirmed in the laboratory of Valladolid NIC; 160 in SNCyL patients (25.8%) and 461 from hospitalized patients (74.2%). During 2019-2020 influenza season, the 58.9% of viruses were identified as influenza A type and 42.9% as influenza B viruses were detected. Globally, the A(H1N1)pdm09 subtype represented 51.4% of all viruses identified, not subtyped influenza B represented 41.1%, not subtyped influenza A viruses represented 3.1%, A(H3) represented 2.4% and co-infections between A and B subtypes represented of 1.8% of the detections (Figure 4). Co-infections between H1 and H3 represented only 0.2% of all viruses detected.

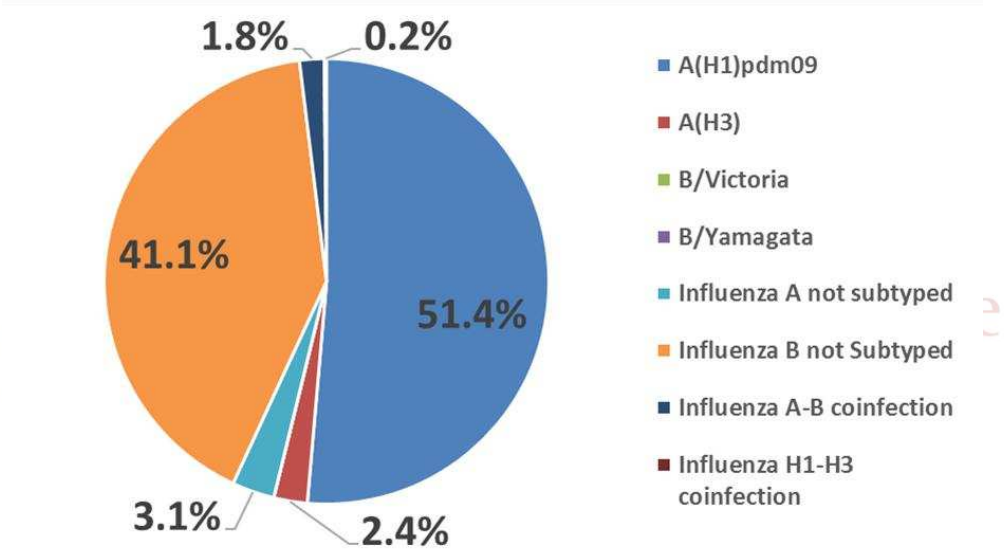

Figure 4. Percentage of detections of the different types and subtypes of influenza A and B viruses in both hospitalized and SNCyL patients. Source: Valladolid NIC.

Hospitalized patients

In hospitalized patients, A type influenza represented 61.0% and B type influenza represented 39.0%. A(H1N1)pdm09 was the subtype more frequently detected (53.4%) and influenza B not subtyped represented 39.3% of viruses identified (Figure 5). The 3.9% was influenza A not subtyped, and A(H3) represented 1.7%. It was detected a co-infection between influenza A and B in 1.7% of the identified viruses.

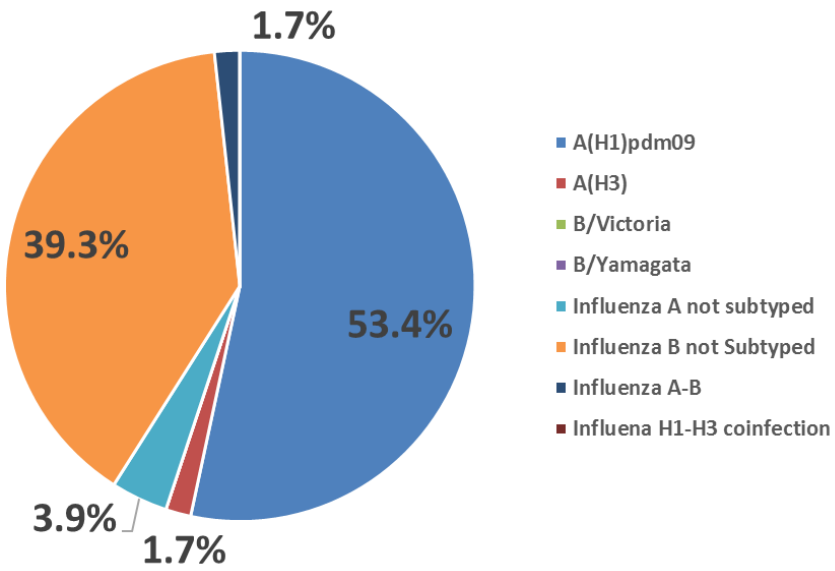

Figure 5. Percentage of detection of the different types and subtypes of influenza A and B viruses in hospitalized patients. Source: Valladolid NIC.

