Poster Reception I

Krista Kniss - AOXI0078

Results of symptom monitoring among persons exposed to highly pathogenic avian influenza (HPAI) A H5N1, February 7 - March 17, 2022, United States

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Background

Highly pathogenic avian influenza (HPAI) A H5N1 viruses belonging to clade 2.3.4.4.b have become the predominant circulating avian influenza strain in birds throughout much of the world including Europe, Africa, and the Middle East beginning in 2021. This virus was first identified in birds in North America in December 2021 in Canada; and first identified in the United States in January 2022 in a hunter-harvested wild bird in South Carolina. Since then, there have been additional detections in wild birds in 24 US states and outbreaks in commercial poultry farms or backyard/hobby flocks in 17 US states. Since little is known about the risk to human health, symptom monitoring of exposed individuals has been instituted in the U.S. to detect any human infections.

Method

For each commercial poultry or backyard/hobby flock outbreak reported, we contacted state and local public health departments to request information regarding human exposures including the number of persons who reported being exposed to infected birds and the number of persons who developed signs or symptoms compatible with avian influenza virus infection during a 10-day postexposure monitoring period. Symptom monitoring was conducted by state or local health departments via telephone, email and/or SMS either daily, or on days 0, 5, and 10 after exposure. If individuals developed signs and symptoms compatible with avian influenza during the 10-day period after exposure respiratory specimens were collected and tested for avian influenza at state public health labs. Some laboratories also performed additional respiratory virus testing including seasonal influenza and SARS-CoV-2.

Result

During February 7- March 17, 2022, 17 outbreaks in backyard flocks and 21 outbreaks in commercial flocks were confirmed as HPAI A H5N1 by the US National Veterinary Services Laboratory. Among the 373 people reported to have been exposed to infected birds, 18 (4.8%) reported symptoms consistent with avian influenza virus infection. None of the symptomatic individuals were positive for influenza A H5N1, six were influenza A H3N2 positive, two were SARS-CoV-2 positive, two were Rhinovirus/Enterovirus positive, and eight were negative for influenza with no other agent identified. All symptomatic individuals reported mild illness.

Conclusion

No human infections with influenza A H5N1 virus were detected through symptom monitoring and testing among individuals exposed to birds infected with influenza A H5N1. Because avian outbreaks occurred during the traditional US respiratory virus season, it is not surprising that some exposed persons had symptoms consistent with avian influenza virus infection.

Gaëlle Simon - AOXI0079

Human case of infection with a swine influenza virus of H1N2 subtype that emerged and spread in pigs in 2020 in metropolitan France

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Background

In August 2021, France, a man in his sixties, with comorbidities, was hospitalized in intensive care unit for acute respiratory syndrome. He tested negative for SARS-CoV-2 and was found to be infected with an influenza A virus (IAV) not identified by seasonal IAV subtyping methods. Whole genome sequencing revealed an A(H1N2)v virus nearly identical to a swine IAV identified in France. The patient reported a one-time exposure, without personal protective measures, to pigs in a fattening farm (F) four days before becoming ill.

Method

Investigations were conducted at the genomic level to compare the human virus to its swine counterparts. Epidemiological surveys were implemented on the animal and human sides to provide information on inter- and intra-species transmission events.

Result

The A(H1N2)v virus exhibited a very high level of identity to a swIAV of H1avN2#E genotype (H1 of clade 1C.2.4; N2 of Gent/84 lineage; internal genes of EA lineage). This swIAV genotype was first identified in Brittany in February 2020, introduced in toto from another European country. This swIAV genotype spread rapidly in the pig population of western France and became the most frequently identified swIAV in France in 2020-2021. Comparative genome analyses of the A(H1N2)v strain and 77 H1avN2#E strains confirmed their close proximity on the eight genomic segments. The A(H1N2)v strain has the same mutations and deletions as those identified in H1avN2#E near the receptor binding site, the impact of which on viral functions is not known. A few non-silent mutations were specifically identified in some A(H1N2)v genes, but none of them involved amino acids known to be markers of IAV adaptation to humans. Moreover, in silico analyses did not reveal any resistance mutations to NA and PA inhibitors.

Epidemiological, virological, and serological investigations in farm F, complemented by analyses in the piglet supplying farm, revealed the circulation of H1avN2#E virus in farm F during a period including the patient's exposure date. Persons who had been in contact with the patient before hospitalization, including one who worked daily on the farm, did not develop any influenza-like illness, and their serological follow-up did not evidence antibodies to the A(H1N2)v subtype.

Conclusion

The patient's clinical course was favorable after treatment with oseltamivir. Although there was no human-to-human transmission after crossing the species barrier during this episode, this case of human infection reminds us that swIAVs, which circulate widely and persist in pig farms, have zoonotic potential and that appropriate biosecurity measures should be adopted on farms.

Sophie George - AOXI0082

Candidate molecular markers of swine influenza A viruses with zoonotic potential

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Background

Almost 11 years after the human influenza A virus pandemic of 2009 (H1N1pdm09) was introduced into Danish swine herds by reverse-zoonosis events, Denmark recorded the first suspected zoonotic case of human infection with a swine-adapted H1N1pdm09 virus. However, the viral genetic determinants enabling viral transmission between pigs and humans remain largely unknown. This study follows the evolution of H1N1pdm09 over 10 years as the virus adapts to the pig population in Denmark.

Method

Next generation sequencing recovered 240 H1pdm09Nx genomes collected from influenza A virus infected Danish pigs between 2010 and 2020, representing ~50% of H1pdm09Nx positive submissions to the Danish swine influenza surveilance program. Phylogenetic relationships, reassortments, evolutionary selection pressures, and post-translational modifications to viral proteins were inferred from the sequencing data using an array of available bioinformatic tools. In addition, viral variants emerging from in vivo experimental studies with pigs and ferrets infected with H1N1pdm09 of swine and human origin were included for comparison.

Result

Phylogenetic analyses revealed the divergence of a distinct H1N1pdm09 lineage evolving exclusively in the Danish pig population. The swine-diverged lineage underwent major positive diversifying selection and formed a swine adapted cluster between 2012 and 2014, which contains the majority of H1N1pdm09 viruses currently circulating in Danish swine. However, transmissions of H1N1pdm09 from humans to pigs continued after 2014, but these viruses failed to establish in the pig population and probably represent sporadic reverse-zoonosis events. In addition, reassortments occuring between other circulating swine NA and NS genes imparted a selective pressure to diverge away and evolve separately from unreassorted H1N1pdm09, thereby creating additional swine divergent clusters.

Conclusion

Comparisons between the swine-diverged and human-like H1pdm09Nx lineages emerging in the pig population have indicated candidate viral genetic markers of host adaptation that could be used to evaluate the zoonotic potential of circulating swine influenza A viruses. However, further experimental characterization and validation is required before implementation of zoonotic risk assessments.

Sukanta Chowdhury - AOXI0109

The environment in live poultry markets in Bangladesh: a potential reservoir for avian influenza viruses

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Background

In Bangladesh, highly pathogenic avian influenza A (H5N1) virus causes repeated outbreaks in poultry and sporadic infections in humans. Since 2007, >560 outbreaks in poultry, eight human cases, and one death have been reported. Live poultry markets (LPMs) are considered an important source of H5N1 virus infection in humans. Bangladesh has a large number of LPMs where live chicken, ducks, geese, quail, pigeon, and other poultry species are sold.

Method

International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) initiated LPM-based avian influenza surveillance in 2007. Each month we collected swab specimens from individual poultry and environment. Swabs from eight environmental sources, including poultry droppings, cages, feed, water, slaughtering sites, chopping boards, market floors, and drains were collected to prepare a one pooled environmental sample for an LPM. From May 2009 to February 2022, 2,465 pooled environmental samples were collected from 30 LPMs (20 in urban areas and 10 in rural areas) in 10 districts. All samples were tested using rRT-PCR to detect RNA for AIVs and subtyped for H5, H7, and H9 at icddr,b laboratories. All samples were also sequenced at CDC laboratories in Atlanta, GA. We performed multivariable logistic regression to identify factors associated with environmental contamination.

Result

Avian influenza A viral RNA was detected in 840 (34%) pooled samples; 283 (11%) tested positive for H5 subtype, 274 (11%) for H9 subtype, 81 (3%) for H5/H9 co-detection and 202 (8%) remained unsubtypable (likely other avian influenza subtypes not tested). RNA for AIV/H5 was detected in samples collected every month, but the months with the highest proportion of samples testing positive for AIV/H5 were December to March of each year (12-17% of samples tested positive). Environmental samples collected during winter (November-February) (OR=1.37, 95% CI: 1.18-1.59) and from urban markets (OR=2.23, 95% CI: 1.48-3.27) were more likely to be AIV/H5 positive than those collected in summer (April-September) and from rural markets, respectively. Multiple AIVs subtypes including H5N1, H5N2, H5N3, H5N9, H9N2, H9N1, H9N9, H7N9, H2N3, H3N2, H11N3 and H11N9 were detected. A total of four clades of H5N1 virus (2.2; 2.3.2; 2.3.2.1; 2.3.2.1a) were identified over the study period.

Conclusion

The environment of LPMs was highly contaminated with AIVs. Year-round detection of AIV/H5 in environmental specimens indicates that the LPM environment might be a potential reservoir for highly pathogenic AIVs. Improving the LPM environment by regular cleaning and disinfection especially during winter months and in urban markets might reduce the environmental contamination and minimize the risk of human exposure to AIVs.

Shikha Garg - AOXI0027

Respiratory Viral Co-detections among Patients Hospitalized with Laboratory-Confirmed Influenza in the United States, FluSurv-NET, 2014-2019

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Background

Data on the epidemiology of respiratory virus co-detections among U.S. patients hospitalized with influenza are limited.

Method

Using data from the Influenza Hospitalization Surveillance Network (FluSurv-NET), a population-based surveillance system for laboratory-confirmed influenza-associated hospitalizations, we determined the frequency of other respiratory virus testing and test positivity by pathogen, age group and season among persons hospitalized with influenza during the 2014-15 through 2018-19 influenza seasons. Among infants <6 months old who were tested for respiratory syncytial virus (RSV), we used multivariable logistic regression to determine whether influenza and RSV co-detection was associated with increased odds of intensive care unit (ICU) admission and invasive mechanical ventilation (IMV).

Result

Of 79,862 patients hospitalized with influenza, 38% were tested for ≥1 other respiratory virus; the proportion tested increased from 32% during 2014-15 to 45% during 2018-19 (p<0.01). The proportion tested was greater in children than adults (Figure A). The highest proportion of testing across all seasons for RSV occurred among infants <6 months old (83%) and for all other respiratory viruses occurred among children 5-17 years (33-52%). Respiratory viruses were co-detected in <5% of patients >5 years (Figure B). Among children <5 years, RSV was detected most frequently (18% among infants <6 months old and 13% among those 6 months to <2 years), followed by rhinovirus/enterovirus (11% among children 2-4 years). Among infants <6 months old hospitalized with influenza who were also tested for RSV, a higher proportion with influenza and RSV required ICU admission (27% vs 16%) and IMV (8% vs 4%) compared with those with influenza only. In adjusted analyses, infants with influenza and RSV had a higher odds of ICU admission (aOR 1.9; 95% CI 1.3-2.9), but the odds of IMV (aOR 1.8; 95% CI 0.9-3.6) did not significantly differ when compared to those with influenza only. Deaths were rare in both groups.

Conclusion

Respiratory virus testing and viral codetections were uncommon among adults hospitalized with influenza. Over 80% of infants <6 months old were tested for RSV and almost 1 in 5 had RSV codetection. Compared with influenza only, influenza and RSV codetection was associated with increased odds of ICU admission in infants <6 months old.

Nicole Wolter - AOXI0034

Summer Circulation of Influenza in South Africa in 2021

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Background

Integrated surveillance for influenza, SARS-CoV-2 and respiratory syncytial virus is performed through three sentinel, syndromic programmes, namely Viral Watch (VW) influenza-like illness in outpatients at private general practitioners, influenza-like illness (ILI) in outpatients at public health clinics, and national pneumonia surveillance in public health hospitals. The annual influenza season usually occurs between late autumn and early spring (April to October). Following the start of the COVID-19 epidemic in March 2020, only one influenza A(H1N1)pdm09 infection was detected in 2020. We aimed to describe influenza activity in 2021.

Method

For individuals meeting the surveillance case definition, from 4 January 2021 (week 1) through 2 January 2022 (week 52), respiratory specimens were collected and tested by reverse transcription real-time PCR. PCR subtyping was performed for all positive specimens. Influenza activity was assessed using ILI surveillance (indicator of transmission) and pneumonia surveillance (indicator of disease impact) using the Moving Epidemic Method (MEM).

Result

Among 8407 individuals tested (253 (3%) VW, 1941 (23%) ILI and 6213 (74%) pneumonia surveillance), 414 (5%) influenza infections were identified. Infections were identified from March (week 9) through December (week 52). In ILI surveillance, the detection rate was 9% (171/1941) and was highest during November (weeks 44 (41%, 21/51) through 47 (40%, 22/55)), reaching a level of moderate transmission. In pneumonia surveillance the detection rate was 3% (208/6213), and was highest between September (week 38) and December (week 49) with a peak detection rate of 17% (18/104) at end November (week 47). During these weeks, influenza disease impact was classified as low. A comparable number of infections were detected in 2021 (n=379) compared to earlier years (ranging from 373 cases in 2019 to 474 in 2017), although the number of specimens tested was higher in 2021. Influenza infections that could be subtyped were dominated by influenza A(H1N1)pdm09 (56%, 215/383), followed by B/Victoria (27%, 102/383) and A(H3N2) (17%, 66/383). Influenza B/Yamagata was not detected.

Conclusion

Influenza infections were identified from March through December 2021, with increased transmission and admissions during the late spring and summer season. The number of infections was similar to pre COVID-19 years but proportion positive lower, likely as a result of increased testing of suspected SARS-CoV-2 cases. The atypical influenza circulation observed is likely due to the immunity gap created as a result of limited influenza circulation during the COVID-19 pandemic, and relaxing of COVID-19 restrictions/ non-pharmaceutical interventions.

Catherine Bozio - AOXI0039

Relative Rates of COVID-19-associated hospitalizations and clinical outcomes by age and race/ethnicity -- March 2020 - March 2021

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Background

The VISION network was established to utilize electronic health record data to examine influenza vaccine effectiveness. It was expanded during the COVID-19 pandemic to monitor COVID-19 clinical impact and vaccine effectiveness. We used VISION data to estimate population-based rates and rate ratios (RR) of COVID-19-associated hospitalizations and pre-specified clinical outcomes, stratified by age and race/ethnicity.

Method

Using data from electronic health records (EHR) and claims from VISION's four U.S. health systems for the period March 2020 through March 2021, we calculated rate and RR by age and race/ethnicity for COVID-19-associated hospitalizations and outcomes among adults (≥18 years). Adults who had ≥1 ambulatory visit within the health system in the 12 months prior to September 1, 2019 were included in the patient cohort. COVID-19-associated hospitalizations were defined based on COVID-19 discharge codes or a positive SARS-CoV-2 result. Proportions of acute exacerbations of underlying conditions were estimated among hospitalized patients with select underlying conditions, stratified by age (18-64 vs ≥65 years) and race/ethnicity.

Result

Among 2.6 million adults included in the patient cohort, 6,879 had COVID-19-associated hospitalizations during March 2020-March 2021 (rate: 264 per 100,000 population). Compared to non-Hispanic White adults aged 18-64 years, non-Hispanic Black and Hispanic adults aged ≥65 years had the highest hospitalization rate ratios (RR: 8.6 (95%CI: 7.6-9.9) and RR: 9.3 (95%CI: 8.5-10.3), respectively). Rate ratios for admission to the intensive care unit were also highest in non-Hispanic Black and Hispanic adults aged ≥65 years (RR: 8.6 (95%CI: 7.6-9.9) and RR: 9.3 (95%CI: 8.5-10.3), respectively). Among hospitalized adults with COVID-19 and underlying renal disease or cardiovascular disease, the highest proportion of acute renal failure (55.5%) or congestive heart failure (43.9%) occurred in non-Hispanic Black patients aged ≥65 years. Among hospitalized adults with COVID-19 and chronic lung disease or asthma, the highest proportion of respiratory failure (62.9%) or asthma exacerbation (66.7%) occurred in Hispanic patients aged ≥65 years.

Conclusion

During the first year of the U.S. COVID-19 pandemic in this cohort, non-Hispanic Black and Hispanic adults aged ≥65 years had the highest relative rates of COVID-19-associated hospitalization and adverse outcomes, and, among those with select underlying conditions, the highest occurrences of acute exacerbations. Continuing use of such EHR data could help in future monitoring and understanding of medically attended respiratory infection, including influenza and COVID-19.

Alicia Budd - AOXI0051

Enhancing U.S. Surveillance of Laboratory-Confirmed Respiratory Viruses through a Network of Emergency Departments

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Background

In the United States, multiple surveillance systems provide information about respiratory virus circulation and acute respiratory illness (ARI), but no existing national system provides weekly patient level pan-respiratory virus testing linked to clinical data. In preparation for circulation of influenza, SARS-CoV-2 (SC2) and other respiratory viruses during the fall/winter of 2021-22, CDC began working with a network of hospitals to collect linked lab and clinical data from a single platform to better understand respiratory virus testing practices and the relative impact of multiple respiratory viruses on causes for ARI.

Method

We assembled a network of 24 hospital systems to collect patient level demographic, pan-respiratory virus testing, clinical, disposition, and vaccination data for all emergency department (ED) visits for ARI. In addition, age and ED disposition were reported for all ED visits. Data extracted from electronic health records were sent to a coordinating site and transmitted to CDC weekly. SAS was used to calculate percent positivity for and relative proportion of multiple respiratory viruses, monitor patient disposition and respiratory virus testing practices, and track the percent of ED visits for ARI. The first hospitals began reporting in late 2021, and as of February, 18 hospitals are reporting weekly.

Result

Approximately 45,000 ED visits for ARI occurred between December 2021, and February 2022. The weekly percent of visits for ARI ranged from 10% to 27%. The percent of ARI patients tested for SC2 or influenza was 74% and 59%, respectively overall and 87% and 71%, respectively for ARI patients admitted to the hospital. The trends in weekly percentage of specimens testing positive for influenza varied by age group, while the percentage of specimens testing positive for SC2 declined for all age groups since early January 2022. As SC2 activity declined, the relative contribution of influenza, rhinovirus, endemic human coronaviruses and human metapneumoviruses as the cause of ARI increased. While SC2 was the predominant virus identified among ARI patients of all ages, the relative contribution of influenza and SC2 infection varied by age group; the largest influenza burden occurred in children, and the largest SC2 burden occurred in adults. Of the 635 influenza positives among patients tested for both influenza and SC2, 42 (6.6%) were also positive for SC2.

Conclusion

Data from this newly established pan-respiratory virus surveillance system provide critical timely information needed to fill surveillance gaps and improve the ability to interpret data from existing surveillance systems during a time when multiple respiratory viruses are circulating.

Carrie Reed - AOXI0054

Trends in influenza testing among hospitalized patients during the COVID-19 pandemic, United States

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Background

Several viral and bacterial respiratory illnesses have similar clinical presentations, yet many infected people never receive diagnostic testing. Use of influenza testing, in particular, varies by care setting, age group, and disease severity, and has been evolving with increasing availability of molecular and multiplex assays. With the emergence of the COVID-19 pandemic, major changes in clinical testing for influenza could influence trends observed in long-standing surveillance systems and introduce new biases into epidemiologic and clinical studies that rely on results of clinical testing.

Method

We used data on inpatient hospital admissions from August 2018-December 2021 (n=14,043,121) in a large electronic health dataset of multiple healthcare systems across the United States to examine trends in influenza testing before and during the COVID-19 pandemic. Influenza and SARS-CoV-2 tests were identified using Current Procedural Terminology (CPT) codes for test orders or Logical Observation Identifiers, Names, and Codes (LOINC). Hospital visits overall and those with respiratory viral testing were aggregated by month and further stratified by presence of acute respiratory illness (ARI) diagnostic codes (ICD-10), intensive care unit (ICU) admission during hospitalization, and age group (children <18 years, adults ≥18 years).

Result

During 2020, the proportion of patients hospitalized for ARI who were tested for influenza declined to levels at or below those seen in prior summer non-epidemic periods in the United States. Testing increased back to pre-pandemic levels by late 2021, with earlier increases among children, but remained at lower levels than testing for SARS-CoV-2. From 2018-2020, 74% of all patients with influenza testing had ARI diagnoses; by December 2022, 44% of influenza tests were among patients with ARI. Conversely, since February 2020, 24% of patients tested for SARS-CoV-2 had ARI diagnoses. During the pandemic, ARI patients in the ICU were more likely to be tested than non-ICU patients (RR=1.2 for influenza, RR=1.8 for SARS-CoV-2). Among non-ARI patients, ICU admission was strongly associated with testing (RR=3.8 for influenza, RR=3.9 for SARS-CoV-2).

Conclusion

While levels of influenza testing among hospitalized ARI patients returned to pre-pandemic levels during the 2021-22 season, increased testing of non-ARI patients, especially severely ill patients, changes the landscape of clinical influenza testing. A better understanding of changes in respiratory viral testing practices during and after the pandemic will improve our ability to interpret potential changes in surveillance data and the epidemiology of influenza in the population.

John Paget - AOXI0059

Age differences in comorbidities, presenting symptoms and outcomes of influenza illness requiring hospitalization: a global perspective from the Global Influenza Hospital Surveillance Network

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Background

The annual impact of influenza varies depending on both virus and host factors, which occur in environmental and geopolitical contexts. The Global Influenza Hospital Surveillance Network (GIHSN) was established in 2012 with the aim of conducting coordinated worldwide influenza surveillance. Here we present results describing the 2018/19 influenza season, focusing on age differences in underlying comorbidities, presenting symptoms, and outcomes.

Method

Between November 2018 and October 2019, GIHSN included 19 sites in 18 countries: 5 intertropical sites with year-round influenza circulation, 3 Southern and 11 Northern hemisphere sites. Active surveillance was conducted using a standardized protocol, based on a Modified European Centre for Diseases Control case definition for Influenza-Like Illness. Influenza was laboratory confirmed with RT-PCR. Data collection included age, sex, presenting symptoms, and underlying comorbidities. Outcomes included hospital length of stay, mortality, ICU admission, and mechanical ventilation. Descriptive analyses were used for comparisons across age groups, and regression models examined risk factors for severe outcomes.

Result

s: There were 16,134 patients enrolled; 3,528 had laboratory-confirmed influenza and were included in these analyses. Influenza A/H1N1pdm09 represented 49.2% of detections, with co-circulation of A/H3N2, B Yamagata and B Victoria, though not all strains were seen at each site. Influenza vaccination coverage among inpatients varied widely across sites, from <5% to >70%. Symptoms varied by age and must be interpreted in context of enrollment criteria; symptoms were not collected for ages <5 yrs. Fever and cough were most common, though decreased with age; 98.9% of those aged 5-17 yrs had fever and 95.0% had cough, decreasing to 80.9% (fever) and 85.6% (cough) in those 80+ ($p<0.001$). Shortness of breath was uncommon among those <50 but increased with age: 58.1% aged 50-64, 61.9% aged 65-79 and 75.5% aged 80+ ($p<0.001$). Underlying comorbidities varied by site and age; cardiovascular (1.5% children; 65.4% 65+), respiratory conditions (2.9%; 37.0%), diabetes (<0.1%; 29.1%), neoplasm (0.6%; 12.1%) and kidney disease (<0.1%; 12.3%) were most common. Adverse outcomes

increased with age; ICU admissions and mortality occurred across the age spectrum from the youngest infants to the oldest adults.

Conclusion

We identified important virus and host factors contributing to influenza burden. The GIHSN provides an ongoing platform to contribute to global understanding of hospitalized influenza illness. Future seasons will integrate whole genome sequencing in the context of ongoing data collection on clinical presentation and outcomes.

Marianne De Bruijn - AOXI0064

Etiology of influenza-like illness (ILI) during Northern Hemisphere (NH) 2020/21 influenza season in children 6 through 47 months of age enrolled in a vaccine efficacy trial

Marianne De Bruijn[1], Derchieh Hung[1], Matthew Hohenboken[1], Jonathan Edelman[1], Deborah Molrine[1]

[1]Seqirus

Background

Circulation of seasonal respiratory viruses, especially influenza, has been dramatically reduced since the WHO declared a COVID-19 pandemic in March 2020. An influenza vaccine efficacy trial provided an opportunity to identify viral and bacterial respiratory pathogens from healthy children actively being monitored for ILI during the NH 2020/21 season.

Method

An ILI was defined by body temperature ≥ 37.8°C and at least one of the following symptoms: cough, sore throat, nasal congestion, rhinorrhea, earache or ear discharge. Nasopharyngeal (NP) swabs were collected within 7 days of ILI onset from subjects 6 to 47 months of age enrolled at study sites in Northern and Eastern Europe. Swabs from subjects whose parents provided permission for additional testing were evaluated in a multiplexed PCR test designed to identify nucleic acids from 23 respiratory pathogens within a single specimen (BioFire® RP2.1 Panel).

Result

A total of 187 subjects provided 243 NP swabs; 46 subjects experienced more than 1 ILI event. At least one pathogen was detected in 162 (67%) swabs from 135 subjects, of whom 28 had multiple pathogens detected from a single swab. Human rhinovirus/enterovirus (44%), coronavirus OC43 (11%) and adenovirus (9%) were the most common pathogens identified (distribution by month shown in Figure). Of the 29 swabs with a co-infection, human rhinovirus/enterovirus, adenovirus, coronavirus OC43 and human metapneumovirus were most frequent in combination with another virus. SARS-CoV-2 was identified in 2.5% of samples and detection of RSV and influenza viruses was 2.5% and 1.2%, respectively. One ILI (human rhinovirus/enterovirus) resulted in a hospitalization for bronchitis.

Conclusion

During the NH20/21 influenza season, viral etiologies were identified for a majority of ILI reported, with human rhinovirus/enterovirus the most frequent respiratory pathogen detected alone or in combination and rarely leading to serious illness. In contrast to pre-COVID surveillance, detection of influenza and RSV was markedly reduced.

Lisa Staadegaard - AOXI0072

Understanding the impact of the COVID-19 pandemic on influenza surveillance data reported to WHO FluNet by National Influenza Centers

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Background

The emergence of SARS-CoV-2 in early 2020 had a major impact on influenza activity and was associated with a massive decline in the number influenza cases reported by National Influenza Centres (NICs) to the WHO's FluNet surveillance platform. The aim of our study was to better understand the impact of SARS-CoV-2 on surveillance data reported by the NICs during the COVID-19 pandemic.

Method

A questionnaire on the influenza and SARS-CoV-2 surveillance activities was prepared and shared with 28 NICs located in 19 countries. NICs were invited to reply to the survey between November 2021 and March 2022.

Result

We received 18 responses from NICs based in 15 countries, five of which are low- or middle-income countries. Influenza data was reported to FluNet by 17 NICs and ten NICs reported their SARS-CoV-2 data to WHO. The majority of responses (12/17) indicated a decrease in the number of specimens being tested for influenza since the start of the pandemic, eight of those reported a reduction of ≥50%. The origin of these samples (e.g. GPs or hospital) differed for most countries and often shifted as a result of the pandemic. All NICs indicated they had suffered an increase in the burden of work as a consequence of the pandemic. However, the NICs also reported that the pandemic had: a) increased the availability of multiplex PCR testing, b) often (7/15) resulted in a larger testing capacity and c) increased (11/17) the overall robustness of their surveillance system (e.g. more funding for equipment and personnel).

Conclusion

Our data suggest that the ongoing SARS-CoV-2 pandemic has had a substantial impact on NICs in the WHO FluNet surveillance system. Overall, NICs reported a reduction in the number of specimens tested for influenza during the COVID-19 pandemic (likely associated with the lower levels of influenza activity and greater focus on SARS-CoV-2) and changes in the sources of these samples. Although the pandemic imposed a burden on influenza surveillance systems it also increased robustness in the form of funding, personnel and equipment. The information gathered through our questionnaire will aid with the interpretation of the surveillance data presented in FluNet. Most importantly, the data highlights the resilience and flexibility of the NICs and addresses aspects that should be considered to ensure the sustainability and pandemic preparedness of influenza surveillance systems in the future.

Yuzo Arima - AOXI0073

Lack of influenza activity during the 2020-21 and 2021-22 seasons in Japan: a pluralistic assessment utilizing multiple information sources

Yuzo Arima[3], Takeshi Arashiro[3], Takuri Takahashi[3], Reiko Shimbashi[3], Yuuki Tsuchihashi[3], Miyako Otsuka[3], Yusuke Kobayashi[3], Osamu Takahara[3], Katsuhiro Komase[3], Kazuhiko Kanou[3], Tomimasa Sunagawa[3], Hiromasa Horiguchi[2], Kiyosu Taniguchi[1], Motoi Suzuki[3]

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Background

Since early 2020, the coronavirus disease 2019 (COVID-19) pandemic has had a major global impact, eclipsing that due to other acute respiratory viral diseases, including influenza. Japan, which has continued to maintain one of the most stringent border closure measures for COVID-19, has seemingly remained influenza-free since the spring of 2020. However, with major changes in healthcare-seeking behaviors, testing, and/or reporting during the pandemic, assessment of temporal trends in influenza activity can be challenging. To account for such surveillance biases, we adopted a pluralistic approach, utilizing various information sources to improve our confidence level in interpreting temporal trends in influenza occurrence.

Method

In our weekly monitoring of trends in influenza activity during the 2020-21 and 2021-22 seasons, in order to minimize and/or account for ascertainment-related biases, we monitored several indicators from multiple data sources (including sources outside of the national influenza surveillance platform).

Result

Based on the national influenza/influenza-like illness (ILI) sentinel surveillance system, influenza activity remained below the season onset threshold throughout both seasons. Representing a more severe outcome likely less affected by healthcare-seeking behaviors and testing practices, incident influenza hospitalizations saw similarly unprecedented low baseline levels. In addition, data from the national hospital organization indicated that-in the context of a reduced number of tests for influenza-the test positivity (proportion of tests performed positive for influenza) consistently remained near zero, substantially lower than that observed in prior years and suggesting that a lack of testing was unlikely to explain the reduction in influenza-positive notifications. Lastly, absenteeism in schools due to ILI-a syndromic indicator of influenza that is likely upstream of healthcare access/testing and thus unaffected by healthcare-seeking behaviors and testing-were also at unprecedented low levels.

Conclusion

Using a pluralistic approach and assessing multiple data sources to explicitly address ascertainment-related biases, our findings indicated a true decline in influenza incidence to historically low levels in Japan during the 2020-21 and 2021-22 seasons. However, with influenza activity returning globally and with borders starting to reopen in Japan, vigilance is warranted. We will continue to monitor influenza with this approach during the upcoming season to maintain situational awareness, inform risk assessments, and facilitate surveillance-informed decision-making.

Maureen Goss - AOXI0098

Surveillance of SARS-CoV-2 and acute respiratory infections in a school-based longitudinal cohort in South Central Wisconsin, 2019-2022

Cecilia He[1], Maureen Goss[1], Shari Barlow[1], Jonathan Temte[1]

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Background

Surveillance of respiratory viruses among school-aged children provides early assessment of virus circulation in the community. Following the start of SARS-CoV-2 (SC2) pandemic in 2020, many school districts implemented public health measures such as virtual learning, social distancing, and mandatory face mask wearing to prevent SC2 transmission. We demonstrate the feasibility of an online survey tool to effectively monitor the prevalence of acute respiratory infections (ARIs) in households within a school district and its association with concurrent public health measures implemented in schools.

Method

The Great ORCHARDS Vaccine Effectiveness Study (GROVES) chronicles ARIs and household SC2 cases in the Oregon School District (OSD; Oregon, WI). Participating households were invited from a group of past surveillance study participant families and asked to complete weekly e-surveys to report household ARI and, starting in October 2020, COVID-19 cases. Study data and surveys were collected and managed using REDCap electronic data capture tools hosted at University of Wisconsin at Madison. Percent of households with ≥1 member with ARI (%HH-ARI) was used as a weekly indicator to track ARI prevalence.

Result

From 12/2/2019 - 3/28/2022, a cohort of 170-204 households participated in GROVES with an average weekly response rate of 95.3%. Significant changes in %HH-ARI were documented in March 2020, September 2021, and late December 2021-January 2022. Two weeks after cessation of in-person education, due to the SC2 pandemic in March 2020, %HH-ARI dropped from 42% to 19%. A steep increase in %HH ARI, from 9/6/21 - 10/4/21 (7.6% to 31%), occurred during the first month of OSD in-person education since the switch to virtual learning in March 2020. A peak in %HH-ARI from 12/20/2021 - 1/17/2022 coincided with the introduction of the SC2 Omicron variant in Wisconsin, and a corresponding peak in reported COVID-19 cases in participating families (Figure 1).

Conclusion

Brief weekly surveys offer a feasible, sustainable method to monitor ARI activity in a school-based community. Observed trends in ARI activity can help visualize the effect of school closure and reopening on families in the school district, the possible contributions of mitigation efforts, and epidemiologic events in the community at large.

Rachael Pung - AOXI0105

Power to detect differences in generation and serial intervals varies across different outbreak periods

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Background

During influenza and SARS-CoV-2 pandemics, variation in the virus incubation period and infectiousness profile, shortening of the time from infection to isolation and changing contact patterns all combine to influence generation and serial intervals. Incorrect estimates of these intervals bias conclusions about the magnitude of transmission and feasibility of control, but it remains unclear how pathogen biology, epidemic response and study design influence estimates over time.

Method

Using a high-resolution dataset on pre-pandemic human social interactions collected in a small town in the United Kingdom, we stratified interactions into household and non-household contacts and simulated SARS-CoV-2 transmission pairs. We investigated, in silico, the power to detect differences in the generation and serial intervals under varying viral epidemiological characteristics, isolation strategies and contact, as well as the ability to correctly recover the true values from available data.

Result

Pre-pandemic household pairs were in contact for about 30% of the measured contact period but this was less than 1% for non-household pairs. Simulating transmission in these contacts, we predicted a difference in generation time of 0.7 days between household and non-household contacts and a 16% power to detect this difference with 100 sampled intervals and only 10% power with 50 samples - power reduction was not proportional to the sample size due to variation in contacts frequency. Using household contacts only, when the mean incubation period is reduced by a day, we estimated a reduction of 0.3 days in the generation intervals with 11% power to detect this difference in the absence of isolation. However, when most cases were isolated by 4 days since onset, this further truncates the generation time distribution leading to a difference of 0.6 days and 40% power to detect this difference. When the duration of infectiousness increases from 14 to 21 days and the mean incubation period is reduced by a day, we estimate a 2-day difference in the generation interval with over 90% power to detect this difference. Early isolation diminishes the effect of prolonged infectiousness with 40% power to detect 1-day difference. Given the greater variance in serial interval, the power to detect a difference in the serial interval distributions is lower.

Conclusion

Variations in outbreak characteristics and study sample size does not bring about a proportional change to the generation intervals and the power to detect this difference. Outbreak interventions such as early isolation can enhance or diminish the power to detect differences in generation intervals when there are contrasting changes in the epidemiological characteristics of the outbreak.

Malania Wilson - AOXI0055

In-field detection of influenza B/Victoria lineage deletion variant viruses by portable triplex real-time RT-PCR and mobile sequencing in Louisiana, 2019

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Background

In Louisiana, the proportion of healthcare visits for influenza-like illness (ILI) began to increase in August 2019, primarily in children and earlier than previous seasons [1]. Between August-November 2019 one large pediatric healthcare facility in New Orleans reported 1,268 laboratory-confirmed B/VIC virus infections, including 23 hospitalizations. Because of the uncharacteristically large outbreak, viral characterization was needed to determine if this was a known circulating virus or a new subclade. During November 2019, Louisiana declared a state of emergency after a cybersecurity attack on state government servers limiting the connectivity of the Louisiana Health Department Laboratory (LHDL) and their ability to perform genetic characterization. Our team deployed to the LHDL with our mobile influenza analysis (Mia) next-generation sequencing pipeline [2] and B/VIC DEL triplex real-time RT-PCR (rRT-PCR) assay which are not reliant on the LHDL systems, to determine the viral subclades.

Method

The B/VIC DEL triplex rRT-PCR diagnostic assay uses a pair of conserved primers and three probes specific for each genetic group: B/VIC V1A.1, VA1.2, and VA1.3 [3]. Eighty-eight B/VIC clinical samples were analyzed with the in-field rRT-PCR assay performed using the portable Quantabio "Q" instrument. Additionally, the influenza genome was amplified from the samples and sequenced using the Mia pipeline.

Result

With the rRT-PCR assay, it was determined that 86 samples were VA1.3, 2 samples were VA1.2 and one sample tested influenza negative after previously testing B/VIC positive. Among the 88 genomes sequenced, 87 samples were in congruence with the rRT-PCR results. The single sample that tested negative via rRT-PCR was determined to be V1A.3 by the HA sequence.

Conclusion

Genetic characterization showed that this outbreak was not due to a new influenza B subclade but was associated with unvaccinated children and likely due to the early circulation of influenza before seasonal influenza vaccine campaigns begun. This study illustrates how portable rRT-PCR and next-generation sequencing can facilitate disease characterization, rapidly at the point of outbreak even in resource-limited settings.

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Joshua Petrie - AOXI0092

Investigating sources of hospital-acquired influenza infection in two seasons.

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Background

Hospital-acquired influenza infection (HA-FLU) can result in severe morbidity and mortality. Whole-genome sequencing (WGS) of influenza viruses has been used to investigate HA-FLU, but most studies have focused on known outbreaks and may not be representative of typical HA-FLU infection. We aimed to identify epidemiologically linked HA-FLU in a large tertiary care hospital and apply WGS to confirm or rule out linkage between patients over two influenza seasons.

Method

The study population included all inpatients testing positive for influenza A during the 2017-2018 and 2019-2020 influenza seasons. For these individuals, we attempted to retrieve all residual clinical respiratory specimens testing positive for influenza; specimens were unavailable for the 2018-2019 season. WGS to generate consensus sequences was attempted for all retrieved specimens. Dates and locations of inpatient service, and clinical influenza testing collection dates and results were retrieved from the electronic medical record. Time-location groups contained at least one presumed HA-FLU case (1st positive ≥48 hours after admission) and all other inpatients who tested previously tested positive and resided in the same unit as the HA-FLU case in the 4 days prior to the order date of their first positive test. Genetic relatedness within time-location groups was assessed by examination of phylogenetic trees.

Result

During the 2017-2018 season, 230 patients who tested positive influenza A (H3N2) or untyped influenza A, and 26 were HA-FLU. Overall, 178 (77%) of the 230 2017-2018 influenza patients had WGS data including 19 (73%) of 26 HA-FLU patients. There were 159 influenza A (H1N1) or untyped influenza A positive patients identified during the 2019-2020 season including 33 HA-FLU. WGS data were available for 57 (36%) influenza patients overall including 14 (45%) HA-FLU cases. There were 10 time-location groups identified in 2017-2018, and 13 in 2019-2020. Two time-location groups from 2017-2018 had genetically linked cases: 3 patients from a group of 4 patients, and 3 patients from a group of 18 had evidence of phylogenetic linkage. No other patients within time-location groups genetically linked, suggesting transmission links were unlikely.

Conclusion

Our results suggest patient to patient transmission or multiple infections from a single source was limited in our study. Instead, most HA-FLU likely result from separate introductions possibly from healthcare workers or visitors. These results further suggest that current infection control practices are sufficient to prevent hospital outbreaks, but additional preventive measures could focus on reducing healthcare worker presenteeism and visitor screening.

Katherine Williams - AOXI0031

Modeling the impact of twice-yearly influenza vaccination in age 65 and up

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Background

The elderly (age 65+) are at high risk of death from flu and are offered a single flu vaccine dose each season. The flu season peak varies, while vaccine effects are believed to wane over a period of months. Two flu vaccine doses in a season for this group could potentially provide early season protection (first dose) and additional protection to offset waning later in the season (second dose). Models of infected individuals (agent-based) are ideal for allowing for differential vaccine dosing schedules and influenza season start dates.

Method

We used the Framework for Reproducing Epidemiological Dynamics (FRED), an agent-based (agent defined as an individual person) modeling platform to model two vaccination strategies based on the timing of the flu season. FRED tracks 1.2 million persons in the Pittsburgh region at their work, school, household, and neighborhood, allowing infection to spread in any locale. A one-season flu model with simulation starting Aug 15, varied flu season start resulting in peak cases from mid-Feb to end-Mar, an effective reproductive rate of 1.5, and increased susceptibility in age 65 and up were used. All infected individuals were symptomatic, susceptibility was reduced to 0 after infection. For flu vaccination, 68.7% of agents 65+ were vaccinated as per CDC 2019 reporting, vaccine effectiveness (VE) was 40% for all for both doses, and waning VE was 7% per month. In the first set of models, all individuals were vaccinated beginning Sept 1. In the next set, individuals age 65+ who received the first dose on Sept 1 received a second dose beginning Jan 1. Vaccinations occurred over 45 days in both cases.

Result

Compared to a single vaccination on Sept 1, a second vaccine dose decreased total cases by 12-19% and had a greater impact with a later season start (Table). Seasonality in this model decreases the transmissibility from its maximum value later in the season, resulting in lower cases with a later season start and peak.

Conclusion

Given variable flu season start dates, the optimal timing of vaccination is unknown; a second vaccine dose may offset this variability. For people age 65+, the proportion of cases prevented with a second dose was greater for all start and peak dates, but a higher estimated proportion was prevented with a later peak presumably because of waned immunity. With a late-season peak, a second vaccination could thwart nearly 1 in 5 estimated cases in vulnerable seniors.

Kylie Ainslie - AOXI0056

The impact of vaccinating adolescents and children on COVID-19 disease outcomes

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Background

Despite high COVID-19 vaccination coverage among adults, there is concern over rising SARS-CoV-2 infections in the coming months. Many countries have extended vaccination to adolescents (12-17 year olds) and may further extend to children aged 5-11 years.

Method

To quantify the benefits of extending COVID-19 vaccination beyond adults we developed a deterministic, age-structured SEIR model. We compare cases, hospital admissions, and intensive care (IC) admissions for vaccination in adults only, those ≥12 years, and those ≥5 years. The model incorporates differences in susceptibility and infectiousness by age, seasonality, and different modes of vaccine protection. Model parameters were estimated by fitting to daily cases in the Netherlands. We performed sensitivity analyses in which vaccine protection waned.

Result

Upon relaxation of all non-pharmaceutical control measures a large wave occurred regardless of vaccination strategy. We found overall reductions of 5.7% (4.4%, 6.9%) cases, 2.0% (0.7%, 3.2%) hospital admissions, and 1.7% (0.6%, 2.8%) IC admissions when those ≥12 years were vaccinated compared to adults only. When those ≥5 years were vaccinated we observed reductions of 8.7% (7.5%, 9.9%) cases, 3.2% (2.0%, 4.5%) hospital admissions, and 2.4% (1.2%, 3.5%) IC admissions compared to vaccinating adults only. Benefits were largest within the age groups included in the vaccination program extension and smaller if vaccine protection wanes.

Conclusion

Our results highlight the benefits of extending COVID-19 vaccination programs beyond adults to reduce cases and severe outcomes in adolescents and children and in the wider population. Additional control measures may be required to prevent a large wave despite vaccination program extensions.

Lin Wang - AOXI0015

Community-wide interventions minimize the opportunity for super-spreading of SARS-CoV-2

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Background

High overdispersion in individual transmissibility and the resulting super-spreading events are believed to drive the SARS-CoV-2 transmission. Estimating these characteristics often requires detailed contact-tracing data, which is challenging to obtain during the pandemic. It is important to develop a simple yet flexible method that uses only routinely reported time series data of incident cases to infer key characteristics of individual transmissibility and assess the impact of control measures.

Method

To facilitate real-time estimation, we develop a likelihood-free inference framework using the approximate Bayesian computation-Sequential Monte Carlo approach, which allows us to evaluate the posterior distribution without formulating complex likelihood functions. We performed the inference by optimizing the similarity between simulated and observed daily time series of community cases, thereby only requiring the use of routinely reported time series data of incident cases.

Result

We applied this framework to the COVID-19 data of daily case counts from regional economic hubs including Singapore and Hong Kong. We demonstrate the ability of our framework in characterizing the changing dynamics of individual transmissibility, reconstructing transmission chains and clusters, and providing more accurate impact assessments of control measures.

Conclusion

Our analyses suggest that the super-spreading of SARS-CoV-2 in the community is driven by large transmission clusters with many generations of infections instead of super-spreading events alone. Community-wide interventions can minimize the super-spreading of SARS-CoV-2.

Jessica Y. Wong - AOXI0019

Assessing the impact of influenza epidemics in Hong Kong

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Background

Influenza viruses cause a substantial burden of morbidity and mortality in Hong Kong and across the world. However, methodology for timely assessment of the impact of influenza virus infection is not standardized. As a result, there is a need to examine the validity of the methodology for the assessment of impact developed by the World Health Organization.

Method

We estimated influenza-associated excess all-cause mortality from 1998 to 2019 in Hong Kong using linear regression models. We also collected severe influenza cases across different age groups. We assessed the influenza impact defined using World Health Organization's pandemic influenza severity assessment framework. We estimated thresholds using 2014 to 2018 data under the WHO averaging method and moving epidemic method, then applied the thresholds to the 2019 data.

Result

Our study estimated an annual influenza-associated excess all-cause mortality rate of 14.4 (95% CI: 11.1, 17.3) per 100,000 person-years. When thresholds were applied to the 2019 data, there was good agreement between excess mortality and severe influenza cases. Impact was characterized as moderate for all ages but high for individuals in the 45-64 years age group. In addition, there was good agreement between the WHO averaging method and moving epidemic method.

Conclusion

Our study assessed seasonal influenza impact using different data sources. The framework will be useful in monitoring circulating influenza strains that could potentially cause influenza pandemics.

Gregory Hoy - AOXI0090

The Spectrum of Influenza in Children in Managua, Nicaragua

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Background

Better understanding of the full spectrum of influenza infection in children is important both for estimating the true burden of childhood influenza and for improving influenza control and clinical care. Establishing the frequency of asymptomatic infection and post-influenza sequelae and the clinical relevance of infecting strain is particularly crucial.

Method

Data from the Nicaraguan Pediatric Influenza Cohort Study (NPICS), the Household Influenza Transmission Study (HITS), and the Household Influenza Cohort Study (HICS), based in Managua, Nicaragua, were used. Children aged 0-14 were tested for influenza using RT-PCR and/or HAI. The frequency of asymptomatic influenza was calculated from children undergoing surveillance for infection, and the frequencies of sequelae were calculated from symptomatic children in NPICS. Associations between virus strain and sequelae were calculated using age-adjusted GLMMs with log-link functions.