The first influenza laboratory confirmed cases in hospitalized patients during the 2019-2020 season were detected between the weeks 43/2019 and 51/2019, and were identified as both A(H1N1)pdm09 and influenza B not subtyped (Figure 6). Since week 1/2020, influenza A(H1N1)pdm09 and influenza B not subtyped were the virus more frequently identified in hospitalized patients until the end of the surveillance period.

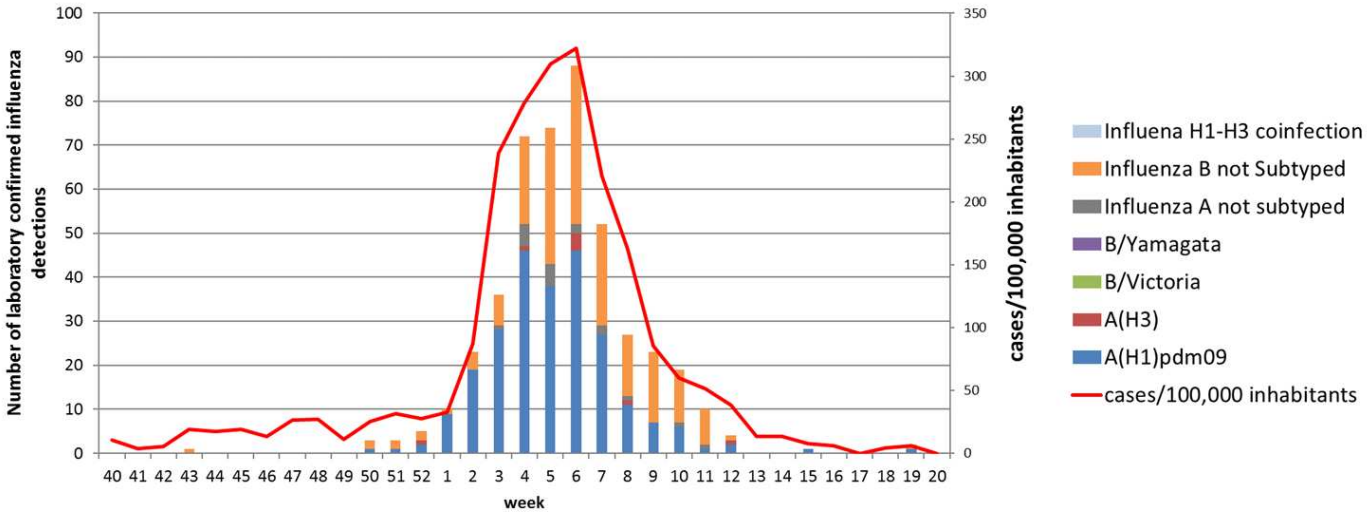

Figure 6. Number of identifications per week of influenza A and B subtypes and lineages in hospitalized patients. Incidence rate of influenza detection. Source: Valladolid NIC.

Almost half of the influenza detections in hospitalized patients were observed in the pediatric (0-4 years) and children (5-14 years) (53.2%), predominantly the A(H1N1)pdm09 subtype (70%). The number of influenza laboratory confirmed cases in the pediatric patients were 2.5 times higher than in the others age groups. The percentage of A(H1N1)pdm09 subtype identified in young-adult patients (15-44 years), adults (45-64 years) and elderly were 52.7%, 91.1%, and 76.7% respectively (Figure 7).

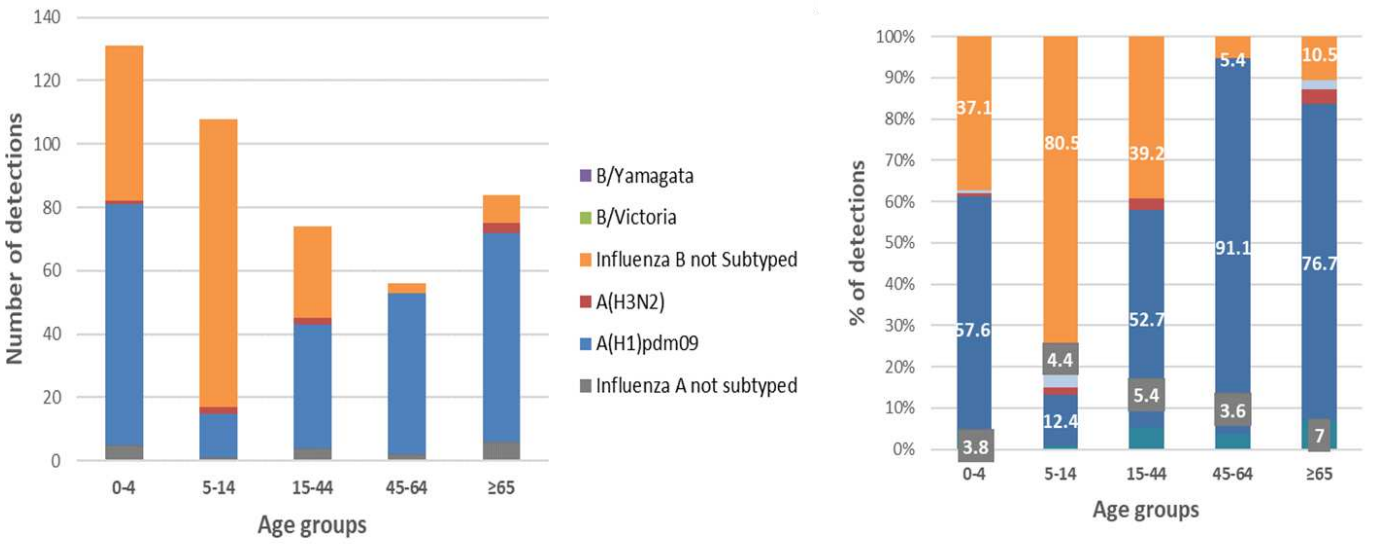

Figure 7. Absolute number and percentage of detections of influenza A and B subtypes and lineages in the different age groups of hospitalized patients analyzed. Source: Valladolid NIC.

Patients from Sentinel Network

In almost the half of the samples of the SNCyL it was identified influenza B not subtyped viruses (45%) and the other predominant virus was A(H1N1)pdm09 (43.8%). (Figure 8). A(H3) subtype represented 5% of identifications. The 1.9% of influenza A type viruses could not be assigned to any subtype, and in 2.5% of samples were detected a co-infection between A(H1) and A(H3) influenza subtypes. The coinfection between A-B represented 1.9%.

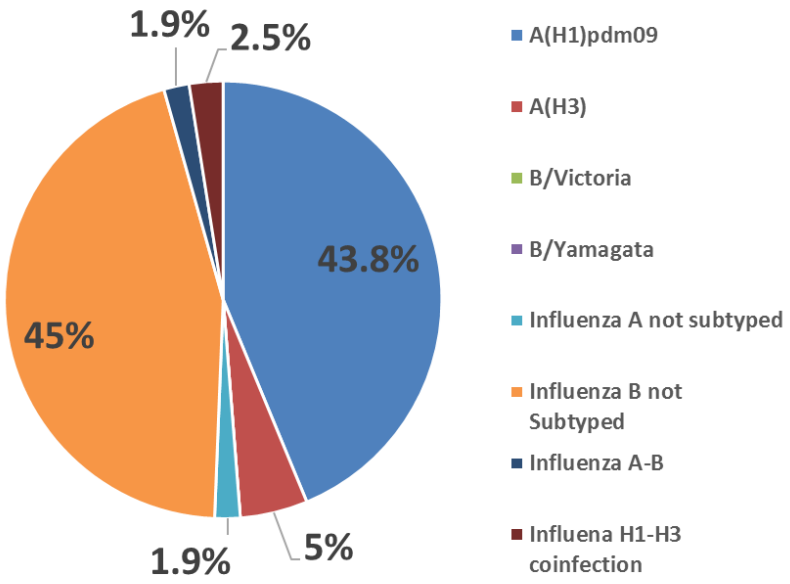

Figure 8. Percentage of detection of the different types and subtypes of influenza A and B viruses in sentinel patients. Source: Valladolid NIC.