Result

From 2012 to 2020, 1272 influenza infections occurred in the household studies, and 6.6% of these had no fever or cough and no more than one other minor symptom. The asymptomatic fraction increased with age; 1.7%, 3.5%, and 9.1% for children aged 0-2, 2-5, and 5-14, respectively (trend $p<0.0001$), and 26.6% for individuals older than 15. Of asymptomatically infected children, 51.2% shed virus detectable by RT-PCR, compared to 92.5% of symptomatic children ($p<0.0001$), and younger children were more likely to shed virus even when asymptomatic (trend $p=0.0329$).

From 2011 to 2020, a total of 2140 cases of symptomatic influenza occurred in the pediatric cohort. Sequelae were rare, the most common being pneumonia (2.4% of cases) and acute otitis media (3.3% of cases); hospitalization occurred in 1.9% of cases. Children under 2 were at higher risk for pneumonia (7.3% of cases), acute otitis media (4.6% of cases), and hospitalization (3.2% of cases). There were no differences in the odds of sequelae between Influenza A and B; however, AOM (OR 1.99, 95% CI 1.14-3.48) and hospitalization (OR 3.73, 95% CI 1.60-8.67) were more likely with A/H1N1pdm than A/H3N2, and pneumonia (OR 10.99, 95% CI 1.34-90.28) was more likely with B/Victoria than B/Yamagata.

Conclusion

In our community studies of influenza, asymptomatic infection was rarer in children than in adults, and the frequency was inversely associated with age. Viral shedding occurred in half of asymptomatic infections and almost all symptomatic infections, and younger children were more likely to shed virus when asymptomatic compared to older children. Post-influenza sequelae were rare in children, and the odds of pneumonia, acute otitis media, and hospitalization differed by strain.

Alison Barkhymer - AOXI0125

Species Differences in the Antiviral Immune Response to Influenza

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Background

Avian influenza is a global public health concern, threatening both human health and agricultural industries. Sporadic outbreaks of avian influenza occur in humans, usually resulting in levels of morbidity and mortality high above that of seasonal influenza. Despite these occurrences, spillover events for influenza are rare. This is due to a number of roadblocks that exist that prevent cross-species transmission. One of these is host immunity. In order to establish a productive infection, viruses must overcome the innate immunity of the host. Interferon (IFN) is an integral part of the early innate immune response to viruses. IFN protects cells by inducing the expression of IFN-stimulated genes (ISGs), which can restrict viral infections through a myriad of mechanisms. ISGs are under high rates of positive selection, causing orthologs to sometimes have divergent functions between species. When a strain of influenza is first introduced to a new species, it encounters ISGs that it has never interacted with before. We hypothesize that there are ISGs that are divergent between birds and humans that block the cross-species transmission of influenza.

Method

We have computationally identified avian orthologs of human ISGs that are significantly divergent between both species. We plan on using knockout and overexpression studies to establish whether divergent ISGs restrict influenza, followed by ectopically expressing the avian orthologs in human cells, and vice versa. Additionally, we also treated chicken and duck cells with IFN or poly(I:C) and performed RNA-Seq to detect upregulated genes in order to generate an independent list of avian ISGs.

Result

We have compiled an independent list of chicken and duck ISGs and have identified several candidate ISGs that may have divergent functions between birds and humans.

Conclusion

By identifying ISGs that contribute to the cross-species transmission barrier of influenza, we hope to gain knowledge that can help predict and combat avian influenza outbreaks in the future.

Charlotte Kristensen - AOXI0128

Preparing for the next pandemic: Impact of pigs challenged with pre-pandemic, swine-adapted and human-adapted influenza A H1N1pdm09 viruses

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Background

Influenza A virus (IAV) causes respiratory disease in a variety of mammals and due to exchanges of IAVs between humans and pigs, the risk of creating new viruses with pandemic potential is present. It is unclear why some IAV strains that evolve in swine can infect and transmit between humans while others seem to be swine specific. This study aimed to compare the infection dynamic and pathogenesis of a presumed pre-pandemic, swine-adapted and human-adapted H1N1pdm09 virus.

Method

A total of 42 seven-week-old Danish Landrace pigs were challenged with 4 ml of 10^7 TCID50/ml of either swine-adapted H1N1pdm09 (n=12), human-adapted H1N1pdm09 (n=12), a presumed pre-pandemic H1N1pdm09 (n=12) or mock (n=6). Nasal swabs, body weight measurements and rectal temperatures were obtained during the study. The control group and eight pigs from each virus-challenged group were euthanized three days post-inoculation (DPI), whereas four pigs from each virus-challenged group were euthanized 14 DPI. Three different areas of lung tissue were collected at necropsy. Quantification of IAV in nasal swabs and lung tissues was investigated by reverse-transcriptase qPCR. The total viral load 0-3 DPI was calculated as the median under the curve (AUC). The clinical impact was evaluated based on observations of respiratory disease symptoms, the proportion of days with rectal temperatures above 40°C and body weight gains.

Result

The highest viral shedding was found in the swine-adapted H1N1pdm09 group at all DPIs until 10 DPI. At 14 DPI, none of the swine-adapted H1N1pdm09 pigs tested positive for IAV, whereas one pig from the human-adapted H1N1pdm09 group and one pig from the pre-pandemic H1N1pdm09 group tested positive for IAV. The total viral load 0-3 DPI was significantly higher in the swine-adapted H1N1pdm09 group compared to the human-adapted H1N1pdm09 group. The highest clinical impact was found in the pre-pandemic H1N1pdm09 group while the lowest clinical impact was found in the swine-adapted H1N1pdm09 group.

Conclusion

A high viral load combined with low clinical impact found in the swine-adapted group and a low viral load combined with high clinical impact found in the human-adapted group demonstrate the importance of host adaptation concerning viral fitness and virulence. This suggests that spillover events of swine-adapted IAVs to humans could potentially result in more severe disease outcome compared to infections with human-adapted IAVs. Further studies investigating antiviral immune responses and viral sequencing are required to determine host factors important for the host adaptation.

Marie Kirby - AOXI0143

Discriminating North American Swine Influenza Viruses with a Portable, One-Step, Triplex Real-Time RT-PCR Assay

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Background

Swine harbor a genetically diverse population of influenza A viruses (IAVs) with demonstrated potential to transmit to and spread among humans causing outbreaks and pandemics. Swine are susceptible to IAV infection from other species, and the mixture of viruses within swine further evolve through antigenic shift and drift. Reverse zoonotic events of IAVs transmitting from humans to swine can lead to sequestration of human, seasonal IAVs within swine populations, leading to antigenically diverse viruses to which humans or subsets of humans have little to no immunity. Ultimately, these IAVs that continue to circulate in swine have the potential for outbreaks or even pandemics if a zoonotic transmission occurs. Therefore, it is important to have a rapid method to detect swine IAV (IAV-S) that have a high potential for causing outbreaks or pandemics if transmitted to humans. This is especially critical at the human-swine interface, where zoonotic transmission risk is high.

Method

We developed a one-step, triplex real-time reverse transcription-polymerase chain reaction (rRT-PCR) assay multiplexed from the CDC H1v_1A, H1v_1B2 and H3v 2010 assays that detects and distinguishes A(H1) subtype IAV-S that belong to the 1A.1 (α), 1A.2 (β), 1A.3 (γ), 1B.2.2 (δ1) and 1B.2.1 (δ2) lineage and A(H3) subtype IAV-S from the H3 2010.1 lineage. The performance of the IAV-S Triplex rRT-PCR was evaluated by comparing its sensitivity with the sensitivity of the Influenza A (InfA) assay from the CDC Flu rRT-PCR Dx panel using 10-fold serial dilutions of relevant viruses. To evaluate specificity of the IAV-S Triplex rRT-PCR, we tested high titer A(H1N1)pdm09, seasonal A(H3N2), HPAI A(H5N1), HPAI A(H5N6), Eurasian lineage A(H7N9), influenza B(Yamagata) and B(Victoria) lineage viruses. We demonstrated the portability of this assay via an in-field test at an exhibition swine show.

Result

The sensitivity of the H1v_1A, H1v_1B2 and H3v_2010 components in the context of the IAV-S Triplex assay is 103.3, 103.9, and 104.1, respectively, and we demonstrate that the IAV-S triplex is highly specific for detection of IAV-S. We identified three IAV-S lineages circulating among pigs at an exhibition swine show within hours of sampling using the IAV-S Triplex rRT-PCR and portable sequencing.

Conclusion

By coupling the IAV-S Triplex rRT-PCR assay with portable methods and instrumentation, we demonstrate that the IAV-S Triplex rRT-PCR assay can efficiently and promptly detect North American IAV-S outbreaks in-field, ultimately allowing timely deployment of interventions to prevent virus transmission to other swine and to humans during IAV-S outbreaks.

Lauren Steele - AOXI0146

Defining the Genesis and Pathogenesis of the Avian Influenza Virus

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Background

Influenza A viruses can readily spread from wild bird species to terrestrial poultry. In terrestrial poultry, influenza A viruses cause a mild/subclinical infection and is thus referred to as low pathogenic avian influenza (LPAI). H5 and H7 LPAI viruses can evolve in terrestrial poultry to become highly pathogenic avian influenza (HPAI) viruses. Unlike LPAI viruses, HPAI viruses can cause 100% mortality in terrestrial poultry. The evolution of LPAI to HPAI is associated with the insertion of a multi-basic cleavage site in the haemagglutinin, which conforms to the Cend rule (CendR). The CendR motif is a short peptide with the sequence R/K-X-X-R/K, which has been experimentally proven to bind to, and be internalised by, neuropilin-1 (NRP-1). Here, we investigate the structure and expression of NRP-1 in several avian cell lines to determine its role in promoting the evolution of LPAIVs to HPAIVs in chicken cells.

Method

To investigate structural differences between avian (chicken and duck) NRP-1, amino acid changes in chicken and duck NRP-1 were introduced into the human NRP-1 protein structure using FoldX to model avian NRP-1 structures. Structural alignments were then conducted using PyMOL to determine structural variations between the two avian species. NRP-1 gene expression was determined by culturing primary aortic endothelial cells isolated from chickens and ducks (ChAEC and DuAEC), before harvesting cellular RNA for quantitative polymerase chain reaction analysis. Protein expression in ChAEC and DuAEC was assessed using fluorescently-labelled NeutrAvidin-coated silver nanoparticles conjugated to a CendR peptide.

Result

Structural differences and mRNA expression levels between chicken and duck NRP-1 were minimal. Conversely, NRP-1 protein expression was significantly higher in ChAEC than in DuAEC, suggesting that there may be greater selective pressure for the genesis of HPAIV variants in ChAEC due to a greater abundance of NRP-1. These results are also seen in chicken and duck fibroblasts, suggesting this phenotype is not cell-type-specific.

Conclusion

The differential protein expression of NRP-1 in ChAEC and DuAEC may explain why HPAIV variants only emerge in terrestrial poultry. Greater levels of NRP-1 at the surface of chicken cells may provide the positive selective pressure for HPAIVs containing the multi-basic cleavage site. These data may provide the molecular basis to genetically engineering chickens that are resistant to the genesis of HPAIVs.

Dillon McBride - AOXI0164

Shortening the duration of swine exhibitions reduces risk of influenza A virus infection at the human-animal interface

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Background

In the United States, diverse lineages of influenza A virus (IAV) infect swine at county fairs and transmit from swine to people at this interface. Since 2011, over 475 confirmed zoonotic IAV cases have been reported in the US, the majority of which were associated with swine contact at agricultural fairs. Transmission of swine-origin influenza to people poses a public health threat, and measures that limit interspecies transmission are critical to mitigate the risk of viral spillovers with pandemic potential. Because IAV is likely to be introduced into county fairs via subclinically infected pigs, it is critical to reduce IAV transmission within swine populations at individual fairs. In this study, we evaluated the effectiveness of shortening swine exhibitions to 72-hours or less to reduce zoonotic IAV risk; a measure offered by the Swine Exhibitions Zoonotic Influenza Working Group.

Method

We longitudinally sampled every pig daily for the full duration of 16 county fair events during 2014 and 2015 for a total 39,768 nasal wipes from 6,768 individual pigs. Additionally, we estimated IAV prevalence at 195 county fair events during 2018 and 2019 to test the hypothesis that fairs which shortened their swine exhibition to 72-hours or less would have lower IAV prevalence in their swine by the end of the fair.

Result

In both longitudinal and cross-sectional studies, we found that shorter duration of swine shows drastically reduces IAV prevalence in exhibition swine at county fairs.

Conclusion

Reduction of viral load in the barn within a county fair is critical to reduce the risk of interspecies IAV transmission and ultimately pandemic potential. An additional benefit is that shortening exhibitions can be implemented from a fair organizer level and does not require individual exhibitor compliance to be effective as a mitigation strategy. We have provided substantial evidence supporting this mitigation strategy, and we encourage fair organizers to consider shortening their swine shows to protect the health both animals and people.

Jasmine CM Turner - AOXI0165

Persistence of Avian Influenza Viruses in Live Poultry Markets and Farms of Bangladesh During COVID-19 Pandemic

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Background

Influenza A has been the cause of four pandemics since the turn of the 20th century; however, the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the cause of the COVID-19 pandemic has led to an unexpected global health crisis. While community measures implemented to mitigate the spread of SARS-CoV-2 have affected the circulation of seasonal influenza amongst people, limited data has been presented to show the impact of these pandemic countermeasures on influenza A prevalence in the poultry sector. Here, we report findings from active surveillance at live poultry markets (LPMs) and free-range poultry farms in Bangladesh wetlands from June 2020 to December 2021 to acquire a more comprehensive understanding of the dynamics of the human/poultry live bird market interface in a country with endemic H9N2 and H5 circulation.

Method

Bimonthly water, fecal, oropharyngeal, and cloacal samples were collected from birds and surfaces in retail and wholesale markets, backyard flocks, and poultry farms. Swabs collected were placed in a PBS/glycerol isolation media and stored at -80°C until shipment. Upon arrival, samples were screened for influenza A via rRT-PCR. All samples tested as positive for influenza A were subsequently tested for H5. All rRT-PCR H5-positive samples were injected into 10-day-old embryonated eggs, whereas only 10% of non-H5 rRT-PCR positive samples were injected into eggs. Isolates obtained were subtyped by sequencing.

Result

A total of 2027 (33%) of the 6150 samples collected were rRT-PCR positive for influenza A via matrix gene. Of the 2027 positive samples, 921 (33% of the 2800 collected) were collected from duck farms, 763 (53% of the 1440 collected) from LPMs, and 343 (17% of the 1910 collected) from wild birds. One hundred isolates were obtained during this surveillance period: 35 H5N1, 34 H9N2, 2 H4N6, 1 H3N2, 1 H1N3, and 27 pending subtyping. All but 3 H5N1 viruses were isolated from duck, while most of the H9N2 isolates originated from chicken and quail. Other LPAI viruses were also found exclusively in duck.

Conclusion

H9N2 and H5N1 viruses continued to be detected in the LPMs of Bangladesh slightly above pre-COVID-19 levels, despite SARS-CoV-2 pandemic driven changes in poultry density, turnover, and bird movement.

Gianpiero Zamperin - AOXI0170

The interplay between avian influenza viruses and their hosts: insights from transcriptomic sequencing of galliformes infected with low pathogenic viruses of the H7 subtype

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Background

Influenza A viruses (AIVs) are important human and veterinary health pathogens, with avian species representing their natural hosts. There are many subtypes of AIVs, each characterized by a specific pair of surface glycoproteins, the hemagglutinin (HA) and the neuraminidase (NA). AIVs infecting poultry can be divided into two groups, according to the severity of the disease they cause. So far, only H5 and H7 subtypes have showed the capability to mutate from low to highly pathogenic avian influenza (LPAI, HPAI). Once this happens, the mutation results in severe epizootics with up to 100% mortality. Although AIVs are inextricably linked to their hosts in their evolutionary history, the contribution of host-related factors in the emergence of HPAI viruses has only been marginally explored.

Method

We selected two pairs of H7 low-pathogenic viruses with a distinctive ability to evolve from LPAI to HPAI under natural conditions. One pair of LPAI virus precursor of HPAI strains (precHP) included the H7N1 A/chicken/Italy/1279/1999 and the H7N3 A/chicken/BC/CN006/2004. The other pair included two viruses that have not evolved into highly pathogenic strains (nevoLP), even after mid- to long-term circulation in Galliformes: the H7N3 A/turkey/Italy/2962/03 and H7N2 A/chicken/Italy/1670/15. We did an in vivo infection of six-week-old female SPF white leghorn chickens. RNA samples were isolated from tracheas at 24, 36, 48 at 72 hours post-infection and subjected to library production and sequencing. High quality data were aligned to host genome to perform differential expression analysis. Differentially expressed genes (FDR < 0.05, |log2FC| ≥ 1) were used for GO enrichment analysis (FDR < 0.05) and pathway analysis with IPA.

Result

NevoLP enriched terms included chromosome segregation, cell division, cell cycle, biosynthetic process, cellular component biogenesis, ATP metabolic process, cellular metabolic process, suggesting that infected cells were busy multiplying and producing proteins, ATP and other components. PrecHP enriched terms included immune response, immune effector process, response to external stimulus, response to biotic stimulus and actin filament-based process, indicating a host immune response as the main reaction to the viral infection.

Conclusion

Our challenge study demonstrated that the number and type of DEGs can profoundly vary between viruses and even within the same HA subtype, pathotype, species and tissue. It is interesting to highlight that both the H7 HPAI precursors showed a very high number of general enriched terms related to immune response. These findings suggest that an exacerbated innate immune response may represent a selective factor shaping AIV pathogenicity evolution.

Stephen Nyarko - AOXI0176

Outbreaks of Highly Pathogenic Avian Influenza AH5N1 during 2021 in Ghana.

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Background

Highly Pathogenic Avian Influenza (HPAIV) AH5N1 subtype continues to pose a significant global health threat, with intermittent outbreaks in poultry. The West African sub-region continues to experience outbreaks of HPAIV AH5N1 among poultry since 2007. In July 2021, outbreaks of HPAIV AH5N1 among poultry in Ghana were investigated. The objectives were to examine backyard poultry in military barracks and assess the possible spillover of any avian influenza infections into the human population.

Method

This study was conducted by the Ghana National Influenza Centre in collaboration with the Ghana Armed Forces and Veterinary Services Directorate. Military barracks as well as nearby poultry farms with reports of sick birds and selected live bird markets in14 regions were visited. Both symptomatic and asymptomatic birds were randomly sampled with bird droppings, feathers, wood shavings, and water collected for influenza virus investigations and phylogenetic analysis. Farmers and birdkeepers were also sampled and tested for the presence of influenza and SARS-CoV-2 viruses. Data obtained was analyzed to reflect proportions and regional distribution.

Result

For 1,363 animals sampled, 86 samples tested positive for HPAIV AH5N1 with 1 AH7 strain detected for positivity of 6.3% for avian influenza infections. Amongst 286 human specimens collected, no avian influenza infection was detected. However, seasonal influenza virus was found in 4 samples [3 AH3N2, 1 A(H1N1) pdm09] using real-time polymerase chain reaction assays. Six samples tested positive for SARS-CoV-2. Greater-Accra region reported the highest number of avian influenza positives among poultry, followed by Central, Ahafo, Upper East, and Upper West regions. Phylogenetic analysis indicated that the circulating H5N1 strain in Ghana is closely related (99% match) to A/chicken/Nigeria/VRD21-37_VIR2288-2/2021(H5N1).

Conclusion

The Greater-Accra region recorded the highest number of avian influenza cases in poultry, probably due to interaction with migratory birds and high poultry trading activities. No spillover of avian influenza was detected in farmers or birdkeepers and genomic sequencing showed that the circulating H5N1 strain does not possess known human adaptive motifs. The presence of SARS-Cov-2 infections in humans was in line with the prevalence of COVID-19 respiratory infections in Ghana in 2021.

Klara Marie Andersen - AOXI0210

Exploring zoonotic markers of influenza A virus using phylogenetic and ancestral inference analyses on large datasets

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Background

The zoonotic potential of Influenza A viruses (IAVs) presents a continuous threat of emerging human pandemics. The virus responsible for the latest IAV pandemic in 2009 was formed as the result of a reassortment of three different swine IAV (swIAV) lineages originating from Mexican swine. However, sequencing data of swIAVs from before 2009 is limited, and thus we have no clear understanding of the specific mutational events that lead to the zoonotic transmission and further spread in the human population.

Method

We collected large IAV sequence datasets from GISAID and NCBI Influenza Virus Database of both swine and human origin. Extensive phylogenetic analyses and inference of ancestral sequences (internal nodes on the phylogenetic trees) then allowed us to gain information about genetic changes occurring on branches in the trees corresponding to zoonotic or reverse zoonotic jumps. Specifically, these were branches where the inferred host was swine on one end and human on the other end. We used a strategy where we first constructed fast Bio-NJ phylogenetic trees for all our data, and then sequentially selected subsets of leaves for which we then built more robust trees that could be used for further analysis of specific evolutionary branches.

Using the same general strategy, we both analyzed swine IAV sequences from around the pandemic emergence separately to look for specific mutational events preceding the pandemic H1N1 subtype (H1N1pdm09) in swine, and we analyzed datasets of human and swine IAVs from 2009 until present, both separately and in combination, to explore adaptation patterns connected with zoonotic or reverse zoonotic jumps.

Result

We have reconstructed ancestral sequences and identified potentially important amino acid substitutions in each viral protein along the evolutionary branches leading to H1N1pdm09. We have also inferred large phylogenetic trees of human and swine IAVs from 2009 and onwards and have identified several subclades of swIAVs in the trees possibly resulting from reverse zoonotic events and continuous circulation in the new host. These subclades provide great opportunities for further analysis of differences in selective pressure following a host jump.

Conclusion

The identified amino acid substitutions on the branches leading to H1N1pdm09 needs further characterization, and analyses of e.g. the selective pressure on any of these sites will help determine the significance of the mutations as zoonotic markers. Combined with analysis of the adaptation patterns in swine and human hosts, respectively, we will gain more knowledge of specific amino acid substitutions with possible importance for the emergence of IAV strains with pandemic potential.

Jonathan Temte - AOXI0148

SARS-CoV-2 co-detection with influenza A and other respiratory viruses among school-aged children and their household members

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Background

Concurrent detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and another respiratory virus in an individual can document contemporaneous circulation. We used an ongoing, community-based study of school-aged children and their households to evaluate SARS-CoV-2 co-detections with other respiratory viruses in a non-medically attended population over a two-year period.

Method

Household enrollment was predicated on an acute respiratory illness in a child residing in that household who was also a kindergarten through 12th grade student in the participating school district. Demographic, symptom and household composition data and self-collected nasal specimens were obtained on the recruitment day, and 7 and 14 days later, from the index child and all other household members. All specimens were tested for SARS-CoV-2/influenza A/B by RT-PCR. Day 0 specimens from the index children were simultaneously tested for 17 viruses using a commercial respiratory pathogen panel (RPP). To assess viral co-detections involving SARS-CoV-2, all household specimens were tested via RPP if the index child's Day 0 specimen tested positive to any of the 17 viral targets in RPP and any household member tested positive for SARS-CoV-2.

Result

Of 2,109 participants (497 index children in 497 households with 1,612 additional household members), two (0.1%) were positive for both SARS-CoV-2 and influenza A; an additional 11 (0.5%) were positive for SARS-CoV-2 and another RPP-covered respiratory virus (figure 1). Co-detections predominantly affected school-aged children (figure 2: 12 out of 13 total) and were noted in 11 of 497 households.

Conclusion

SARS-CoV-2 co-detections with other respiratory viruses were uncommon and predominated in school-aged children.

Mira Patel - AOXI0151

Recent trends in influenza antiviral susceptibility monitoring

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Background

The US Centers for Disease Control and Prevention (CDC) participates in national and global influenza surveillance. In addition to genetic and antigenic characterization, viruses are assessed for their susceptibility to neuraminidase inhibitors (NAIs) and a polymerase inhibitor, baloxavir (BXA). Since the implementation of the Sequence First Initiative for influenza virologic surveillance, the antiviral testing algorithm has changed.

Method

Illumina MiSeq is used for Next Generation Sequencing (NGS) to generate codon-complete genome sequences of viruses (clinical specimens and isolates). Virus susceptibility to NAIs and BXA is assessed by NA inhibition (NI) assay and high-content imaging neutralization test (HINT), respectively.

Result

NGS analysis has become the CDC's primary tool for monitoring NAI susceptibility. In a typical season, genomic sequences of >6,000 viruses are analyzed, with nearly half of the viruses being collected abroad. NA sequences were screened for changes (markers) known to confer resistance or reduced inhibition by NAI(s). Numerous NA substitutions/deletions and their combinations have been reported, including those derived from virus culturing. Flagged viruses, as well as ~5% of all submitted viruses without markers, are tested by NI assay to determine their drug susceptibility. Many US Public Health Laboratories (PHLs) conduct in-state antiviral surveillance using pyrosequencing, mainly to detect the most common marker, N1-H275Y. A transition from pyrosequencing to NGS has recently begun, which would streamline and enhance in-state surveillance.

BXA is a new drug for which markers of resistance are not fully elucidated. This puts an emphasis on phenotypic testing. The cell culture-based HINT has been successfully used to test hundreds of viruses in recent seasons. Its streamlined version (IRINA), developed at CDC, does not require a sophisticated cell imager. This assay is posed to improve throughput and ease implementation at PHLs. Several changes in polymerase acidic (PA) subunit have been associated with reduced susceptibility (> 3-fold increase in EC50). Hence, sequences of submitted viruses are screened to detect known and suspected PA markers. By using a combination of NGS and HINT data, we identified new markers (e.g., PA-K34R) of reduced susceptibility and showed that some previously reported markers (e.g., PA-L28P) had no effect on drug phenotype.

Conclusion

As technologies are improving, algorithms of antiviral testing are undergoing necessary updates. NGS allows high-throughput analysis for drug resistance markers and provides a framework for selecting viruses to test phenotypically. The development of streamlined assays will facilitate the expansion of baloxavir susceptibility testing.

Sandra Chaves - AOXI0215

Ten-year anniversary of the Global Influenza Hospital Surveillance Network (GIHSN)

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Background

The Global Influenza Hospital Surveillance Network (GIHSN) currently includes more than 100 hospitals in 20 countries, collecting, analyzing, and sharing epidemiologic, clinical and laboratory data on influenza and other respiratory viruses. The network operates under a public-private partnership governance: the Foundation for Influenza Epidemiology (FIE).

Method

An independent multidisciplinary scientific committee manages the scientific direction of the network. Using standard protocols, the sites collect demographic and clinical information from patients admitted with respiratory illnesses. Respiratory specimens are collected to test for influenza and other respiratory virus. The GIHSN promotes sharing of surveillance data with local health authorities, WHO and the scientific community at large. The network has evolved over time to focus on linking epidemiologic and clinical data with whole genome sequencing (WGS) information to facilitate exploring viral phenotypes as they relate to severity or vaccine-breakthrough cases. Despite the pandemic, the network has been able to pursue its activities with limited disruption and it is currently active year-round.

Result

The GIHSN has been progressively expanded since 2012 to include sites in both hemispheres and in the inter-tropical area. A total of 110,827 patients hospitalized with respiratory illness have been enrolled so far, including laboratory-confirmation of 21,159 Influenza cases and 30,125 patients with other respiratory viruses. The annual positivity rate for influenza has ranged from 29% in 2019 to 2% in 2020-2021 (COVID-19 pandemic period). The network has contributed to more than 20 published manuscripts and numerous local and international meetings and conferences since its initiation. More recently, the FIE is also supporting research activities that leverage the community of scientists to use data gathered through the GIHSN and expanding collaborations to better understand the burden of influenza. GIHSN data are also shared with WHO to support vaccine strain selection.

Conclusion

The COVID-19 pandemic has highlighted the need for resilient and ready surveillance systems, targeted genetic sequencing scale up and a multi-stakeholder approach. The pandemic has also shown the critical importance of understanding the circulation and burden of respiratory viruses to guide public health decision making and research and development initiatives. Emerging infectious diseases represent an ongoing threat and GIHSN illustrates the feasibility and pertinence of public and private sector coming together to optimize global efforts.

Mary Krauland - AOXI0131

Impact of Enhanced Influenza Vaccines for People 65 and Over

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Background

Influenza vaccines have relatively modest effectiveness in people > 65 years. Several enhanced vaccines (high dose, adjuvanted and recombinant vaccines) providing higher levels of effectiveness are licensed for people >65 years but it is unclear whether minor differences in vaccine efficacy among them would make one preferable to another. Agent-based models are ideal for allowing assignment of differential vaccine effectiveness by host characteristics, including age. We used the Framework for Reproducing Epidemiological Dynamics (FRED), a large agent-based modeling platform that can follow individuals and that accounts for household, community, and work exposures, to model the impact of enhanced vaccines in persons > 65 years.

Method

An agent-based model of influenza was implemented in FRED using a city population of ~1.2 million. Simulations covered one influenza season. The model included vaccination at rates derived from reported vaccine uptake in the US. 80% of vaccinated persons > 65 years received an enhanced vaccine, to match rates in the US. Enhanced vaccine efficacy was modeled as providing 40, 45 or 50% reduction in susceptibility to infection. The remaining 20% of vaccinated persons 65 and over received a standard vaccine, modeled at 35% reduction in susceptibility in that age group (40% reduction in susceptibility in persons < 65). Season start date was varied from November 15 to January 1. Two levels of influenza burden were included with reproductive rates of ~1.2 and 1.3. Waning of immunity was modeled as a 10% increase in susceptibility per month for persons over 65.

Result

The model produced reasonable influenza burden in the population >65 years in simulations with start date in November. Later season starts resulted in lower influenza burden. Use of enhanced vaccine with 45% and 50% efficacy in 80% of seniors resulted in modest decrease in cases relative to the lower efficacy enhanced vaccine (40% efficacy), with reductions of ~5-6% in infections in seasons with an earlier start date but lower impact in seasons with later starts, with <1% reduction in a season starting January 1. Waning immunity and reduced transmission rate due to seasonality contributed to decreased impact of the more effective vaccine in seasons with a later start.

Conclusion

There was an overall modest impact of increased vaccine efficacy, probably due to current high levels of uptake of an enhanced vaccine in the target age group in the US. The impact depended on vaccine efficacy as well as the season start date, with earlier seasons having overall higher influenza burden but also greater impact of use of more effective vaccines.

Lotte van Heuvel - AOXI0129

The Impact of Influenza and Pneumococcal Vaccination on Antibiotic Use: A Systematic Review and Meta-Analysis

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Background

Antimicrobial resistance (AMR) remains a major threat to global health and vaccination is increasingly seen as an effective public health intervention to address AMR. Immunization can prevent bacterial and viral infections that are often (inappropriately) treated with antimicrobial medicines. As stated in the WHO Action Framework on Leveraging Vaccines to Reduce Antibiotic Use, there is a need to expand and share knowledge on the impact of vaccines on AMR. We therefore performed a systematic literature review and meta-analysis describing the impact of influenza and pneumococcal vaccination on antibiotic use.

Method

We updated two systematic literature reviews that studied the link between vaccination and antibiotic use, carried out by Buckley et al. (2019) and Doherty et al. (2020). We took a number of steps to further enhance the reviews by: 1) including the latest publications (from November 2018 onwards); 2) adding modelling and cost studies; 3) stratifying the results by region; and 4) studying the antibiotic use data collection methods in randomized controlled trials (RCTs). The risk of bias for all included studies was assessed using various tools (e.g. RoB 2).

Result

In our literature review, we identified 1409 articles; assessed 32 full-text reports; included 25 new studies on influenza (n = 10) and pneumococcal (n = 15) vaccination (in addition to systematic reviews by Buckley (87 studies) and Doherty (26 studies)). The following results are limited to influenza. The meta-analysis included a total of 15 RCTs (2 new RCTs) performed in the WHO European Region (n = 7), the Americas (n = 5), the Western Pacific (n = 1) and in mixed regions (n = 2). The overall result among influenza-vaccinated vs. unvaccinated individuals is a reduction in the proportion of people receiving antibiotics (Risk Ratio 0.63: 0.51 - 0.79) and a reduction in the number of antibiotic courses or prescriptions (Ratio of Means 0.71: 0.62 - 0.83). One RCT was rated as high quality, 6 as moderate and 8 were categorized as low or very low.

Conclusion

There is a limited number of RCTs with high quality of evidence that explore the association between influenza vaccination and antibiotic use, and efforts to collect and assess antibiotic use data in new vaccine trials should be encouraged. In our study, we will propose standard indicators for antibiotic use data collection in future trials. Overall, our findings confirm the Buckley study's conclusion that influenza vaccination may reduce antibiotic use and it highlights the value of vaccination in AMR policies.

J. Kevin YIN - AOXI0196

First-year experience of implementing the preferential recommendation of Standing Committee on Vaccination (STIKO) for high dose quadrivalent influenza vaccine for adults 60 years and older in Germany

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Background

STIKO preferentially recommended high-dose quadrivalent influenza vaccine (HD-IIV4) over other standard dose vaccines to all adults 60 years and older (older adults) in Germany during 2021/22 influenza season. This was based on STIKO's systematic review (including Grading of Recommendations, Assessment, Development and Evaluations analysis), which demonstrated improved protection by HD-IIV4 vs. standard dose vaccines against influenza infection and influenza-related hospitalizations, and also the robustness of clinical data. It is the first nationwide, preferential recommendation of a new influenza vaccine in Europe that was implemented during the COVID-19 pandemic. Here we review our experiences of the HD-IIV4 roll out during the first season in 2021/22.

Method

We collected and analysed information from various sources on the number of HD-IIV4 doses distributed, cohort size of older adults, and vaccine uptake in Germany.

To assess the safety profile of HD-IIV4 in routine care, we passively collected data as part of the Enhanced Passive Safety Surveillance (EPSS) for 2021/22 in Germany. The EPSS is a requirement of the European Medicines Agency aiming to rapidly detect any unexpected safety signal of influenza vaccines in routine use. In this surveillance framework, HD-IIV4 vaccinees were instructed by participating healthcare practitioners to report the occurrence of adverse events of interest (AEIs) seven days after vaccination. These data were used to derive the rates of AEI accordingly.

Result

In 2021/2022, 9.3 million HD-IIV4 doses were distributed for the 24.1 million of older adults in Germany. Assuming the vaccine uptake in the current season was the same as 2020/2021 (47.3%; corresponding to 11.4 million older individuals vaccinated), up to 9.3 million older adults may have received HD-IIV4.

To assess the safety of HD-IIV4, 903 individuals were vaccinated as part of the EPSS between 18 October and 2 December 2021. Of these, 19 (2.1%) persons reported 47 AEIs, all of which were non serious. Of the 47, severity was reported for 39 AEIs: 16 were mild (1.8%); 14 were moderate (1.6%); and 9 were severe (1.0%). The most frequently reported AEIs were injection site reactions (18/47), headache (6/47), and myalgia (6/47).

Conclusion

Despite the challenges due to the COVID-19 pandemic, STIKO's preferential recommendation of HD-IIV4 (issued in January 2021 and incorporated in Vaccination Guideline since April 2021) was successfully implemented in the first year, with high acceptance amongst older adults. Enhanced pharmacovigilance surveillance in Germany confirmed the reassuring safety profile of HD-IIV4, consistent with that is known or expected as per the Summary of Product Characteristics.

Mary Patricia Nowalk - AOXI0144

Effect of Mild COVID-19 on Physical and Mental Function

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Background

Previous research has shown that individuals have a variable response to hospitalization for influenza in terms of overall physical and mental functioning as measured by the Short Form Health Survey (SF-12). The SF-12 is a validated self-reported survey assessing the impact of health on everyday life. In early 2020, the SARS-CoV-2 virus began to circulate and soon resulted in a W.H.O.-declared pandemic causing hundreds of millions of COVID-19 illnesses, hospitalizations and deaths worldwide. As a respiratory virus, SARS-CoV-2 causes symptoms resembling influenza and other acute respiratory infections, but little is known about the effects of a mild SARS-CoV-2 infection on physical and mental functioning.

Method

This study conducted from 3/30/2020 to 4/30/2021, was a prospective observational study of symptomatic adults (18-87 years) who sought testing to confirm a case of COVID-19 that did not require hospitalization. After informed consent, participants completed an enrollment survey that included the SF-12 to report their physical and mental health and well-being prior to symptom onset, then completed another SF-12 an average of 6-8 weeks later (FU). Viral testing was performed centrally using PCR tests. Results were reported in the electronic medical record (EMR) and were pulled from the EMR using a clinical surveillance software system. Participants were divided into COVID-19 cases and non-cases to compare overall physical function (PF) and mental function (MF) at enrollment and FU, using paired t-tests. Multivariable regression modeling was used to determine predictors of PF and MF at FU.

Result

Of 3,295 participants enrolled in the study, 973 completed surveys at both enrollment and FU: 426 COVID-19 cases and 547 non-cases. PF improved significantly ($P<0.001$) from enrollment to FU for both cases (5.4±0.41) and non-cases (3.3±0.32); whereas MF improved significantly for cases (1.4±0.51; $P<0.001$) and decreased significantly for non-cases (-0.8±0.37; $P=0.23$). Enrollment PF and time between surveys were positive predictors and FU MF and age were negative predictors of FU PF for cases. Enrollment PF was a positive predictor and FU MF, age and non-white race were negative predictors for FU PF in non-cases. There was a significant negative impact of non-white race ($\beta=-3.39$; $P<0.001$) on PF for non-cases that was not observed for cases ($\beta=-0.78$; $P=0.437$). In contrast, male sex had a significant positive impact ($\beta=2.37$; $P=0.006$) on MF for non-cases that was not seen in cases ($\beta=1.48$; $P=0.111$).

Conclusion

The effect of mild COVID-19 on physical and mental functioning during convalescence differed from that of non-COVID-19 respiratory illness cases and bears further study.

A. Danielle Iuliano - AOXI0150

Estimating influenza- and COVID-19-attributable unrecognized deaths in the United States from March 2020-February 2022

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Background

After the emergence of Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) in the United States in February 2020 and the implementation of prevention measures, influenza activity declined and remained low until the 2021/22 season. Causes of death are reported on death certificates to the National Vital Statistics System (NVSS), though reporting of influenza as the underlying cause of death remains rare. Both COVID-19 and influenza deaths may not be completely recognized and reported on death certificates because of limitations in testing, sensitivity of assays used for testing, time between illness onset and test, exacerbation of chronic health conditions listed as the cause of death, or delays in reporting. We first aim to estimate COVID-19 deaths accounting for both SARS-CoV-2 and influenza virus circulation and then to expand the model to also estimate influenza-attributable deaths.

Method

We estimated unrecognized COVID-19 deaths accounting for influenza virus circulation, from October 2021-February 2022, using all-cause deaths reported to NVSS by week and six age groups (0-17, 18-49, 50-64, 65-74, 75-84, and ≥85 years) for 50 states, New York City, and the District of Columbia using a linear time series regression model. Reported COVID-19 and influenza deaths were subtracted from all-cause deaths first. Weekly expected deaths, assuming no SARS-CoV-2 or influenza circulation and predicted all-cause deaths using the SARS-CoV-2, influenza A, and influenza B weekly percent positive as covariates were modeled by age group and included the jurisdiction as a random intercept. COVID-19-attributable unrecognized deaths were calculated for state and age group by subtracting the expected all-cause deaths from the predicted deaths and added to reported deaths to calculate total estimated COVID-19 deaths.

Result

We estimated that 240,806 deaths attributable to COVID-19 occurred in the United States from October 1, 2021-February 19, 2022. Of these, 36,952 (15%) COVID-19 deaths were not documented on death certificates. Sixty-eight percent of unrecognized deaths were among persons aged ≥65 years. Most COVID-19-attributable deaths were not captured during the December 2021 and January 2022 when SARS-CoV-2 activity and influenza virus activity were both increasing.

Conclusion

Estimating COVID-19-attributable unrecognized deaths in the context of both SARS-CoV-2 and influenza virus circulation provides a better understanding of the mortality burden and population subgroups that might be at increased risk of death.

Ian McGovern - AOXI0178

A Retrospective Database Analysis to Estimate the Epidemiology and Burden of Influenza in Children 0-14 Years Over 10 Consecutive Seasons

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Background

In Europe, influenza vaccination is not commonly recommended (or recommended but not reimbursed) for healthy children and vaccination coverage in the pediatric population is low, which may be potentially due to a lack of data, awareness or recognition of the impact of influenza in this age group. This study aimed to describe the incidence and impact of influenza disease on the pediatric population in Italy and the associated health care utilization.

Method

The analysis used the Pedianet database, a pediatric (aged 0-14 years) primary-care database collecting specific data from computerized clinical files of more than 150 family pediatricians [FP] in Italy to evaluate the 2010-2011 through 2019-2020 influenza seasons. Incidence rates over 1000 person-months of influenza cases and related sequelae and associated healthcare resource use were evaluated using diagnostic (ICD-9-CM), prescription, ambulatory exam, and physician note data. Additional hospitalization data was available for the Veneto Region, allowing evaluation of influenza-related emergency room (ER) visits and hospitalizations from the 1st of January 2017 to the 1st of March 2020.

Result

Overall, around 150,000 children were included each season (ranged from 133,452 in the 2019-2020 season to a maximum of 155,328 in the 2015-2016 season). There was an average of 8,892 included influenza cases each season (ranged from 4,700 in 2019-2020 to 12,419 in 2010-2011). Influenza (FP visit, emergency room visit, or hospital admission) incidence was highest among children 1-4 years of age and lowest among children under 6 months of age (Figure 1). Children were prescribed an antibiotic in 38.7% of the influenza cases and the rate of antibiotics prescribed varied from 49.2% in children less than 6 months of age to 32.4% in children 10-14 years of age. No children were prescribed antivirals. Across influenza seasons, there were approximately 30 acute otitis media and 5 pneumonia cases within 30 days per 1000 influenza cases. In the Veneto from January 2017 to March 2020, there were 12,416 reported influenza cases which were associated with 220 ER visits and 111 hospitalizations.

Conclusion

This study showed a significant burden of influenza among children aged 0-14 over a ten-year period in Italy.

Jesús Ruiz-Aragón - AOXI0206

Cost-effectiveness of quadrivalent adjuvanted influenza vaccine with MF59 versus a standard-dose quadrivalent influenza vaccines in Spain

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Background

Quadrivalent influenza vaccines (QIVe) are designed to provide protectionagainst all four influenza subtypes.

Nevertheless, adjuvanted QIV (aQIV), indicated for people aged 65yrs+, combines MF59 adjuvant (an oil-in-water emulsion of squalene oil) and a standard dose of antigen, and is designed to produce, stronger and longer immune response, especially in the elderly where immunosenescence reduces vaccine effectiveness.

The objective of this study is to evaluate the cost-effectiveness of aQIV vs. QIVe in the elderly (65yrs+), from the payer and societal perspective in Spain.

Method

A dynamic transmission model was used to predict the number of medically attended infections in Spain using the two vaccines.

The model uses a decision tree structure to forecast influenza-related costs and benefits from7 seasons (2010-2018) considering available data from Sistema Centinela de Vigilancia de Gripe in Spain (ScVGE).

Likewise, the model includes recent immunization rates published by the Minister of Health in Spain for Season 2020/21. Based on two different meta-analysis, we used as the relative vaccine effectiveness (rVE) of aQIV vs. QIVe in two scenarios; one with a rVE=34.7% (CI95% 2%-66%) which is the results of including laboratory-confirmed influenza studies only and the rVE=13.9% (CI95% 4.2%-23.5) which includes different influenza-like-illness real world evidence medical encounters outcomes.

Influenza-related probabilities of outpatient visit, hospitalization, work absenteeism, mortality, with associated (dis)utilities and costs were extracted from Spanish and European published literature.

The model includes tender prices in Spain, €7 for QIVe and €13 for aQIV, all costs are expressed in 2021 euros. Deterministic and probabilistic sensitivity analyses were conducted.

Result

Replacing QIVe with aQIV in the Spanish elderly population will prevent 38,982 influenza complicated cases, 988 hospitalizations and 495 deaths (with a rVE=34.7%) or 16,824 influenza complicated cases, 433 hospitalizations and 219 deaths (with a rVE=13.9%).

When the rVE of aQIV vs QIVe is 34.7% the incremental cost per quality adjusted life years (QALY) gained was €2,726.55 and cost-savings from the payer and societal perspective, respectively. If the rVE of aQIV vs QIVe is 13.9% the incremental cost per QALY was €7,840.89 and €4,901.20 from the payer and societal perspective, respectively.

Sensitivity analyses validated the robustness of these findings

Conclusion

This analysis demonstrated that aQIV is highly cost-effective compared to QIVe and should be the preferred influenza vaccine option for the Elderly population in Spain.

William Cracknell - AOXI0219

Epizootic & Zoonotic Influenza Surveillance is a vital component of Rapid Pandemic Response

William Cracknell[3], Ray Longstaff[2], Pedro Vieira[1], Beverly Taylor[2]

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Background

Our experience with COVID-19 has graphically demonstrated the dangers posed when viruses pass from animals to humans. Influenza is an avian disease which has made exactly that jump. As we look to better protect ourselves from the next pandemic it behoves us to look very closely at avian influenza outbreaks and how they are affecting human populations.

Method

Influenza viruses have a long history of spilling into humans and causing significant disease outbreaks, four influenza pandemics have occurred in the last hundred years with the 2009 'Swine Flu' pandemic being the most notable recent example. Many influenza viruses have been circulating on the edges of human outbreaks in recent years e.g. H5N1 since the 1990's, H7N7 in the early 2000's and more recently the repeating waves of H7N9 in China, a virus which was quite mild in birds, but caused severe disease and death in humans.

Worryingly, we are now seeing steadily rising numbers of reports of highly pathogenic avian influenza, A(H5N1) infection in birds, with a much wider geographical spread, particularly in Europe but also in Asia and Africa and increasingly in the US, as well as of zoonotic infections in humans with a range of A(H5) and A(H9N2) viruses. Increasing numbers and spread multiply the potential for a reassorting event which may give rise to another pandemic.

Result

It is vital that we support the WHO as they conduct rigorous and detailed surveillance of these zoonotic influenza infections so that we can be properly prepared. As vaccine reference viruses are highlighted and genetic sequences published it is essential they are shared rapidly, made freely available and that their use is unencumbered by national access and benefit sharing (ABS)/Nagoya Protocol legislation.

Manufacturers can then work with WHO, Academia and Government agencies to build banks of 'seed' viruses (a stated goal of the G7/CEPI), allowing earlier understanding of virus characteristics and their potential for vaccine manufacture. Such work provides a running start in the event of a pandemic, especially if the causative virus is a close strain match or shown to have cross-reactive capability.

In parallel with this is an urgent need to accelerate work on the provision, and acceptability to regulators and reference laboratories, of new influenza potency assays to speed up the release of vaccine once it is produced.

Conclusion

It is through this combination of surveillance, proactivity and innovation that we will continue to meet, and even improve upon, an influenza pandemic response within 100-days of declaration.

Bianca Zecchin - AOXI0247

Highly pathogenic avian influenza H5N1/H9N2 reassortant virus in West Africa: a potential threat for humans?