The first laboratory influenza confirmed case in sentinel patients during the 2019-2020 season was detected in week 48/2018, corresponding to a not subtyped B virus. Two weeks later (50/2019), it was detected an A(H1N1)pdm09 virus. Influenza A(H1N1)pdm09 and not subtyped B cocirculate in the community since week 2/2020 until week 11/2020. The percentage of A(H1N1)pdm09 and not subtyped B viruses identified was similar (approximately 50%), but since week 6/2020 the not subtyped B was the virus most identified in sentinel patients till the end of influenza circulation.

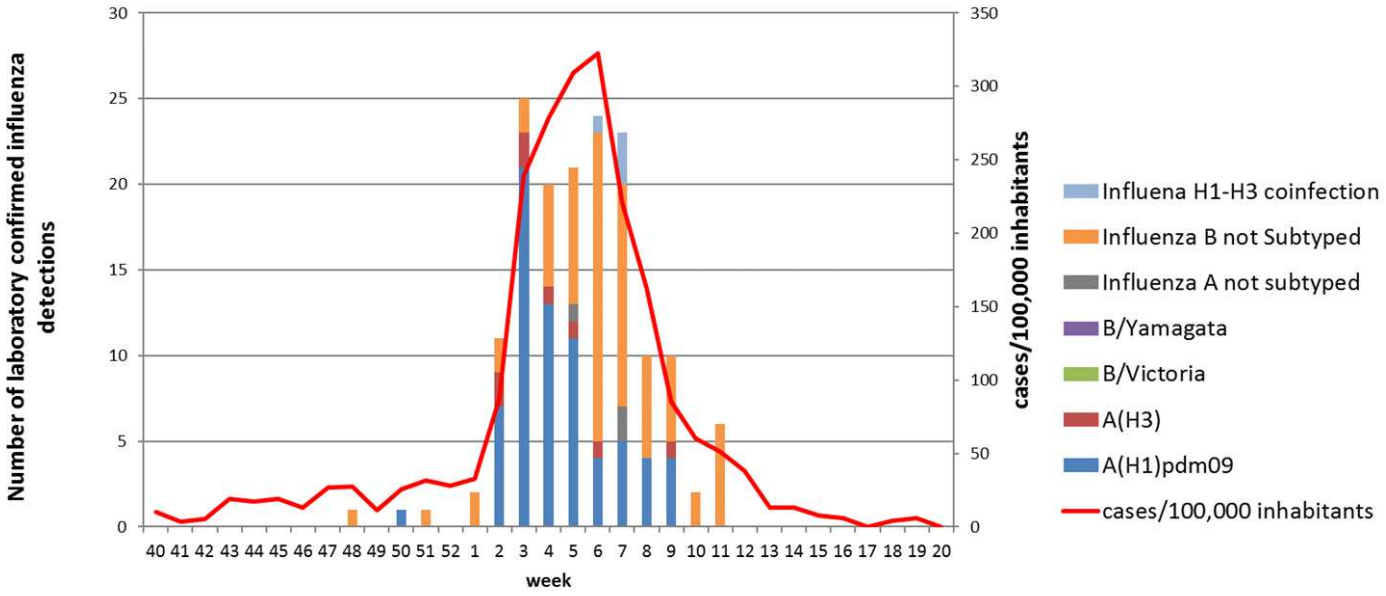

Figure 9. Number of identifications of influenza A and B subtypes and lineages per week in SNCyL patients. Source: Valladolid NIC.

The highest number of influenza detections was observed in children (5-14 years) (35.71%), predominantly the not subtyped B (39%). The number of influenza laboratory confirmed cases between the groups of pediatric patients (0-4 years), young-adults (15-44 years) and adults (45-64 years) was a bit lower, but lowest number of cases was in the elderly (3%) (Figure 7). The number and percentage of A(H1N1)pdm09 viruses identified was similar than not subtyped B.

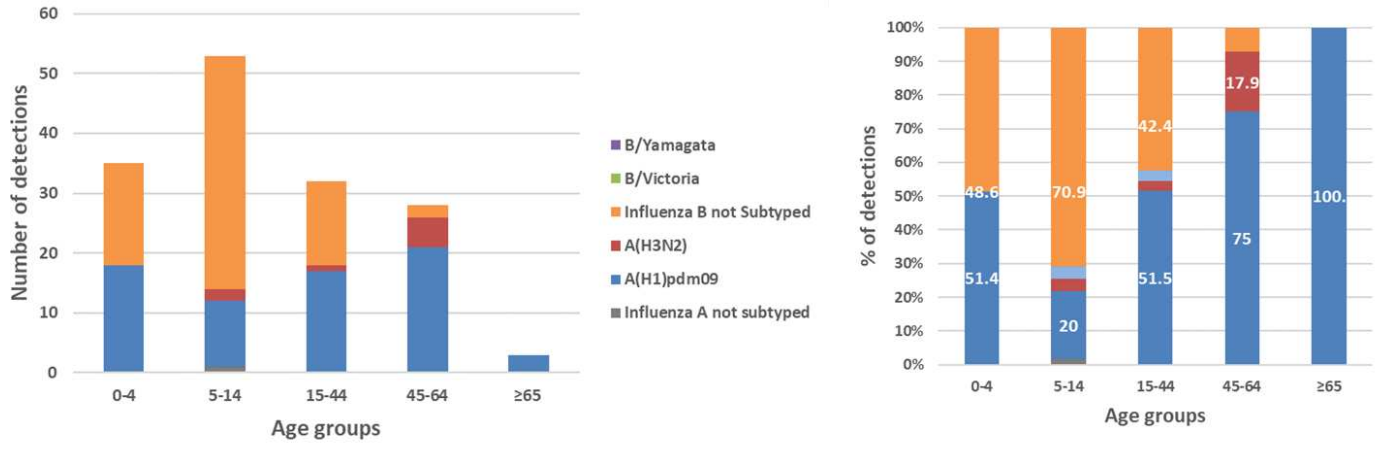

Figure 10. Absolute number and percentage of detections of influenza A and B subtypes and lineages in the different age groups of sentinel patients analyzed. Source: Valladolid NIC.

Co-infections of influenza and other respiratory viruses

Co-infections between influenza and others respiratory viruses were identified in 17.6% of the hospitalized patients and in 19.3% to of the sentinel patients. These data show that co-infections with others respiratory viruses were in similar frequency identified in both groups. The influenza virus most frequently detected in co-infection with other respiratory virus was A(H1N1)pdm09 in hospitalized (9.8%), and influenza B not subtyped in sentinel patients (12.7%) (Figure 11).