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Background

Since 2006, the West African poultry population has been seriously hit by different waves of highly pathogenic avian influenza (HPAI) H5Nx viruses, brought by migratory birds, with the last introduction of the H5N1 subtype reported in late 2020. In January 2017, the H9N2 subtype of the G1 lineage was identified for the first time in Burkina Faso and since then it has been reported in several West African countries. The co-circulation of these two zoonotic subtypes in this region is a cause for concern not only for animal health and economic damage, but also for the possible emergence of reassortant viruses with unknown biological properties and public health implications.

In December 2021, three HPAI H5N1 outbreaks were reported in poultry farms from three distinct regions of Burkina Faso. Here we describe the complete genome characterization of the first H5N1/H9N2 reassortant virus in West Africa.

Method

By using an Illumina MiSeq platform, we generated the whole genome sequences of three H5N1 viruses from Burkina Faso. Maximum likelihood phylogenetic trees were obtained for all the eight gene segments using IQTree v1.6.6 and the time to the most recent common ancestor (tMRCA) was estimated for the hemagglutinin (HA) gene using the BEAST v.1.10.4 package.

Result

Phylogenetic analysis of the HA gene shows that the HPAI H5N1 viruses from the three distinct outbreaks in Burkina Faso cluster together (similarity of 99%-99.2%) within clade 2.3.4.4B, and are closely related to HPAI H5N1 viruses identified in Nigeria and Niger in 2021-2022. The phylogenetic trees of the other gene segments confirm this clustering, except for the PA gene where the three H5N1 viruses from Burkina Faso cluster with H9N2 viruses collected in West Africa between 2017 and 2020. The tMRCA of the three H5N1 under study was June 2021 (95% HPD March-August 2021).

These reassortant viruses possess several mutations that may be associated to an increased zoonotic potential, including the HA-S137A (H3 numbering) mutation, which has been demonstrated to increase virus binding to human receptors, and the PA-367K mutation, which has been associated to a more efficient H5N1 virus replication in primary human bronchial epithelial (NHBE) cells, in A549 and Calu-3 cells.

Conclusion

Although it is difficult to ascertain where and when the reassortment event occurred, the emergence of an H5N1/H9N2 reassortant virus in West Africa raises concerns about its possible impact on animal and human health. Further studies to evaluate the biological significance of this emerging genotype and to assess its spread are urgently required.

Angel Ma - AOXI0279

Tropism and replication competence of canine influenza virus in canine and human respiratory tract explants

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Background

Dogs are close friend of human, zoonosis and reverse zoonosis therefore raise our concern. Avian-origin canine H3N2 influenza virus (H3N2 CIV) is enabled to cross species and infect a wide range of hosts. Although no human cases have been reported, H3N2 viruses are one of the human pathogens causing seasonal flu epidemic, indicates the zoonotic risk of H3N2 CIV. In this project, we aim to risk assess for the zoonotic potential of H3N2 CIV and its possibility of further reassortment with human and avian influenza A viruses in canines and humans using ex-vivo respiratory explant culture models.

Method

Ex-vivo explant cultures of human lung and bronchus were used to study the replication kinetics of H3N2 CIVs and Ex-vivo explant cultures of canine trachea was used to study the reassortment between H3N2 CIVs, 2009 H1N1 pandemic and avian H9N2 viruses. Sialic acid receptor distribution of the canine respiratory tract explants was also examined.

Result

Limited viral replication of the H3N2 CIVs were found in the human ex-vivo lung and bronchus explants. In canine trachea explants, both human and avian influenza viruses showed productive replication and it can be due to the abundance expression of both human and avian sialic acid receptors in canine trachea explants. The reassortment between H3N2 CIVs, 2009 H1N1 pandemic and avian H9N2 viruses are unlikely to occur in canine tracheal explant culture.

Conclusion

Canine influenza viruses have limited replication in human respiratory tract and the result is consistent with the absence of human cases. Zoonosis and reverse zoonosis have low preference to occur. However, continuous risk assessment and surveillance of the reassortment between canine influenza viruses and other human and avian viruses is recommended, it can reduce the opportunity of spillover during outbreak.

Cyril Barbezange - AOXI0222

Sentinel SARI surveillance in Belgium in times of COVID-19 pandemic

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Background

Sentinel severe acute respiratory infection (SARI) surveillance was recommended by WHO following the 2009 H1N1 influenza virus pandemic. It was originally developed to monitor the severity of influenza infection in hospitals. It uses a case definition based on clinical criteria, making it relevant to monitor the severity of other respiratory viruses such as SARS-CoV-2. The Belgian sentinel SARI surveillance has been in place since 2011 and we present here its performances during the COVID-19 pandemic.

Method

The Belgian sentinel SARI network is composed of six representative hospitals. The original case definition was based on the 2014 WHO SARI case definition. Following the emergence of SARS-CoV-2, a more exhaustive list of symptoms was reported by the hospitals, in addition to basic demographic data, information on known risk factors/comorbidities, influenza and SARS-CoV-2 vaccination status, administration of antiviral or antibiotics, complications during hospitalization, and outcome. Respiratory samples were sent to the National influenza center for RT-qPCR testing for influenza virus, SARS-CoV-2 and 16 other respiratory viruses.

Result

During the first phase of the pandemic (Feb-March 2020), the SARI network operated normally (covering the end of the influenza epidemic) and was able to capture the local spread of SARS-CoV-2 in Belgium at the same time as the national emergency monitoring. In phase 2 (May 2020-January 2021), coinciding with the first waves of the pandemic when the strongest Non-Pharmaceutical Interventions were in place, the SARI surveillance was disrupted due to a high workload in the hospitals dealing with the surge of hospitalized COVID-19 cases. In phase 3 (January-December 2021), the SARI surveillance resumed in a lighter mode (using comprehensive sampling on specific days to provide more flexibility to the hospitals). The adapted method enabled us to monitor the COVID-19 pandemic and the resurgence of other respiratory viruses such as RSV and parainfluenza viruses, and to contribute to European COVID-19 vaccine effectiveness studies. Phase 4 started in January 2022, with the re-emergence of seasonal influenza viruses and their co-circulation with SARS-CoV-2.

Conclusion

Although sentinel SARI surveillance, originally implemented for influenza, suffered greatly in the initial phase of the COVID-19 pandemic due to the increased workload in the hospitals, it proved to be resilient and adaptable. It now allows to monitor SARS-CoV-2 virus in addition to influenza and other respiratory viruses. Sentinel SARI surveillance should thus be considered as a centerpiece of respiratory infection surveillance and as a priority for policy makers for further consolidation.

Francois Dufrasne - AOXI0223

Was SARI surveillance successful at monitoring SARS-CoV-2 circulation and its genomic evolution in Belgium throughout the pandemic?

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Background

After two years of crisis due to the SARS-CoV-2 pandemic, many countries are now entering the recovery phase and plan for long-term surveillance of infectious diseases. Sentinel surveillance networks have been operating for influenza virus for many years. In particular, severe acute respiratory infections (SARI) surveillance has proven very useful to evaluate the severity of such infections. We present the results of SARS-CoV-2 genomic surveillance based on the Belgian SARI surveillance during the pandemic.

Method

Belgian sentinel SARI surveillance has been in place since 2011 and is composed of six hospitals. Samples (nasopharyngeal swabs or aspirate, or broncho-alveolar lavage) were taken from adults and children fulfilling the Belgian SARI definition (adapted from WHO 2014 SARI case definition). Samples were sent, alongside clinical information, to the National Reference Centre for influenza, where they were tested by RT-qPCR for seasonal influenza viruses (A and B), SARS-CoV-2, and 16 other respiratory viruses. Whole Genome Sequencing of SARS-CoV-2 was performed on positive samples with sufficient viral loads (Ct<25) on a MinION or Illumina sequencing platform. Clades and lineages were determined using the open web applications provided by Nextstrain and Pangolin.

Result

SARS-CoV-2 was first detected within the SARI surveillance on a patient sampled on 02/03/2020. Since then, out of 2717 samples received between March 16th 2020 and April 15th 2022, 974 were positive for SARS-CoV-2 and 643 (66%) had a Ct value allowing sequencing. To date, 441 samples were sequenced successfully, covering the different SARS-CoV-2 waves of the pandemic in Belgium. Only the second wave (August 2020 till February 2021) was missed due to a temporary disruption of the surveillance. Lineage analysis showed a similar pattern to that observed in the national Belgian Baseline Genomic Surveillance by the Belgian Sequencing Consortium aiming at sequencing 5 to 10% of all COVID-19 cases in Belgium.

Conclusion

Our results clearly show that sentinel SARI surveillance was able to reflect the circulation of the different SARS-CoV-2 variants, in a comparable way to the exhaustive Baseline Genomic Surveillance that was implemented in Belgium during the pandemic. Sentinel SARI surveillance may therefore represent a cost-effective and sustainable tool for public health policy makers. To obtain a global view on circulating SARS-CoV-2 variants and for future analyses on variant severity and vaccine effectiveness, replacing a seasonal by a year-round SARI surveillance should nonetheless be implemented.

Ana Torres - AOXI0225

The Added-Value of a SARI Surveillance System for COVID-19 and Influenza Surveillance in Portugal

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Background

Severe Acute Respiratory Infections (SARI) syndromic surveillance is recommended not only, for early detection of respiratory infection outbreaks, such as COVID-19 and influenza, but also to assess severity of disease. In 2021, the National Health Institute of Portugal started to collaborate with two central hospitals, located in the main cities of the country, to develop a pilot SARI surveillance system using hospital registers of case-based data on ICD-10 codes. In this work, we describe the results of this surveillance system, to the 2021/2022 season (week 40/2021 to 15/2022).

Method

Since week 40/2021, weekly anonymized data on hospitalizations, including primary diagnoses at admission, were reported. We identified SARI cases based on ICD-10 codes for influenza-like illness, cardiovascular diagnosis, respiratory diagnosis and respiratory infection. Pearson correlation and cross-correlations between weekly SARI hospitalizations, weekly COVID-19 cases (obtained from the national surveillance system) and the number of weekly positive samples for influenza (made available by the Portuguese Laboratory Network for the Diagnosis of Influenza Infection) were estimated.

Result

A high correlation ($\rho = 0.8$) between SARI hospitalizations and COVID-19 incidence was obtained. Weekly SARI hospitalizations detected COVID-19 epidemic peak for about a week earlier. A weak correlation was observed between SARI hospitalizations and the number of positive samples for influenza ($\rho = -0.2$). However, if restricted to hospitalizations due to cardiovascular (CV) diagnosis, a moderate correlation was observed ($\rho = 0.5$). Moreover, CV hospitalizations detected the increase of influenza epidemic activity for about a week earlier. This early warning was not observed between COVID-19 and CV hospitalizations.

Conclusion

In 2021/2022, the SARI surveillance pilot was able to early detect the 5th COVID-19 epidemic wave peak, in January 2022, and the increase of influenza activity, in March 2022. Although, the relation between influenza and cardiovascular major events is known, more weeks of SARI surveillance are needed, in order to understand if CV admissions are an earlier sign of influenza circulation in our population. The integration of clinical and laboratorial data is in progress and is vital, in order to explain changes in SARI patterns, in real time.

Amanda Bolt Botnen - AOXI0226

Impact of the COVID-19 pandemic on respiratory virus detection in the ILI sentinel surveillance system in Denmark

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Background

The COVID-19 pandemic greatly affected sentinel surveillance of influenza-like illness (ILI). The ILI system integrates clinical and virological data and incorporates virological characterization. In light of COVID-19, WHO recommended adapting the system to include the inter-season. Here, we describe findings from the adapted Danish sentinel surveillance system from 2019-W40 and onward.

Method

The Danish sentinel surveillance system monitors ten types of respiratory viruses and their subtypes. These data are linked with individual-level information in national registries. Until 2020, each participating general practitioner (GP) in the system would send up to 10 samples/season for characterization from ILI. From 2020-W13, the system was expanded to more doctors and up to five ILI patients and five asymptomatic patients/week but analysed for influenza and SARS-CoV-2 only. For the 21/22 season, the system changed to two swabs/GP/week year-round.

Result

The 2019/20 season was dominated by rhinovirus, enterovirus, RSV, and other coronaviruses. SARS-CoV-2 was first spotted in 2020-W10. The 21/22 influenza season saw an unusually late start following the end of most COVID-19 restrictions, dominated by Influenza A H3N2, clade 3C.2a1b.2a.2.

Conclusion

The COVID-19 pandemic interfered with the ILI sentinel surveillance system, which was therefore quickly adapted to include SARS-CoV-2 and increased sampling frequency. Year-round surveillance facilitates the capture of viral signals circulating in the population during the inter-season. The adapted and expanded system will be used in the future for integrated surveillance of respiratory viruses including SARS-CoV-2 in the Danish population.

Jocelyn Moyes - AOXI0250

Home-based testing for influenza, SARS-CoV-2 and respiratory syncytial virus (RSV): exploring ways to improve surveillance and vaccine effectiveness estimates, South Africa, 2022

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Background

Surveillance programmes for influenza and other respiratory pathogens are important to inform vaccine formulations and vaccine effectiveness estimates. During 2020, fewer people attended primary care facilities, highlighting the limitations of traditional facility-based surveillance. We aimed to explore the feasibility and acceptability of a home-based testing surveillance programme.

Method

In 3 of 9 provinces in South Africa, we established a referral system for individuals with acute respiratory symptoms to enable access to self-administered nasal swabs. Participants were also identified through an electronic participatory surveillance platform called CoughWatchSA. All participants were enrolled through a webpage link or QR code. Electronic consent forms were signed followed by an electronic data collection questionnaire. Once these forms were completed participants were able to set up an appointment for delivery and collection of swab collection material and instructions. The testing laboratory conducted PCR testing for influenza, SARS-CoV-2 and respiratory syncytial virus (RSV). Results were delivered by text message to the participant within 24 hours. A reference laboratory conducted influenza and RSV subtyping. Participants received a feasibility and acceptability questionnaire after receiving their results. Descriptive statistics were applied to describe demographic, symptoms reported, vaccine coverage and acceptability indicators.

Result

Adult participants (N=595) were enrolled 1 December 2021 through 30 March 2022. The median age was 37 years (interquartile range (IQR) 28-51 years). Median duration of symptoms 2 days (IQR 1-4 days). We received 79 (13%), 258 (43%) and 258 (43%) samples from Gauteng, KwaZulu-Natal and the Western Cape provinces, respectively. Of these 71 (12%) had received influenza vaccination in 2021 and 483 (81%) had received at least one COVID-19 vaccine. SARS-CoV-2, influenza (all influenza A) and RSV were detected in 189 (33%), 6 (1%) and 6 (1%) participants respectively. No coinfections were detected. Of those who completed the acceptability questionnaire 123/127 (97%) would make use of the service again. Access to testing was through self-referred by accessing the testing centre's webpages 46/127 (36%), social and print media (17/127 (13%), and 29/127 (22%) respectively. Word of mouth was identified as an additional source of referral, accounting for 46/127 (36%).

Conclusion

Home-based swabbing for the detection of respiratory viruses was feasible and acceptable, especially. Detecting viruses through this mechanism may provide a simple platform to expand surveillance programmes to inform virus circulation and vaccine effectiveness estimates.

Amanda Perofsky - AOXI0266

The impact of physical distancing on respiratory pathogen transmission in Seattle, Washington

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Background

Many studies have used mobile device data to model SARS-CoV-2 transmission, yet relationships between mobility behavior and seasonal respiratory pathogens are less well understood. We studied the impacts of physical distancing on the transmission of influenza, respiratory syncytial virus (RSV), rhinovirus (RV), and SARS-CoV-2 in the greater Seattle region from February 2020 to September 2021.

Method

Respiratory specimens collected by the Seattle Flu Study, the Greater Seattle Coronavirus Assessment Network, and two Seattle-area hospital systems were screened for the presence of 27 pathogens using RT-PCR (N = 50,995 samples). We adjusted pathogen-specific percent positive values by age, clinical setting, and syndromic respiratory illness rates to reconstruct daily incidences. We obtained aggregated mobile device location data from SafeGraph and characterized patterns of within-city mixing, in-flows, and foot traffic in Seattle. We used time series cross-correlations and lasso regression to assess trends in the daily effective reproduction number (Rt) over time in relation to mobility.

Result

Endemic pathogen transmission dropped substantially after the emergency declaration on 29 February 2020 and stay-at-home orders on 23 March 2020. We observed strong relationships between mobility and Rt in the early months of 2020, where mobility is a positive, leading indicator of transmission across all endemic pathogens and lagging behind and inversely correlated with SARS-CoV-2. RV rebounded after the easing of COVID-19 restrictions in July 2020, while increases in influenza and RSV detections were not observed until Fall 2021. Mobility indicators, especially proxies for travel into Seattle and movement within and between neighborhoods, led or coincided with increases in RV and SARS-CoV-2 during July 2020 but relationships were less clear in later stages of the pandemic.

Conclusion

Mobility metrics may be reliable proxies of contact patterns that are predictive of seasonal respiratory virus transmission, but this may only apply during large perturbations. The lag between COVID-19 Rt and mobility in the early months of the pandemic suggests that population behavior was responsive to COVID-19 case counts or restrictions rather than the reverse. The relationship between Rt and mobility diminished over time, potentially due to a more refined understanding of high risk activities, pandemic fatigue, increasing population immunity, or because mobile device data do not track the movements of children <13. Future analyses will incorporate the 2021-2022 respiratory virus season and consider non-linear relationships between Rt and mobility, other behavioral indicators (e.g., masking, school closures), and the effects of prior immunity on pathogen rebound.

Aspen Hammond - AOXI0291

Addressing challenges to timely reporting of GISRS-supported respiratory virus surveillance data to global platforms, 2020-2022

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Background

In March 2020, the Global Influenza Surveillance and Response System (GISRS) incorporated SARS-CoV-2 into laboratory algorithms for testing specimens from sentinel and non-sentinel surveillance sources. Data from such influenza surveillance systems can efficiently monitor the circulation of different respiratory viruses. Successive versions of guidance, aligned with the temporary recommendations of the International Health Regulations (2005) Emergency Committee on COVID-19 and WHO's COVID-19 monitoring and evaluation framework, encouraging integrated surveillance and reporting of this information (separately for sentinel and non-sentinel data) to the global platform (FLUMART) managed by the WHO Global Influenza Programme have been published, most recently in January 2022. Outreach activities such as training and webinars have also been implemented to encourage the integration of SARS-CoV-2 and reporting of surveillance data. We evaluated the progress made by countries and timely reporting of routine surveillance testing data, including those from sentinel sources.

Method

To assess the trends in reporting on SARS-CoV-2 testing of routine influenza surveillance samples, data on the number of countries reporting such information to FLUMART by source (sentinel or not) for each week of 2020-2022 was extracted on 1 April 2022. The number of countries ever reporting sentinel data was determined. Timeliness was defined as the reporting of results on the same week or by the following week and trends were assessed by reporting data from all sources.

Result

Overall, since the beginning of the COVID-19 pandemic, 95 countries, areas, and territories have tested and reported SARS-CoV-2 sentinel data through established syndromic surveillance systems of GISRS. As of 1 April 2022, the number of countries, areas, and territories reporting timely data on testing surveillance samples for SARS-CoV-2 to FLUMART has steadily increased from 9 in March 2020 to 82 in 2022.

Conclusion

We demonstrate progress in integrating SARS-CoV-2 surveillance into routine influenza surveillance systems, especially sentinel syndromic systems and the reporting of this data to a global platform. Continued actions to facilitate reporting of quality data can contribute to COVID-19 surveillance. Strengthening core surveillance capacities and learning from experiences in data reporting will allow for improved responses to future threats and emergency situations.

Isabel Bergeri - AOXI0298

Lessons learnt from SARS-CoV-2 First Few Cases and household transmission studies for influenza and future novel respiratory viruses

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Background

With the emergence of SARS-CoV-2, the WHO Unity Studies adapted and further developed standardised early investigation protocols, including for First Few X cases (FFX) investigations and Household transmission investigations (HHTI). The objective was to encourage rapid generation of local data for public health action and to facilitate comparison of key epidemiological parameters, such as pathogen transmissibility and infection-severity. We conducted a systematic review and meta-analysis of investigations aligned with the WHO Unity Studies HHTI protocol to describe the implementation of investigations in time and place, assess methodological quality of aligned investigations, explore the sources of heterogeneity, and calculate a pooled estimate of SARS-CoV-2 household secondary infection rate (hSAR) as appropriate.

Method

We searched Medline, Embase, Web of Science, Scopus and medRxiv/bioRxiv for 'Unity-aligned' First Few X cases (FFX) and HHTIs published between 1 December 2019 and 26 July 2021. Standardised early results were shared by WHO Unity Studies collaborators (to 1 October 2021). We used a bespoke tool to assess investigation methodological quality. Estimated hSAR and 95% confidence intervals (CIs) were extracted or calculated from crude data. Heterogeneity was assessed by visually inspecting overlap of CIs on forest plots and quantified in meta-analyses.

Result

Of 9988 records retrieved, 80 articles (64 from databases; 16 from Unity Studies collaborators) were retained in the systematic review and 62 were included in the primary meta-analysis. 32 countries were represented across all 6 WHO regions including 15 lower-and-middle income countries. The majority of investigations (n=50/62) were completed before July 2020. hSAR point estimates ranged from 2%-90% (95% prediction interval: 3%-71%; I2=99.7%); I2 values remained >99% in subgroup analyses (by income setting, predominant circulating strain, testing protocol and risk of bias), indicating high, unexplained heterogeneity and leading to a decision not to report pooled hSAR estimates.

Conclusion

FFX and HHTI remain critical epidemiological tools in all resource settings for early and ongoing characterisation of novel infectious pathogens. We recommend the design of country-specific pre-planned "sleeping" FFX and HHTIs which are exercised in inter-pandemic periods. The large, unexplained variance in hSAR estimates emphasises the need to further support standardisation in planning, conduct and analysis, and for clear and comprehensive reporting of FFX and HHTIs in time and place, to guide evidence-based pandemic preparedness and response efforts for SARS-CoV-2, influenza and future novel respiratory viruses.

Ashley Fowlkes - AOXI0308

High SARS-CoV-2 seroprevalence and rapid neutralizing antibody decline among agricultural workers in rural Guatemala, June 2020-March 2021

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Background

While occupational factors might increase the risk of SARS-CoV-2 exposure for agricultural workers, subclinical illness can lead to underestimation of COVID-19 cases. Serologic SARS-CoV-2 antibody assays identify previous mild COVID-19 and asymptomatic SARS-CoV-2 infections typically missed by traditional respiratory virus surveillance, but seroprevalence studies in agricultural workers in low-and-middle-income countries are underrepresented in the literature. Understanding occupational risk factors can help to inform targeted workplace mitigation strategies.

Method

Using data from the Guatemala AGricultural workers and Respiratory Impact (AGRI) study and anti-SARS-CoV-2 nucleocapsid IgG (anti-N) testing to estimate past infections, we analyzed risk factors associated with seropositivity at enrollment in relation to lab-confirmed SARS-CoV-2 infection. We assessed the stability of neutralizing antibody (NAb) response using a lentivirus-based pseudovirion assay in a subset of samples from workers with two visits from June 2020 ì¶ March 2021, prior to vaccine roll-out. Relative risk (RR) for seroprevalence at enrollment was obtained using a modified Poisson regression model adjusted for age, sex, ethnicity, number of household members, chronic illness, household monthly income, cough at enrollment, and job role.

Result

From June 15-December 30, 2020, 1334 (93.2%) participants were tested for anti-N IgG (Roche Elecsys® immunoassay) at enrollment and provided baseline clinical, demographic, and socioeconomic data. The majority were male (84%), young (mean age 31 years), and healthy (<13% had chronic medical conditions). At enrollment, 616 (46.2%) participants had anti-N IgG suggestive of prior SARS-CoV-2 infection. Cough ≤10 days prior to enrollment (RR=1.29, 95% CI: 1.13-1.46), working as a packer (RR=2.00, 95% CI: 1.67-2.40), and as a packing plant manager (RR=1.82, 95% CI: 1.36-2.43) were associated with increased risk of seropositivity at enrollment. Of 718 seronegative workers, 2.1% had lab-confirmed COVID-19 during follow-up compared with 0.3% of the 616 seropositive workers. COVID-19 incidence density for seropositive workers was 0.4/100 Person ì¶ Years (P-Y), lower than those who were seronegative (2.3/100 P-Y). At enrollment, anti-N IgG titers in serum correlated with neutralizing antibody titers (R2=0.26, p<0.0001). In <6 months from enrollment, most workers with follow-up NAb testing (65/77, 84%) exhibited a 95% decrease in neutralizing antibody titers.

Conclusion

Seroprevalence among workers was substantial. Natural infection may have offered some protection against reinfection but was short-lived and underscores the need for multipronged SARS-CoV-2 infection prevention strategies, including vaccination.

Matthew Keller - AOXI0316

Targeted Amplification and Genetic Sequencing of the Severe Acute Respiratory Syndrome Coronavirus 2 Surface Glycoprotein

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Background

The SARS-CoV-2 surface glycoprotein (Spike) is a highly immunogenic and mutable protein that is the target of vaccine prevention (Thompson, et al. 2021) and antibody therapeutics (VanBlargan, et al. 2022). This makes the encoding S-gene an important sequencing target. During the COVID-19 pandemic, it was critical to develop a method for obtaining rapid sequence information-specifically the S-gene-to serve as a complement to viral whole-genome sequencing methods, which can miss important information due to coverage gaps. For this purpose, we developed SpikeSeq, a targeted method to amplify and sequence the S-gene.

Method

We performed in silico analysis using SARS-CoV-2 genomes from both the NCBI and GISAID databases to identify optimal SpikeSeq primer locations and to select candidates that target highly conserved regions. The amplification performance of 20 distinct primer designs was evaluated across varied reaction conditions to select the optimal primer pairs and run conditions. Further in silico analysis evaluated the analytical specificity of the selected primer pairs and assessed the relative selective pressure on the targeted locations. To verify the method, we compared SpikeSeq Nanopore data to whole-genome data previously collected on 322 clinical samples representing SARS-CoV-2 diversity from the early lineage B.1.1 through Omicron BA.2.

Result

We selected two highly sensitive and specific primer pairs for SpikeSeq. The selected primer binding locations are highly conserved for SARS-CoV-2 (<1.3% mismatches at any position) and conserved for closely related Bat- and Pangolin-coronaviruses (0-4 mismatches/primer). We show through statistical and in silico analyses that the SpikeSeq primers are specific to the amplification of the S-gene, with no cross-reactivity to other known human coronaviruses, including SARS-CoV-1, and the primers are in areas that have not undergone negative or positive selection pressure. For 322 clinical samples, Nextclade variant assignment showed 100% concordance between SpikeSeq and whole-genome data.

Conclusion

SpikeSeq can serve as a complement to whole-genome sequencing data with S-gene coverage gaps or be leveraged as a tool for projects in which only S-gene sequencing is of interest. Because SpikeSeq targets a portion of the genome, a given amount of surveillance capacity could cover several times more samples compared to whole-genome sequencing on the same platform. Moreover, the Nanopore platform used by SpikeSeq is compatible with low to moderate throughputs, and its simplicity better enables users to achieve accurate results, even in low resource settings.

Aspen Hammond - AOXI0317

A scoping review of influenza surveillance systems using traditional and alternative sources of data

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Background

While the World Health Organization's recommendation of syndromic sentinel surveillance for influenza is perhaps the most efficient method to collect high-quality data, several limitations are undoubtedly present. Aligned with the Research Recommendation 1.1.2 of WHO Public Health Research Agenda for Influenza to identify complementary influenza surveillance systems which provide timely estimates of influenza activity, we performed a scoping review to map the extent, range and nature of published literature on the use of non-traditional sources of surveillance data for influenza.

Method

We searched three electronic databases (PubMed, Web of Science, and Scopus) for articles in English, French, and Spanish, published between January 1, 2007 and 28th January 2022. Studies were included if they directly compared at least one non-traditional surveillance system with a traditional influenza surveillance system in terms of correlation in activity or timeliness.

Result

We retrieved 823 articles of which 57 were included for analysis. 15 articles considered Electronic Health Records (EHR), 11 participatory surveillance, 10 online searches and webpage traffic, 7 Twitter, 5 absenteeism, 4 telephone health-lines, 3 medication sales, 2 media reporting and 5 looked at other miscellaneous sources of data. Several articles considered more than one non-traditional surveillance method.

Conclusion

We identified eight categories and a miscellaneous group of non-traditional influenza surveillance systems with varying levels of evidence on timeliness and correlation to traditional surveillance systems. Data from electronic health records and participatory surveillance systems appeared to have the most agreement on timeliness and correlation to traditional systems. No studies suggested a non-traditional surveillance system as a replacement of the current system, but rather, the non-traditional systems were proposed as complements to traditional systems.

Aryse Melo - AOXI0319

Genetic characterization of Influenza A(H3N2), circulating in Portugal during 2021/2022 season

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Background

National Influenza Surveillance Program (NISP) and the Portuguese Laboratory Network for the Diagnosis of Influenza (PLNDI) promote the surveillance on Influenza and other respiratory viruses since the 50s and 2009, respectively. The season 2020/2021, was considered atypical, since our surveillance network did not detect any Influenza case. In 2021/2022 season, were detected a late circulation of influenza with an increase of cases since the beginning of March 2022, with a predominant circulation of A(H3N2). In this context, the aim of this work was to perform the genetic characterization of the Influenza virus circulating in Portugal during the season 2021/2022.

Method

We accessed data regarding the diagnosis of respiratory viruses (RV) reported weekly by laboratories from the hospitals of the PLNDI, and data regarding respiratory samples collected in primary care facilities on NISP . All positive samples for Influenza from NISP with CT<30 and a systematic selection of samples reported in the PLNDI (CT<25) were selected to genetic characterization. Whole genome sequencing was performed by next generation sequencing. The sequences analysis and the phylogenetic analysis were performed using the software INSAFLU (https://insaflu.insa.pt/), MEGA 7.0 and FluSurver (https://flusurver.bii.a-star.edu.sg).

Result

Between the week 40/2021 until week 13/2022, 87910 samples were tested in the PLNDI, of which 3725 were Influenza positive , being 2955 Influenza A, and from the subtyped, 427 Influenza A(H3N2). From NISP, 20 cases were positive for Influenza [18 Influenza A(H3N2), 1 Influenza B and 1 Influenza A(H1N1)], among 498 cases of flu-like illness. From the 191 virus A(H3N2) sequenced, 189 were genetically characterize as Bangladesh/4005/2020-like virus (clade 3C.2a1b.2a.2), and 2 as Denmark/3264/2019-like virus (clade 3C.2a1b.1a). The amino acid mutation I222V was detected on neuraminidase (NA) protein in two viruses.

Conclusion

Clade 3C.2a1b.2a.2 is predominant in Portugal so far in the 2021/2022 season, and the clade 3C.2a1b.1a was detected recently. Both clades detected are antigenically different from the 2021/2022 NH vaccine virus, and it can contribute to a lower influenza vaccine-effectiveness. Regarding antiviral susceptibility monitoring, two viruses presented I222V mutation in NA, which confers reduced susceptibility to oseltamivir. The epidemic curve of Influenza is still increasing on week13/2022, thus, it is important to keep the surveillance programs running after the end of the season, to monitor the circulating A(H3N2) viruses, the emergence of new genetic clades or the circulation of other type/subtype.

Natalie Lee - AOXI0248

A Virtual Information Management System for Analysis and Integration of Genomic and Epidemiological Surveillance

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Background

Integration and analyses of viral genomic data with clinical and epidemiological data can provide critical insight into evolution, transmission, and clinical disease during outbreaks. It can also allow for more timely and nuanced influenza surveillance for vaccine strain selection. A major limitation towards this effort is access to technological solutions that provide linkages between these rich datasets that are cost effective and easy to use by non-specialists across the public health space. Importantly, these integrated data platforms need a built-in capability for cross-talk between partners to enable selective data sharing.

Method

We developed a multi-user virtual information management system (VIMS) that utilizes a distributed architecture to perform federated requests for information across self-managed nodes.

Result

VIMS is a pathogen-agnostic customizable data collection and analysis platform that supports multiple data streams and is scalable based on operational needs specific to end-users. It features configurable early event statistical anomaly detection algorithms, such as EWMA and CUSUM, to draw attention to data aberrations and supports temporal and spatial analysis through a wide variety of visualizations. Data sets can be overlaid on top of visualizations for comparison and integrated analysis. Instances of VIMS have absolute control over how data, or aggregations, can be shared with other users in order to facilitate rapid information sharing with stakeholders. The system can be modified to pull data from other surveillance systems and databases in order to enable interoperability between silos.

Conclusion

We have developed a technology solution that is able to facilitate the ability to share, manage, and coordinate health information in a regionally collaborative and timely manner that promotes local and regional partnerships, enables decision making, and serves to build nations' capacity for integrated health surveillance. Incorporation of this capability into public health surveillance programs will empower organizations to implement easier, streamlined sharing of public health information trans-nationally for routine situational awareness across borders as well as promote data-driven decision-making during emergency operations while maintaining control and sovereignty over their data.

Laura Van Poelvoorde - AOXI0280

Exploring The Added Value Of Whole Genome Sequencing Data In Influenza Surveillance

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Background

WGS can be a valuable alternative for influenza surveillance compared to traditional approaches that often only target HA & NA. The aim of this study was to evaluate the added value of WGS for routine surveillance.

Method

Using a dataset of 253 H3N2 samples from the 2016-2017 Belgian influenza season, we propose: (1) a new influenza classification based on the whole genome instead of only HA, which allows reassortment detection, (2) tracking mutations across the whole genome to explore potential associations with patient data & (3) developing a workflow to detect low-frequency variants (LFV) in routine surveillance.

Result

1) Using a powerful phylogenomic approach, BEAST, we show that the posterior probability in the whole genome phylogenetic tree was higher compared to HA. This higher confidence due to additional genomic information from WGS can improve the vaccine strain selection. Also, WGS also provides the opportunity to identify reassortments & we found that samples from patients with severe symptoms were more likely to have reassortments.

2) We could also detect mutations across the whole genome & link these to the patient data. We found that 9 mutations were significantly linked to the sampling period, which may be of interest when selecting the vaccine strain for the next season. As the H3N2 subtype is very diverse, we proposed to reduce the diversity between the samples by stratifying the samples according to their phylogenetic classification. This resulted in significant associations between 5 mutations & renal insufficiency, which could possibly improve patient treatment.

3) Finally, WGS makes it possible to detect the majority variant & LFV. LFV may be interesting to detect, as their evolution may lead to escaping from neutralizing antibodies & antiviral drugs. It is challenging to distinguish LFV from experimental errors that occur due to PCR & sequencing errors. Therefore, we developed a workflow in which we defined two thresholds based on a minimal frequency of the LFV & a minimal viral concentration. This workflow was applied to the 253 samples which resulted in a selection of 59 samples. In 37 out of 59 samples, LFV were found. More LFV were present in samples coming from patients with mild symptoms compared to patients with moderate & severe symptoms.

Conclusion

This study demonstrates the added value of using WGS for routine surveillance & linking this genomic information to patient data. This can lead to a better vaccine strain selection & an improved clinical management. However, our analyses were performed on a limited number of samples & have to be seen as a proof of concept. There is thus a need for a large database on a European or global level that includes both the genomic & detailed clinical data.

Norman Hassell - AOXI0293

Dynamic Integration of Phylogenetic, Antigenic, and Sample Data for the Surveillance of Seasonal Influenza Evolution

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[1]Centers for Disease Control and Prevention

Background

The genomic surveillance of epidemics from influenza viruses requires continual analysis of timely information from a multitude of disparate data types. The most common way to analyze virus evolution is through the use of phylogenetics, providing a basic framework of viral genetic change. Several other data types need to be related back to the phylogeny to gain insight into evolutionary trajectories and better inform public health decisions, such as optimal vaccine virus recommendations.

Method

We have implemented an internal informatic pipeline of automated phylogeny generation and display. Maximum likelihood and time scaled trees are generated for both nucleotide and amino acid sequences for all influenza gene segments using IQ-TREE and treetime. Ancestral reconstruction, glycosylation inference, transformation of the phylogeny to tabular structure, and Hadoop database upload of the trees complete the pipeline process. This pipeline outputs are incorporated into a highly dynamic Tableau dashboard that integrates virus sample, geographic, temporal, antigenic, positional mutation, and population dynamics data.

Result

This flexible integrated analysis format enables the discovery of patterns within the data that previously required separate individual data analyses. The configurable Tableau dashboard format speeds analysis and visualization of different data types which can be added and modified with ease, enabling custom purpose displays to address biological questions in real time. Additionally, by using a Hadoop-based distributed database system in conjunction with the automated analytical toolkit, many large data sources can be configured together without the long retrieval time of traditional relational database systems. For example, dashboards displaying phylogenetic trees can toggle underlying data sources (nucleotide or amino acids), methods (maximum likelihood or time-scaled phylogenies) or gene segment. Since each node of the tree is joined back to different data sources, the display of patterns of geography, temporal relationships between gene segments, and antigenic results can be customized, in addition to the visualization of phylogenetic trees. These analyses are helpful in showing the genetic determinants of antigenic change and create geographic and temporal context.

Conclusion

The composition of disparate data using flexible, scalable systems provides timely access to layered trends and patterns not apparent when viewed in isolation. These data are continually updated from available information, providing critical insights that inform public health strategies for the prevention and control of epidemic influenza viruses.

Laurent Coudeville - AOXI0305

Using a dynamic transmission model to produce influenza activity scenarios for the winter of 2022/23: France, Germany, Italy, Spain and the United Kingdom

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Background

The SARS-CoV-2 pandemic and associated non-pharmaceutical interventions (NPIs) have had an important impact on influenza activity in Europe, especially during the 2020/21 winter when there was little to no influenza activity. We will apply a combined influenza and COVID-19 dynamic transmission model to assess reasonable future scenarios of influenza activity in France, Germany, Italy, Spain and the United Kingdom for the next winter.

Method

The modelling scenarios will be assessed by pairing an influenza and COVID-19 model. Both models are age-structured dynamic transmission models, where the population can be either Susceptible (S), Exposed (E), Infected (I), or Removed (R) from the transmission process. Vaccination will be taken into account using a leaky approach. The models, which have been previously published, have assessed the evolution of the COVID-19 epidemic and impact of NPIs, or the impact of influenza vaccination in various settings. The COVID-19 model is able to account for multiple variants and estimate the impact of NPIs. Estimates of NPIs impact will be inputted into the influenza model which is able to simulate several epidemic seasons in a row in order to properly account for the evolution in time of the immune status of the population. The age-groups analyzed will be based on the immunization policies in each country. The models will take into account the patterns of influenza circulation in the last two years and the modelling strategies will be first tested in Australia before the Southern Hemisphere 2022 winter (June-August).

Result

The paired model will be used to make projections on reasonable future scenarios regarding the healthcare burden (e.g. hospitalizations) generated by both influenza and COVID-19 (the primary focus will be the 2022/23 winter) for France, Germany, Italy, Spain and the United Kingdom. The scenarios will involve a high, medium and low impact of SARS-CoV-2 on influenza activity, with the high impact scenario involving widespread use of NPIs (e.g. due to the emergence of a new variant with high severity). To what extent an increase in influenza vaccination coverage rates can help mitigate the risk of a severe influenza epidemic will be also presented as exploratory results.

Conclusion

The modelling activities are under development and will be presented during the Options conference so that scenarios for influenza activity in Europe will be available before the 2022/23 Northern Hemisphere winter.

Birgitte Klüwer - AOXI0240

Changing patterns in influenza vaccine coverage by educational attainment as coverage rates increased in Norway, 2014/15-2020/21

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Background

The aim of this study was to map influenza vaccine coverage in the risk roup, among individuals working in patient care and in the general population, and to study whether vaccine coverage varied by educational attainment, employment status, age, sex, marital status or place of residence, and if any social or demographic patterns of vaccine coverage changed over time.

Method

Vaccine coverage was estimated by self-report in a nationally representative survey among 14 907 individuals aged 18-79 years from 2014/15 to 2020/21. Associations between belonging to a vaccination target group (>=65 years of age, >=1 medical risk factor, or having patient-centred work), educational attainment, employment status and vaccination status was explored using logistic regression.

Result

During the 7 influenza seasons, coverage increased from 27% to 66% among individuals >=65 years, from 13% to 33% among individuals 18-64 years in the medical risk group, and from 9% to 51% among health care workers with patient contact. Being elderly, having a medical risk factor, working in patient care, and having higher educational attainment, as well as retirement, disability pension, being female, being married and living in a city were significantly associated with higher vaccine coverage in the multivariable logistic regression analysis.

While coverage was at its lowest (seasons 2014/15-2017/18), educational attainment was not significantly associated with vaccine coverage. In contrast, individuals with higher education reported significantly higher coverage both in 2018/19 and 2019/20, compared to intermediate (OR=0.59, 95%CI 0.45-0.78 & OR=0.68, 95%CI 0.54-0.87, respectively) and lower (OR=0.55, 95%CI 0.38-0.79 & OR=0.70, 95%CI 0.50-0.95, respectively) education. While vaccine coverage increased once again in the last season (2020/21), educational differences diminished and was no longer significant.

Conclusion

Educational differences widened as vaccination coverage increased following the severe influenza season of 2017/18. However, the significant increase in educational differences observed in seasons 2018/19-2019/20 was counteracted in the pandemic season of 2020/21, when vaccination was restricted to the target groups and free or nearly free of charge.

Wendy Boivin - AOXI0259

Pediatric influenza vaccination uptake and intentions in Canada and the role of health care providers

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Background

Utilizing a national survey of parents of children, perceptions of the importance of pediatric influenza vaccination, as well as the role of health care providers (HCPs) in influenza vaccination was determined.

Method

A national online survey of 1,500 parents of children between the age of 6 months and 17 years was conducted. Data was collected between February 10-19, 2022. All respondents were adult residents of Canada who were parents or guardians of at least one child between the ages of 6 months and 17 years on September 1, 2021.

Result

Key findings of this research included: 1. A lack of perceived threat of influenza; 2. Parents' influenza vaccination status strongly corelated to children's influenza vaccination status; 3. HCPs were key to increasing influenza vaccination rates among children. Thirty percent of Canadian children received influenza vaccination every year, while 50% never did. There was a strong correlation between parents' vaccination status and their child's, with 92% of parents who never received an influenza vaccine saying their child never did as well. Survey respondents that spoke to any HCP about influenza vaccination, were more likely to get their child vaccinated, with 66% reporting that a recommendation from their child's HCP was a reason for doing so. Conversely, 29% of those whose child did not receive an influenza vaccine said not having this discussed by their child's HCP was a reason for not receiving the vaccine. Outside of Quebec, 33% of children received their last influenza vaccination at a pharmacy and 33% at a physicians office. In Quebec, 40% of children received vaccination at local community service centre and 25% at a pharmacy.

Conclusion

s: Canadian parents perceive a lack of threat of influenza for their children. HCPs have the opportunity to increase vaccination awareness and uptake rates in adults, as well as in the high risk (6 to 59 months) and general pediatric population, through direct communication. Increasing the number of accessible healthcare providers to both discuss and administer vaccinations may improve influenza immunization rates in both general and pediatric populations.

Samir Sinha - AOXI0278

Understanding Influenza Vaccination Uptake During the COVID-19 Pandemic in Canada

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Background

Canada's COVID-19 vaccine rollout has been especially successful, helping its population achieve one of the world's highest vaccination coverage levels. There continues to be a significant gap, however, in immunization rates for other vaccine-preventable diseases, including influenza where only 39% of Canadians aged 12 years and older have been vaccinated against it in 2020. 1

To better understand the persistent influenza vaccination gap, we will conduct an on-line survey across Canada in June 2022. The objectives of this survey include understanding: 1. the knowledge gap in immunization against influenza, 2. the impact of the COVID-19 pandemic on influenza vaccination intentions and uptake, 3. the latest influenza season immunization rates in adults against influenza, 4. the perspectives and comfort level of Canadians around vaccine co-administration.

Method

An on-line survey of 1,500 adults from across Canada, representative by province, age and gender will be conducted in June 2022. Post-stratification weights will be applied to the sample based on census population parameters to ensure representation by province of Canada, age and gender. Results will be compared to previous survey data collected over the past few years.

Result

Survey result themes that will be explored will include an understanding of the current knowledge and awareness of influenza and COVID-19 vaccination, influenza vaccination views, uptake and intentions, as well as COVID-19 impact on views and intention amongst Canadians. Results will be analyzed after the date of abstract submission and will be available at the time of the conference.

Conclusion

It is anticipated that our survey results will provide the latest insights into the influence that the COVID-19 pandemic has had on vaccination awareness and intentions that could help to guide decision-making heading into the upcoming influenza season. This study can help determine the best evidence-based policy options that could improve influenza vaccine uptake and better address long-standing coverage gaps.

1. Statistics Canada. Table 13-10-0096-25 Influenza immunization in the past 12 months, by age group

Mohammad Hossain - AOXI0330

Detection of a novel highly pathogenic avian influenza (A/H5N1) virus subclade 2.3.4.4B in a duck in Bangladesh

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Background

Diverse influenza virus genotypes are circulating among Galliformes and Anseriformes in live-bird markets in Bangladesh. In Bangladesh, the highly pathogenic avian influenza (HPAI) (H5N1) virus became enzootic in domestic poultry, with 561 animal outbreaks reported from February 2007 to December 2018. Co-circulation of low pathogenic avian influenza (LPAI) and HPAI viruses could contribute to the emergence of new genotypes and clades through reassortment.

Method

We used specimens collected from an avian influenza sentinel surveillance system from 2021 and 2022. Surveillance officers collected at least 135 cloacal swabs from ducks, geese, commercial and backyard chickens, and wild birds, as well as pooled environmental samples each month from seven live poultry markets in Dhaka and three other districts in Bangladesh. All samples were tested for avian influenza viruses (AIVs) using qRT-PCR to detect the viral RNA and common HA subtypes H5, H7, and H9. Whole genome sequencing (WGS) of AIVs untyped by PCR and a subset of those subtyped by PCR was done by the Nanopore MinION platform at icddr,b laboratories in Dhaka.

Result

During the period between January 2021 and February 2022, 1,890 cloacal swabs and pooled environmental samples were collected. Of the tested samples, avian influenza A virus was detected in 308 (16.3%) samples; 115 (6%) were A/H5 subtype, 81 (4.3%) A/H9, a single A/H7, 32 (1.7%) A/H5/H9 co-detection, and 79 (4.2%) unsubtyped by PCR. The period between December 2021 and March 2022 had the highest proportion, 46%, of samples test positive for HA/H5. WGS of the unsubtyped and known HA genotype reveals multiple circulating subtypes, including HPAI H5N1 and LPAI: H1N3, H2N1, H2N5, H2N9, H3N2, H3N3, H3N8, H4N6, H5N3, H5Nx, H6N1, H6N9, H9N2, H9N5, and H11N2. Three clades of H5N1 viruses (HPAI; 2.3.2.1a, 2.3.4.4B, low pathogenic Eurasian lineage "EA-nonGsGD") and the predominant G1 lineage of H9N2 and H9N5 viruses were detected. WGS also confirmed the presence of a European/Middle Eastern/African lineage H5N1 subclade 2.3.4.4B virus in a duck from a district where the H5N6 viruses of the same clade was reported in ducks in 2017. The NA protein of the subclade 2.3.4.4B virus carried a virulence determinant, a 22 aa stalk deletion; none of the other A/H5N1 viruses identified in Bangladesh possessed this deletion.