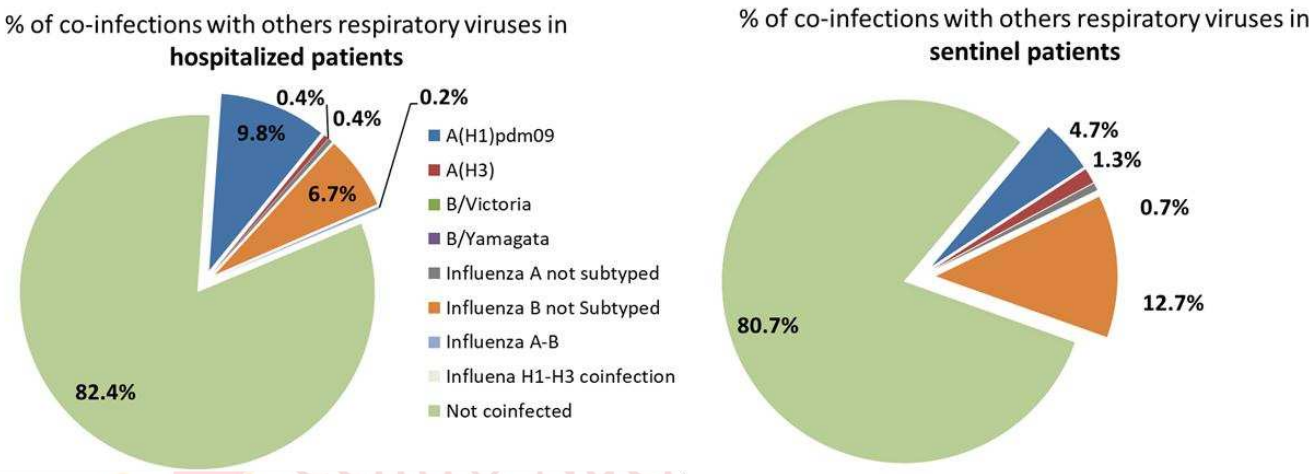

Figure 11. Percentage of co-infections of influenza A and B viruses with other respiratory viruses in hospitalized and sentinel patients. Source: Valladolid NIC.

5. Antigenic and genetic characterization. Antiviral characteristics

The results of antigenic and genetic characterization of the viruses analyzed this season, performed by the London WHO Collaboration Center (Francis Crick Institute; Dr. John McCauley and collaborators), are shown below:

- A(H1N1)pdm09:
    - All but one A(H1N1)pdm09 viruses analyzed during this season were well recognized by the antiserum raised against the vaccine strain of the 2019-2020 season, A/Brisbane/02/2018. The genetic analysis included these viruses in different subgroups of the genetic group 6B.1A5, presenting the amino acid substitutions D187A and Q189E. However, the strain A/Valladolid/5/2020 was only

recognized by the antiserum raised against A/Hong Kong/110/2019, include in the subclade 6B.1A2, with and N156K substitution. All viruses analyzed were sensitive to oseltamivir and zanamivir and showed normal inhibition.

- A(H3N2):
    - Currently it continues to be very difficult to hemagglutinate A(H3N2) subtype viruses with RBCs from different species, and it was not possible to perform antigenic and genetic characterization in all viruses. The genetic analysis showed that the virus shipped belonged to the clade 3C.2a1b + T131K that were the most frequent clades that circulated during 2019-2020 influenza season. All viruses analyzed were sensitive to oseltamivir and zanamivir and showed normal inhibition.

- B influenza viruses:
    - All influenza B viruses shipped belonged to the B/Victoria lineage. One strain, the B/Valladolid/303/2019, present a double deletion (Δ162-163), and other eight presente a triple deletion (Δ162-164). Seven of the B viruses shipped wer.e well recognized by the B/Washington/02/2019 antiserum. All viruses analyzed were sensitive to oseltamivir and zanamivir and showed normal inhibition.

6. Conclusions

The 2019-2020 influenza season in Castile and Leon and in Spain was characterized by the mixed circulation of both influenza A (H1N1)pdm09 and influenza B not subtyped , being predominantly the A(H1N1)pdm09. The predominant virus in hospitalized patients was A(H1N1)pdm09 (53.4%) and B type virus in sentinel patients (45.0%). The diversity of influenza viruses identified in hospitalized and sentinel patients were similar. A total of 110 co-infections between influenza A(H1N1)pdm09 and influenza B not subtyped were detected by molecular methods. The most affected age group in hospitalized was the pediatric patients (28.6%), while children (5-14 years) were the age group most affected in sentinel patients (35.7%). Co-infections of influenza and other respiratory viruses were similar frequently detected in hospitalized patients (17.6%) than in sentinel (19.3%), being the A(H1)pdm09 subtype the most frequently detected in co-infection. The genetic and antigenic characterization showed a good recognition of

the A(H1N1)pdm09 viruses with the vaccine strain A/Brisbane/02/2018, belonging to the genetic group 6B.1A5. No antiviral resistances were observed in the viruses characterized.

7. Acknowledgments

We thank all the institutions that make our work viable. To all the general practitioners of the SNCyL for the logistics and work involved in the submission of samples for identification. To ”Instituto de Estudios de Ciencias de la Salud de Castilla y León” and “Consejería de Sanidad de la Junta de Castilla y León”, for the financial support to the NIC work. To the Epidemiology Unit of Castile and Leon government, for coordinating the SNCyL, and also to “Hospital Clínico Universitario de Valladolid” and University of Valladolid for housing the facilities of the National Influenza Center of Valladolid. To the Francis Crick Institute, WHO Collaboration Center, London, UK, for all its supervision and support with the techniques and reagents that we use to carry out our work.

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