Conclusion

Detection of diverse circulating LPAI subtypes and emergent HPAI clades indicates potential threats to poultry and ultimately to humans. In endemic countries like Bangladesh, implementation of the Nanopore based WGS approach has promise as a routine laboratory test, detecting diverse subtypes in real-time, providing data to inform surveillance.

Magdi Samaan - AOXI0337

Pandemic Risk Assessment of Avian Influenza A(H5N1) Clade 2.3.2.1c Viruses Using the WHO TIPRA

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Background

A total of six human infections with avian influenza A(H5N1) clade 2.3.2.1c viruses have been reported with the most recent in October of 2020. These 2.3.2.1c viruses had been widespread in poultry throughout Asia and parts of Africa, but more recently have been confined primarily to Southeast Asia. A risk assessment exercise using the Tool for Influenza Pandemic Risk Assessment (TIPRA) for avian influenza A(H5N1) clade 2.3.2.1c viruses was conducted in December 2020 to analyse the pandemic potential of these viruses.

Method

TIPRA was used to assess the global risk of the zoonotic 2.3.2.1c viruses. A literature review was conducted to collect and formulate the virus profile of evidence available for each TIPRA risk element. The profile was reviewed and updated by experts who participated in the TIPRA exercise. The risk was characterized by using a multi-attribute additive model, where standardized risk elements, evaluation algorithms, and assessment processes were used. Technical experts scored risk elements based on information available about the virus at the time of assessment, and discussions based on the scores were used to characterize the risk and develop recommendations. Ten risk elements concerning the properties of the virus (4 elements), attributes in the human population (3 elements), and virus ecology and epidemiology (2 elements) were used to characterize the risk. The scores for each of the ten risk elements and their relevant weight per component (likelihood and impact) were applied to calculate the overall risk score. TIPRA risk map is represented as a scatter plot graph, Impact on the Y-axis and Likelihood on the X-axis. Risk is categorized on a scale of 1-10 for likelihood and same for impact. 1-3 is low , 4-7 is moderate and 8-10 is high.

Result

Influenza A(H5N1) clade 2.3.2.1c viruses were deemed to have a moderate likelihood (4.7 out of 10) to develop sustained human-to-human transmission capacity with upper moderate (6.7 out of 10) impact on the human population if the event was to occur. Confidence in the risk assessment results was moderate for likelihood and for impact. The assessed risk was informed by the data available prior to October 2020 as well as the knowledge provided by Technical Experts through the TIPRA exercise.

Conclusion

A risk map is a scientific evidence-based approach to identify the relative risks of zoonotic influenza viruses for preparedness activities and relevant policy making. Clade 2.3.2.1c viruses pose moderate to upper moderate risks (as of October 2020) to public health. Gaps in scientific evidence were identified and be shared for action.

Raquel Guiomar - AOXI0356

Highly pathogenic Influenza A(H5N1) in Portugal: epidemiological and genetic investigation of multiple outbreaks

Aryse Melo[4], Ana Margarida Henriques[7], Teresa Fagulha[7], Margarida Duarte[3], Catarina Martins[5], Renata Carvalho[2], Joana Mendonça[6], João Paulo Gomes[1], Vitor Borges[1], Raquel Guiomar[5]

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Background

Highly pathogenic avian Influenza (HPAI) A(H5N1) is a panzoonotic virus with pandemic potential, which dispersion is associated with long-distance migratory movements of wild birds. Although transmission from birds to human is rare, humans often develop severe disease. In Portugal, the detection of Influenza A(H5) had already occurred in the past. However, until 2021, HPAI A(H5N1) had not been detected in domestic birds. In this work, we combined epidemiological and viral genetic data to unravel the phylogenetic characteristics of the HPAI A(H5N1) strains detected on infected birds and to unravel its origin.

Method

On November 30th, 2021, the first case of avian flu caused by HPAI A(H5N1) was detected in Portugal. Since then, 20 outbreaks were detected in birds so far, affecting wild birds, backyard flocks and commercial poultry farms. The detection and subtypification of the viruses were performed by molecular methods targeting the matrix, hemagglutinin (HA) and neuraminidase genes. The results obtained were communicated to the National Veterinary Authority in compliance with the European Legislation. Positive samples from 19 out of the 20 outbreaks were subjected to single reaction viral genome amplification and Next-generation sequencing (NGS). Genome assembly, phylogenetic analysis and data visualization were performed using INSAFLU (https://insaflu.insa.pt/), MEGA 7.0 and Microreact (https://microreact.org/).

Result

Genetic characterization of Influenza A(H5N1) was achieved for 15 of the 20 Influenza A(H5N1). Based on hemagglutinin (HA) diversity, all sequenced viruses were classified as clade 2.3.4.4b. Still, preliminary phylogenetic analyses strongly suggest the occurrence of at least three independent introductions of HPAI H5N1 in Portugal, all most likely linked (genetically and/or epidemiologically) to indirect contact with infected wild birds. Three Influenza A(H5N1) isolates showed HA genetically very similar to some viruses isolated in Spain in this season, while one was very similar to a strain isolated in Ireland. No mutations related to antiviral resistance were detected in neuraminidase gene.

Conclusion

In this study, we describe the unprecedented detection of highly pathogenic virus Influenza A(H5N1) in domestic birds in Portugal, as well as the follow-up epidemiological and genetic investigations of several outbreaks, detected in a short-period in the country. Viruses belonging to clade 2.3.4.4b were also detected in several outbreaks in the Northern hemisphere this season. Systematic surveillance is fundamental to the early detection and tracking of the virus circulation of this potential threat for Animal and Public Health following the outbreaks.

Philipp Petric - AOXI0378

Increased polymerase activity of zoonotic H7N9 allows partial escape from MxA

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Background

The interferon-induced MxA protein is a potent restriction factor preventing zoonotic infections with the influenza A virus (IAV) subtype H7N9. Individuals expressing antivirally inactive MxA variants are highly susceptible to such infections. Human adapted IAVs, however, acquired specific mutations in the viral nucleoprotein (NP), allowing escape from MxA-mediated restriction, none of which were observed in MxA-sensitive, human H7N9 isolates. So far it is unknown, whether H7N9 can adapt to evade MxA antiviral action.

Method

We infected Rag2-knockout (Rag2-/-) mice with a defect in T and B cell maturation carrying an human MxA transgene (MxAtg/-Rag2-/-). In these mice virus replication can occur for several weeks, facilitating adaptation to the host. Viruses isolated from the lungs of infected mice were subjected to next generation sequencing to analyze the occurrence of adaptive mutations. Specific mutations were tested on their effect on MxA resistance via reverse genetics.

Result

In MxAtg/-Rag2-/-, but not in Rag2-/- mice, the well-described mammalian mutation E627K in the viral polymerase subunit PB2 was acquired, but no variants with MxA escape mutations in NP were selected. Utilizing reverse genetics, we could show that acquisition of PB2 E627K allowed partial evasion of MxA restriction in MxAtg/tg mice. Pretreatment with type I interferon, however, decreased viral replication in these mice, suggesting that PB2 E627K is not a bona fide MxA escape mutation.

Conclusion

Based on these results, we speculate that it might be difficult for H7N9 to acquire MxA escape mutations in the viral NP. This is in line with previous findings showing that MxA escape mutations cause severe attenuation in IAVs of avian origin. Instead, general polymerase-enhancing mutations might be a viable option for H7N9 viruses to overcome MxA-mediated restriction.

Eduardo Azziz-Baumgartner - AOXI0401

Global Reporting of Avian Influenza Outbreaks in Animals and Human Infections with Avian Influenza Increased in 2013-2022

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Background

Avian influenza (AI) is a health, economic, and food security risk, and while many outbreaks have been reported in the past year, it is unclear whether outbreaks are occurring more frequently or in more places. We analyzed AI reports submitted to animal and public health authorities from January 2013-April 2022, and compared them to 2005-2012 reports, to assess changes in AI global spread.

Method

We abstracted information about AI from the World Organization for Animal Health (OIE) World Animal Health Information System for animal outbreaks and from the World Health Organization (WHO) Event Information Site for human infections with AI. We described the subtypes, pathotypes, and geographic locations of animal AI outbreaks by year. For human infections, we summarized subtype and pathotype, geographic location, bird exposure, age, and outcome. Data was compared to published data from 2005-2012. Multivariable regression analyses were used to evaluate associations between potential risk factors of interest including income classification, yearly poultry production, and animal exposure, and the number of reported animal AI outbreaks or reported human infections with AI.

Result

From 2013-2022, 51% (92/182) of OIE member states identified 34 AI virus subtypes (15 high pathogenic [HPAI] and 19 low pathogenic) during 17,801 animal outbreaks; 16 (47%) subtypes were reported for the first-time and 92% of outbreaks were HPAI. The most frequently reported subtypes were HPAI H5N1 (6690, 38%) and HPAI H5N8 (6681, 38%). One in four member states (25/92) reported AI outbreaks in animals for the first time. Of 194 WHO member states, 17 (9%) reported 1,994 AI infections of 9 virus subtypes among humans. Most infected humans (75%; 1456/1947) had a known animal exposure, 62% (1221/1984) were among working age adults (i.e., 18-64 years), and 22% (445/1994) died. AI animal outbreaks (β=0.37, p=0.0002) and human infections with AI (β=1.15, p<0.0001) were associated with increased poultry production. A 10-fold (95% CI: 6.7-17.3) increase in human infections with AI was associated with known animal exposures prior to illness onset. Lower income member states reported fewer AI animal outbreaks (β=-0.82, p=0.0001) but more human infections with AI than higher income member states (β=1.35, p<0.0001).

Conclusion

AI outbreaks in animals occurred in more member states than previously reported with 25 member states reporting their first outbreak; 16 new virus subtypes were identified representing a two-fold increase compared to 2005-2012. Most human infections were associated with animal exposure. Continued monitoring for AI in animals and humans will be essential for pandemic preparedness.

BORANN SAR - AOXI0420

Second Human Infection of Infection with Avian Influenza A(H9N2) Virus in the Kingdom of Cambodia, March 2022

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Background

Avian influenza A(H9N2) viruses are endemic in Cambodian poultry. The first human infection with influenza A (H9N2) virus detected in Cambodia occurred in February 2021 in Siem Reap province. On 3 March 2022, severe acute respiratory infection (SARI) surveillance detected a second A(H9N2) virus infection in a 1-year-old girl admitted to a Siem Reap hospital with fever and dyspnea; her village had a bird die-off one month prior. A One Health field investigation was conducted.

Method

An influenza A(H9N2) positive nasal sample at the National Institute of Public Health (NIPH) was confirmed positive at the National Influenza Center. A One Health investigation occurred March 9-13, 2022. Household and community members were interviewed. Nasal and serum samples were collected from close contacts of the patient, and tracheal and cloacal samples from backyard poultry at five close contacts households. Molecular detection was performed using US-CDC and FAO real-time RT-PCR protocols for influenza virus and SARS-CoV-2. Virus was isolated in embryonated chicken eggs. Sequencing was performed on Illumina and Oxford Nanopore technology and serology on the patient and contacts was determined by standard hemagglutination inhibition assay.

Result

The patient is from Chi Kreng District, Siem Reap province, a village with 240 households (1241 habitants). 80% of the families conduct small-scale poultry farming. The patient's residence has an enclosure with about 20 chickens, and the family had regular contact with birds. Thirteen close contacts were identified among 5 households: 3 persons were <15 years old, and 7 were female. All reported being asymptomatic immediately before and during the investigation. Nasal swab and serum samples from 13 close contacts tested negative for influenza viruses; three were positive for SARS-CoV-2. Health education on safe poultry farming practices was provided to community members. No birds were visibly ill. Out of 16 chickens tested, four were positive for influenza A(H9N2) virus. Sequencing and phylogenetic analysis revealed close association between viruses from household poultry and the patient.

Conclusion

Endemic avian influenza viruses in poultry remain a concern for zoonotic infections in Cambodia. Interdisciplinary One Health investigation efficiently identified the likely source of human infection and informed local action. Strengthening surveillance for early detection and control in poultry and humans, and education on safe poultry rearing practices are critical to prevent transmission and mitigate risk of reassortment and continued evolution that could result in influenza viruses with increased adaptation for human-to-human transmission.

Sushant Bhat - AOXI0427

Reassortant H9N9 emerged following an experimental coinfection of chickens with H7N9 and H9N2 viruses carries a zoonotic infection risk

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Background

An H7N9 low-pathogenicity avian influenza virus (LPAIV) emerged in 2013 through genetic reassortment between H9N2 and other LPAIVs circulating in birds in China. Since the emergence of H7N9 virus in 2013 in China, the virus has continued to reassort with other subtypes leading to emergence of H7N2 and H9N9 viruses. The H9N9 viruses are also emerging as one of the dominant subtypes in China and have also been reportedly isolated from surrounding countries including Bangladesh.

Method

To examine a reassortment scenario between H7N9 and G1 lineage H9N2 viruses predominant in the Indian subcontinent, we performed an experimental co-infection of chickens with A/Anhui/1/2013/H7N9 (Anhui/13) virus and A/Chicken/Pakistan/UDL-01/2008/H9N2 (UDL/08) virus. Plaque purification and genotyping of the reassortant viruses shed via oropharynx of contact chickens was performed. The predominant genotypes identified were rescued by reverse genetics and assessed for their egg lethal dose and replication kinetics in chicken and human cells. The reassortant H9N9 virus emerged as a dominant subtype and was further characterized for its receptor binding to sialic acid receptor analogues. We further assessed the reassortant H9N9 virus for its transmission in a ferret model to further ascertain any potential zoonotic characteristics.

Result

To identify the genotype of reassortant viruses emerged and shed by contact chickens, the swab samples collected via the oropharynx were plaque purified. All the reassortant viruses shed by contact chickens also showed selective enrichment of polymerase genes derived from H9N2 virus. The viable "6+2" reassortant H9N9 (having nucleoprotein [NP] and neuraminidase [NA] from H7N9 and the remaining genes from H9N2) was found to be a dominant genotype in the contact chickens and showed more egg lethality compared to H7N9 and H9N2 viruses. The H9N9 virus also showed an increased replication fitness in human A549 cells and a significantly increased receptor binding avidity for both α2,6 and α2,3 sialoglycans compared to H9N2 virus. The H9N9 virus also showed a lower pH fusion and a similar ability like H7N9 to replicate in directly inoculated ferrets. While H7N9 transmission remained restricted only to the direct contacts, H9N9 on the other hand showed a low-level aerosol transmission as evidenced by seroconversion, when the ferrets were exposed via indirect contacts. This suggests that the reassortant H9N9 can pose a zoonotic infection risk.

Conclusion

Our study demonstrates that co-circulation of H7N9 and G1 lineage H9N2 viruses could represent a threat for the generation of novel reassortant H9N9 viruses with greater virulence in poultry and a zoonotic potential.

Venkatesh Vinayak Narayan - AOXI0321

Epidemiology of influenza, respiratory syncytial virus, and other respiratory viruses among hospitalized children

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Background

Severe acute respiratory infections (SARI) are the leading cause of hospitalizations and deaths among children aged <5 years in India. However, limited data are available on the contribution of different viruses to SARI.

Method

Through Taqman Array Card (TAC), a real-time reverse transcription polymerase chain reaction (rRT-PCR) multipathogen testing platform, we assessed the prevalence of select respiratory viruses [influenza viruses types A & B, respiratory syncytial virus (RSV), metapneumovirus (hMPV), parainfluenza virus (PIV) types 1-4, human rhinoviruses (HRV), adenoviruses, enteroviruses and human coronaviruses types 229E, NL63, OC43 and HKU1] among children <5 years hospitalized with SARI. We randomly enrolled two eligible SARI cases aged <5 years per day, at a tertiary care children's hospital in Delhi from August 2013 to July 2015. SARI was defined as hospitalization and either (a) <7-day history of fever with cough or (b) in children aged 8 days-3 months, physician diagnosis of acute lower respiratory infection. An age-group matched control without any acute illness was enrolled from the outpatient clinic within 24 hours of case enrolment. Naso- and/or oro-pharyngeal swabs were collected and stored at -720C until testing. Prevalence of each virus detection among cases and controls was compared using ï£2 or Fisher's exact test(p<0.05).

Result

We enrolled 840 cases and 419 outpatient controls. Almost half the children were aged <6 months (42%; 95%CI:39-45%). Viral detections were more common among cases (71%; 95%CI:68-74%) than controls (35%; 95%CI:30-40%). RSV (32%; 95%CI:28-35%) was the most common virus detected among cases. Detections of influenza A, RSV, HMPV, PIV type 1 and 3 were significantly more common among cases than controls (p<0.05). In contrast, detections of human coronaviruses 229E and NL63 were significantly more common among controls than cases (p<0.05). Influenza A and B viruses were detected among 24 (3%;95%CI: 2-4%) and 5 (1%;95%CI:0-1%) cases, respectively. Among SARI cases, influenza detections were more common among children aged 2-5 years (6%;95%CI:2-12%) while most RSV detections occurred among children <6 months (46%;95%CI:40-51%).

Conclusion

Using a multi-pathogen molecular detection method, RSV was the most common virus detected among children <5 years hospitalized with SARI. These findings suggest that TAC assays could be useful tool for pathogen detection, particularly in surveillance and outbreak settings.

Alvin X. Han - AOXI0329

Low testing rates limit the ability of genomic surveillance programs to monitor SARS-CoV-2 variants: a mathematical modelling study

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Background

Genomic surveillance is essential for monitoring the emergence and spread of SARS-CoV-2 variants. SARS-CoV-2 diagnostic testing is the starting point for SARS-CoV-2 genomic sequencing, but testing rates in many low- and middle-income countries (LMICs) are low (mean = 27 tests/100,000 people/day between 2020 and March 2022), leading to spatiotemporal biases in sample collection. Various public health agencies and academic groups have recommended optimal sample sizes and sequencing strategies for effective routine genomic surveillance. However, these recommendations assume high volumes of diagnostic testing that are currently well beyond reach in most LMICs.

Method

To investigate how testing rates, sampling strategies and degree of spatiotemporal bias in sample collection impact variant detection outcomes, we used an individual-based model to simulate COVID-19 epidemics in a prototypical LMIC. We simulated a broad range of diagnostic testing rates, accounted for likely testing demand and applied various surveillance strategies including sentinel surveillance.

Result

Diagnostic testing rates play a substantially larger role in monitoring the emergence and prevalence of new variants than the proportion of genomic sequencing (Figure). Robust genomic surveillance programs would need to achieve average testing rates of at least 100 tests/100,000 people/day and sequence 5-10% of test-positive specimens to enable detection and monitoring of emerging variants in a timely manner, which may be accomplished through sentinel or other routine surveillance systems. Under realistic assumptions, this translates to a mean of ~10 samples for sequencing/1,000,000 people/week.

Conclusion

For countries where testing capacities are low and sample collection is spatiotemporally biased, genomic surveillance programs should prioritize investments in wider access to diagnostic testing to enable more representative sampling, ahead of simply increasing the proportion of sequenced samples. Our findings are equally important for high-income countries as they dismantle parts of testing and surveillance infrastructure in the post-crisis phase of the pandemic.

Estefania Benedetti - AOXI0344

INFLUENZA SURVEILLANCE IN ARGENTINA IN THE CONTEXT OF SARSCOV-2. NEW STRATEGY

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Background

In Argentina, as in many countries, the influenza circulation was disrupted with the arrival of the COVID-19 pandemic, partly due to SARSCoV-2 mitigation strategies; during 2020-2021 years the detection of FLU viruses was the lowest. Since 2022, new surveillance strategies were implemented. In the molecular detection of FLU and RSV, a percentage of outpatients is included in addition to severe hospitalized cases and deaths that were regularly studied. Since EW46 2021, an unusual FLU A (H3N2) increment of activity in the Tropical and Temperate Regions of South America was detected. Particularly in Argentina, this increased activity is still detected in May 2022. This report describes the characteristics of the early outbreak of FLU 2022.

Method

FLU A and B viruses detected by immunofluorescence assay and rt RT-PCR are sent to the NIC for further FLU A subtyping, FLU B lineage identification and genomic characterization. A subset was selected for HA1 segment sequencing and phylogenetic analysis including the vaccine and circulating viruses was performed using BioEdit program and MEGA 7 with Neighbor Joining distance method and a bootstrap of 1000. Sequences obtained were deposited in GISAID database. Clinical, laboratory and epidemiological FLU data was analyzed based on the information available in the National Health Surveillance System database SNVS 2.0.

Result

Between EW1-14 2022, from a total of 34,608 pediatric and adult inpatient and outpatient clinical samples notified in SNVS 2.0 9,252 FLU viruses were detected (26.7% of positivity). From them, the NIC received 2600 positive samples from different locations of the country. Up to now, 2554 were subtyped as FLU A (H3N2) and no FLU A (H1N1) was detected. 62 viruses were recovered in MDCK and SIAT cells. Phylogenetic analysis of 40 FLU A (H3N2) viruses selected showed that the vast majority fell into genetic clade Bangladesh like 3C.2a1b.2a.2 (2a.2) with the HA1 substitutions Y159N, T160I, L164Q, G186D, D190N, F193S and Y195F.

Conclusion

At the beginning of 2022 an unusual incremented activity of FLU A (H3N2) was detected in Argentina. Fortunately, the majority of the circulating viruses fall into the Bangladesh subclade. These viruses retained good recognition by post-infection ferret antisera raised against A/Darwin/9/2021-like virus recommended for egg- and cell-based vaccines used in the actual 2022 Southern Hemisphere season. In the context of the current COVID-19 pandemic, it is important to maintain surveillance of FLU and other respiratory viruses in order to respond in a timely manner to public health demand.

Faith Ho - AOXI0346

Accounting for the potential of overdispersion in estimation of the time-varying reproductive number

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Background

Regularly monitoring the time-varying reproduction number (Rt) is crucial in informing the public health authorities the level of transmissibility in the community and the effectiveness of control measures. Currently, Poisson framework is often used to measure Rt. In the context of COVID-19, superspreading plays an important role in transmission. Using conventional approach to estimate Rt did not take dispersion in transmission into account. Here we develop an alternative approach of measuring Rt of COVID-19 to account for overdispersion in transmission.

Method

We developed an approach using negative-binomial distribution to estimate Rt and a time-varying dispersion parameter. We applied the framework to data on the third and fourth COVID-19 epidemic waves outbreaks in Hong Kong from July 2020 to February 2021. We further estimated the proportion of proportion of cases responsible for 80% of transmission over time using inferred time-varying dispersion parameter. We compared the model performance of our model with the Poisson approach using simulated data on a 70-day epidemic under different epidemic scenarios and assumptions of the true values of dispersion.

Result

In the beginning of the third wave, we estimated that Rt based on negative binomial approach peaked around 3.5 (95% CrI: 3.13, 4.30), which was similar to the Poisson approach (Rt = 3.7, 95% CrI = 3.07, 4.37). Estimated time-varying dispersion parameter was around 0.5 (95% CrI: 0.46, 1.04). During the early stage of the fourth wave, the largest cluster across numerous dancing venues was identified in Hong Kong. Dispersion during that period decreased to around 0.4 indicating approximately 20% of cases were responsible for 80% of transmissions. The two approaches estimated mostly similar Rt during the fourth wave, however, the negative binomial model had a better model fit. Simulation analysis showed estimates of Rt under the two approaches covered the true values under different scenarios. When the dispersion is apparent, the negative binomial model had a better model fit.

Conclusion

Our approach was able to timely estimate Rt and monitor when superspreading plays a major part in transmission. Detecting key change-points in dispersion parameters could provide evidence to public health authorities to escalate control efforts in superspreading events.

Charlotte Kjelsø - AOXI0369

Participatory surveillance - ILI in the Danish Population 2016-2022

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Background

Influmeter is the Danish version of a uniform online participatory system, called the European Influenzanet consortium, - monitoring self-reported influenza-like-illness (ILI) in populations, - and collaborating with participating countries. Influmeter was established in 2013, and considered an important supplement to existing Danish influenza surveillance systems, because it captures ILI in individuals who might not seek medical help when ill with influenza symptoms.

Method

Danish Influmeter participants receives during influenza season (week 40 - week 20) a weekly reminder email, with an invitation to report any symptoms, as well as health care seeking behavior in the previous week. We used these Influmeter data to analyze participant´s rates of health care contact and to compare rates of ILI activity among participants in Influmeter with rates among contacts in Danish sentinel and on call-doctors surveillance systems since 2016. We defined an Influmeter ILI case by sudden onset of at least one of either symptoms; fever, tiredness, exhaustion, headache and muscle ache. Supplemented by at least one of either cough, sore throat and, shortness of breath.

Result

Number of participants per month rose since 2016 from 1.500 to 34.000, and stabilized in 2021-22 at 10.000, after a large influx in 2020 related to the covid19 pandemic, and initial COVID surveillance in Influmeter, until establishment of a separate COVIDmeter. Among Influmeter participants 68% are 25-64 years of age, and with twice as many females as males. In the past six influenza seasons only 16-22% of participants who reported ILI symptoms sought medical attention/help. When comparing the weekly proportion of ILI cases observed in Influmeter with other Danish ILI surveillance systems, the observed ILI activity in Influmeter increased one to three weeks before an increase in ILI activity was observed in the sentinel- and on call doctors systems (figure 1). Figure 1 shows the weekly proportion of ILI consultations in the Danish Sentinel system and the Danish on-call doctors system, together with the weekly proportion of ILI cases in Influmeter, during the Influenza seasons 2016-17 to 2021-22.

Conclusion

Despite uneven representation of the Danish population we still regard Influmeter as a usefull supplement to existing ILI surveillance systems and as an alert tool in the population that do not seek medical care. Further similar participatory surveillance systems has recently, successfully also monitored and delivered self-reported COVID-19 to both Denmark and the rest of Europe.

Faith Ho - AOXI0372

Impact of influenza vaccination on cardiovascular diseases: a systematic review and meta-analysis

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Background

Winter peaks in both influenza and cardiac deaths have been observed and observational studies suggest acute respiratory infections may be associated with increased risk of cardiovascular (CV) outcomes including myocardial infarction, stroke and heart failure. Observational and randomized evidence has been accumulating on the effectiveness of influenza vaccination in prevention of acute CV events. We conducted a systematic review and meta-analysis to assess the impact of influenza vaccination on cardiovascular diseases (CVD).

Method

We performed literature search on PubMed, Embase and the Cochrane Central Register of Controlled Trials up to 6 January 2022. Studies that included a fatal or non-fatal CV outcome under any of the following categories: major adverse cardiovascular events (MACE), stroke, ischaemic heart disease, heart failure, acute coronary syndrome and myocardial infarction were included. Randomised control trials (RCTs) and observational studies such as ecological, case-control and cohort studies describing efficacy of any influenza vaccine were included. Studies that used intermediate outcomes including inflammatory markers, cardiac enzyme levels, or electrocardiogram changes were excluded. Risk of bias assessment was conducted by two independent reviewers. We used random effects models stratified by study design to estimate the pooled effect of influenza vaccination on each CV outcome. I2 statistic was used to assess heterogeneity. Possible publication bias was described by Egger's test and generation of funnel plots.

Result

We identified 5,451 studies and included 4 RCTs and 48 observational studies published between 2000 and 2021 in the review. Among the included observational studies, 29 used cohort designs, 17 were case-control and 2 were ecological studies. Of the five CV outcomes included in RCTs, significant risk reductions following influenza vaccine were observed only with MACE (37%, 95% CI: 0%, 60%). For observational studies, influenza vaccination was associated with relative risk reductions of 24% (95% CI: 4%, 39%) in heart failure hospitalizations, 22% (95% CI: 12%, 30%) in non-fatal myocardial infarction, 18% (95% CI: 7%, 27%) in stroke hospitalizations and 19% (95% CI: 6%, 31%) in CVD mortality. We did not identify evidence of publication bias.

Conclusion

Influenza vaccination is associated with reductions in some but not all major CV outcomes. Future powered RCTs are needed to confirm the value of influenza vaccines at preventing CV events, and mechanistic studies to understand causal pathways.

Raquel Guiomar - AOXI0376

Differential laboratory diagnoses in the atypical influenza season 2021/2022

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Background

National Influenza Surveillance Program (NISP) promotes the surveillance of Influenza and other respiratory viruses (RV), integrates Sentinel and the Non-Sentinel Networks and the Portuguese Laboratory Network for the Diagnosis of Influenza - Hospitals (PLNDI). The Influenza 2020/2021 season was very atypical with few detected Influenza virus, and an off-season increase of RV cases, during spring-summer months. During the ongoing season, 2021/2022 the amount of Influenza and other respiratory virus cases detected has increased. This work aims to report the influenza and RV detection during the SARS-CoV-2 pandemic period in the 2021-2022 season.

Method

Weekly, respiratory samples collected by the sentinel network belonging to the National Influenza Surveillance Program were sent to the National Reference Laboratory for the Influenza Virus and Other Respiratory Virus (NRL) to be analyzed. All samples were tested for Influenza A and B, including sub-typing, SARS-CoV-2, and RV (ADV, EV, HBOV, HCOV; HMPV, HRV, PIV, RSV). All diagnostic assays were performed by RT-PCR methodology. Regarding the Non-Sentinel surveillance, data on Influenza, other respiratory viruses and co-infections were reported weekly by 21 hospital laboratories from the PLNDI.

Result

Between week 40-16/2022, from the sentinel network, were analyzed at the NRL 530 cases of SARI/ILI, in which, 29 Influenza virus were detected: 27 A(H3) and 1 A(H1)pdm09.Were identified 104 SARS-CoV-2 virus and 255 RV. Co-infections were detected in 18 cases, one of these by Influenza virus and SARS-CoV-2. In the PLNDI, a total of 106464 cases of respiratory infections were reported, in which 6424 were positive for Influenza virus. Among the positive samples, 6259 were typed as Influenza A [4977 A not subtyped, 1245 subtype A(H3), and 37 subtype A(H1)pdm09], 84 of type B and 81 of undetermined type. RV were detected in 5081 cases. The increase of Influenza virus started to be reported since week 8/2022. From week 2/2022, co-infections by SARS-CoV-2 and Influenza started to be reported, 159 cases were detected since then. Genetic characterizations of SARS-CoV-2 and Influenza virus detected in co-infections are being performed.

Conclusion

Influenza virus epidemic started later than usual in this season. We also noticed a higher number of positive cases for Influenza and RV that could be related with over testing. Co-infections by SARS-CoV-2 and Influenza represents a new concern regarding surveillance. In this sense, it is important to continue monitoring the circulation of the respiratory virus, even during the off-season period to better understand these new circulation dynamics of all respiratory viruses.

Sibongile Walaza - AOXI0392

Risk factors for COVID-19 associated hospitalisation and mortality in a setting with high HIV prevalence, April 2020-January 2021: data from sentinel surveillance

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Background

Data on risk factors for COVID-19 associated hospitalisation and mortality in settings with high HIV prevalence are limited.

Method

Using active syndromic surveillance for influenza-like illness (ILI) and severe respiratory illness (SRI), we describe clinical and epidemiological characteristics of laboratory-confirmed SARS-CoV-2 cases presenting with ILI or suspected COVID-19, and hospitalised with SRI or physician-diagnosed COVID-19, and identify factors associated with (i) COVID-19 hospitalisation by comparing the characteristics of SARS-CoV-2-positive SRI cases (cases) to those of SARS-CoV-2-positive ILI cases (comparison group); and (ii) in-hospital mortality among SARS-CoV-2-positive patients with SRI at sentinel sites in public sector facilities in South Africa. HIV testing and CD4 counts were conducted as part of clinical management.

Result

During 1 April 2020 to 31 January 2022, SARS-CoV-2 was detected in 24.5% (643/2627) of outpatient and 34.0% (2217/6514) of inpatient cases. HIV prevalence was 20.0% (125/626) and 26.4% (541/2046) among SARS-CoV-2 positive outpatient and inpatient cases, respectively.

Factors associated with increased risk of COVID-19 -associated hospitalisation included: older age (45-64 years [adjusted odds ratio (aOR) 5.8 , 95% confidence interval (CI) 3.6-9.3] and ≥65 years [aOR 21.4, 95% CI 11.6-39.4] compared to 15-24 years); black race (aOR 2.8, 95% CI 1.9-4.2); obesity (aOR 2.3, 95% CI 1.4-3.9); asthma (aOR 4.0, 95% CI 1.5-10.3); diabetes mellitus (aOR 4.6, 95% CI 2.7-8.0); HIV with CD4 <200/mm3 (aOR 5.1, 95% CI 2.5-10.5) compared to HIV-uninfected; and history of tuberculosis or current TB (aOR 10.0, 95% CI 2.2-45.4).

Of the 2148 SARS-CoV-2 patients with in-hospital outcome data, 373 (17.4%) died. Factors associated with SARS-CoV-2 in-hospital mortality included older age (45-64 years [aOR 2.9, 95% CI 1.8-4.5] and ≥65 years [aOR 5.6, 95% CI 3.5-9.0]) compared to 25-44 years, admission for <3 days (aOR 1.6, 95% CI 1.2-2.3) compared to 3-7 days, and HIV with CD4<200/mm3 (aOR 2.3, 95% CI 1.4-4.0) compared to HIV-uninfected. Compared to Delta

variant, infection with Omicron variant was less likely to be associated with in-hospital mortality (aOR 0.3, 95% CI 0.1-0.7).

Conclusion

Active syndromic surveillance combining clinical, laboratory and genomic data is important for understanding setting-specific risk factors associated with SARS-CoV-2 disease severity and mortality to prioritize COVID-19 vaccine distribution. The association of severe disease with older age and independently with HIV with CD4<200/mm3 highlights the importance of increasing access to antiretroviral therapy and to prioritise such groups for COVID-19 vaccines and boosters.

Joseph Servadio - AOXI0402

Evaluating cyclic and seasonal patterns of influenza in Vietnam

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Background

Despite annual seasonality of influenza being well established in temperate world regions, such as North America and Europe, the existence of annual or non-annual cycles or seasons of influenza is less well established in tropical world regions, including southeast Asia. Previous works have provided evidence both for and against the existence of regular seasons, but few have prioritized establishing seasonality as the primary study aim. This study aims to explicitly identify annual or non-annual cycles of influenza in Vietnam.

Method

We developed a mathematical model based on the SIRS framework to identify cycles in influenza. The model incorporates periods of increased transmission through parameters φ_i that represent timings of peak transmission, τ_i representing the distance between adjacent φ_i, and δ for the duration of increased transmission. The standard deviation of the τ_i represent the strength of evidence for the existence of cycles: a low standard deviation is stronger evidence of regular cycles, and higher standard deviation is weak evidence of cycles. We fit the model to data collected at fifteen hospitals participating in sentinel surveillance in northern, central, and southern Vietnam, fitting data for (sub)types A/H1, A/H3, and B, as well as combined positive influenza (ILI+). For comparison, we also fit the model to ILI or ILI+ data from the Netherlands, Denmark, and two regions within the United States. Model fitting was done using a Bayesian framework, using diffuse priors and Markov Chain Monte Carlo simulations to produce posterior distributions for each parameter.

Result

Estimated standard deviations of the τ_i parameters were substantially higher in the models for ILI+ in the three regions of Vietnam (104-108 days) compared to the four temperate locations (50-64 days). This was also seen in model fitting for individual (sub)types. During periods of increased transmission, the relative magnitude of increase was substantially larger for model fits in Vietnam (30-34%) compared to temperate regions (6-12%). The duration of increased transmission was typically higher in temperate regions (114-158 days) compared to Vietnam (70-85 days).

Conclusion

The results of this study indicate that cyclic patterns of influenza in Vietnam are notably weaker compared to regions representing North America and Europe. Model fits were weaker for the data from Vietnam compared to temperate regions, particularly the fits for influenza type B. This suggests that the dynamics of influenza in Vietnam likely include contributing factors outside those typically incorporated in modeling.

Anne Mosnier - AOXI0364

What about concomitance of seasonal influenza and Covid-19 vaccination campaigns? The French case

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Background

In October 2021, the seasonal influenza vaccination campaign was launched in France in the context of concomitance with the Covid-19 booster campaign. Concerning the influenza campaign, some changes were proposed by Health Authorities, e.g. extension of the vaccinators' list, first weeks of campaign dedicated to the population targeted by vaccination recommendations, possible co-administration of the two vaccines. A high dose influenza vaccine was also newly available for use in the over 65 years of age.

The COVIGIE group, a consortium of non-governmental primary care organizations, created during the first wave of Covid-19, decided to survey its primary health care workers (PHCW) network about their experience and perception of the vaccination campaigns' concomitance. The COVIGIE project is based on a specific platform allowing PHCW in particular to participate in specific surveys.

Method

Based on the COVIGIE network, we performed an internet survey about the 2021-2022 influenza vaccination campaign, in the specific context of Covid-19 circulation and booster vaccination period. The survey (23 questions) was proposed online to the PHCW between January and March 2022, with several reminder emails. Participation was anonymous. Analyses were conducted with Stata 11.2.

Result

A total of 1 101 non-hospital vaccinators have clicked on the survey link, of which 795 participants completed all the questions. Participants were mainly GPs (49%) and pharmacists (41%), women (61%), aged between 40 and 60 (53%), themselves vaccinated against influenza (87%) and Covid-19 (97%). More than half of them (55%) felt having vaccinated less patients against influenza than previous campaign. Covid-19 crisis seemed to them having variably impacted patients' behaviour against influenza vaccination. Despite the possibility of co-administration, only 41% of the PHCW favoured it. Other Health Authorities recommendations were mainly positively received.

As regards the high dose vaccine availability, 27% of the PHCW have used it during this first winter. Main reasons for not using it were, respectively for GPs/pharmacists: no patients coming with (67%), GPs ignorance of this vaccine (36%)/didn't order it (72%), no prescription or recommendation by GPs (67%). However, when vaccinators proposed this vaccine to their patients, 88% of them agreed to be vaccinated with it.

Conclusion

PHCW seem to have implemented most of the new measures. Two points may need more PHCW targeted information to be better implemented: the possible co-administration of influenza and Covid-19 vaccine and the possible access to high dose influenza vaccine for people over 65 years old.

Joaquin Mould - AOXI0397

THE U.S. INFLUENZA IMMUNIZATION RATE REDUCTION AND ITS IMPACT ON HOSPITAL SYSTEM RESOURCES. AN INFLUENZA AND COVID-19 CO-CIRCULATION SCENARIO

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Background

Influenza (flu) immunization is a critical public health tool to protect against flu, avoid the risk of co-infection from flu and COVID-19, and minimize the burden of flu on the healthcare system. During the 20/21 flu season, U.S. healthcare providers achieved an overall flu immunization rate of approximately 52%, equating to an estimated 172 million people being vaccinated against flu, an all-time high. In season 21/22, the overall flu immunization rate dropped to 45%, which is below pre-pandemic levels. This study evaluated the impact of the reduced flu immunization rate in the U.S. on hospital system resources under a flu and COVID-19 co-circulation scenario.

Method

The impact of the reduced flu immunization rate on hospital resources was estimated using a dynamic age-stratified transmission model. Two U.S. flu seasons (2011-2012 for low incidence and 2017-2018 for high incidence) were used in the analysis to simulate the variation of flu epidemic. Outcome measures include the number of acute hospital beds and Intensive Care Unit (ICU) hospital beds. The COVID-19 variants (Alpha, Delta and Omicron) were used to create an average scenario of the impact on acute beds and ICU beds utilization from COVID-19. The flu vaccine effectiveness (VE) rate was taken from CDC reports to estimate an average VE for all ages for the last 10 seasons (42%). Vaccination rates by age group were estimated using CDC reports and this model assumed immunization with standard-dose, egg-based, quadrivalent flu vaccines for all ages. Total number of acute hospital and ICU hospital beds was assumed in the U.S. at 1,000,000 and 100,000, respectively; with a regular occupancy rate of 70% related to other diseases.

Result

Staying at the current U.S. flu immunization rate (45%) over a high flu incidence season, the number of acute hospital beds and ICU hospital beds used for influenza are estimated at 183,778 and 27,891, respectively; and for a low flu incidence season those will be estimated at 57,521 and 8,850, respectively. These results, within a COVID-19 pandemic setting, will generate significant pressure on the US hospital system (especially within the high flu incidence season) and would saturate the number of ICU hospital beds in high or low incidence seasons. Only increasing the flu immunization rate up to 70% or higher may prevent any saturation of acute hospital or ICU hospital beds regardless on the incidence of the flu season.

Conclusion

The U.S. analyses shows the need to increase the current U.S. flu immunization rate, within a co-circulation scenario, to improve health outcomes and avoid saturation of hospital system resources, especially those associated to ICU hospital beds.

Susan Detmer - AOXI0453

Influenza zoonosis at the human-pig interface in Canada

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Background

While most influenza A viruses in swine (IAV-S) never result in transmission to another species, there are several IAV-S genetic clusters that have been identified as having higher potential for zoonosis and reverse-zoonosis between pigs and people. The IAV-S strains found in humans are called variant influenzas and are denoted by adding a "v" after the subtype (e.g., H1N2v). While there were only 79 positive detections of IAV during the 2020-2021 influenza season, there were four detections of variant influenza (IAV-S detected in humans). There were only two previous detections of variant influenza in Canada prior to this.

Method

All cases of variant influenza were discovered through routine SARS-CoV-2 PCR testing and follow-up IAV testing per provincial procedures.

Result

All four cases had influenza-like illness (ILI) and negative SARS-CoV-2 PCR testing. All four cases also recovered without serious complications. These viruses were easily traced back to pig production by public health officials and genetically matched viruses in swine surveillance data, further supporting the findings by health officials. The genetically distinct viruses were H1N2v from the α3a subclade, H1N2v from the α3 subclade, H1N1v from the pdmH1N1 clade, and H3N2v from the Canadian H3N2 IVE2 group. The first case in a juvenile in Alberta in October 2020 had no direct pig contact but a relative living in the household worked on the farm with a genetic match to the virus isolated from that person. While ILI symptoms were reported one of the Manitoba farms in the past and previous nasal and oral swab samples yielded negative results. The second case was another H1N2v but from the α3 subclade, similar to a case detected in Minnesota in 2016. The third case was a pandemicH1N12009 (pdmH1N1) that was still circulating on a farm after human-to-pig transmission of the virus circa 2018. The pdmH1N1 viruses are of particular interest as human-to-pig transmission is detected by the Detmer Lab on an annual basis as new virus introductions to pig farms with viruses matching the strains circulating in people. The H3N2 virus detected was from a uniquely Canadian genotype IVE2 found in Western Canada. The human-like 2010.1 H3 annually detected in juveniles at pig exhibitions in the Midwestern USA is not currently endemic in Canada.

Conclusion

While there was no evidence of any community or sustained human-to-human spread of these viruses, which is consistent with previous cases of variant influenza, these cases demonstrate that interspecies transmission of IAV-S does occur a limited level and these viruses need continued monitoring through animal and human surveillance practices.

Lorin Adams - AOXI0469

Two zoonotic infections with A(H1N1)v in Denmark highlight the need for development of new candidate vaccine viruses for pandemic preparedness.

***Rodney Daniels*[1], *Ruth Harvey*[1], *Lorin Adams*[1], *Burcu Ermetal*[1], *John McCauley*[1]**

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Background

Over the course of 2021 the National Influenza Centre in Denmark notified the World Health Organization (WHO) of two human cases of infection with swine influenza A(H1N1)v viruses. The viruses, designated A/Denmark/1/2021 and A/Denmark/36/2021 (not recovered), were reported as swine clade 1A.3.3.2 (A(H1N1)pdm09-like) based on whole genome sequencing.

Method

The antigenicity of A/Denmark/1/2021, and a matched swine A/Denmark/36/2021-like virus (A/swine/Denmark/S19922-5/2021) was assessed using haemagglutination inhibition (HI) assays. The two viruses were tested against a panel of ferret antisera raised against all five A(H1N1)pdm09 vaccine viruses recommended to date. A ferret antiserum raised against A/Denmark/1/2021 was tested against the A(H1N1)pdm09 virus panel and a panel of swine origin H1N1 viruses.

The level of antibody response to these viruses that exists in the general population was assessed using panels of human sera from blood samples taken during 2020 and 2021; The potential of recent seasonal influenza vaccines to protect against these two viruses was assessed using panels of pre- and post-vaccination sera from adults receiving the northern hemisphere (NH) 20-21 and NH 21-22 vaccines with representative seasonal H1N1pdm09 viruses used as controls.

Result

Both of the A(H1N1)v viruses possess a number of haemagglutinin amino acid substitutions that render them unrecognisable by antisera raised in ferrets against all five A(H1N1)pdm09 vaccine viruses recommended to date. The same was also true for anti-A(H1N1)pdm09 antibodies, induced by vaccination and/or infection, present in panels of human sera representing the general population in Wales and the pre-/post-vaccination panels tested.

Conclusion

The implications of these observations, together with the diversity of clade 1A.3.3.2 virus evolution in swine, are discussed in relation to the need for development of a candidate vaccine virus to target European-lineage swine clade 1A.3.3.2 viruses for potential pandemic preparedness purposes.

Punam Mangtani - AOXI0488

Cross-sectional sero-epidemiologic and virologic study of avian influenza A(H5N1) and A(H9N2) virus exposures in live bird market workers in Dhaka, Bangladesh

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Background

Avian influenza A virus (AIV) subtypes H5N1 and H9N2 are enzootic in poultry in Bangladesh and poultry are frequently purchased at live bird markets (LBMs). We assessed virologic and serologic evidence of exposures to H5N1 and H9N2 viruses among LBM workers.

Method

A cross-sectional study was conducted from January to May 2017 among 702 randomly sampled workers at 42 LBMs (selected probability proportional to LBM size) in Dhaka, Bangladesh. Information was collected about workers' activities at LBMs. Nasal and throat swabs collected from workers and air samples (using cyclonic and impactor air samplers) from LBMs were tested for influenza A viruses by rRT-PCR. Sera were collected from 695 workers and follow-up sera were collected several weeks later from 89 workers who had at least one respiratory sample positive for influenza A. Sera were tested by microneutralization assay with serial 2-fold dilutions starting at 1:10 to detect neutralizing antibodies to clade 2.3.2.1a H5N1 and G1 lineage H9N2 viruses circulating in poultry in Bangladesh in 2017. A seropositive result was defined as a neutralizing antibody titer ≥1:40.

Result

Of 702 workers, slaughtering and defeathering work was reported by 93.3% and 84.3%, respectively. 14.1% of workers had ≥1 respiratory sample that tested influenza A positive (H1 and H3 negative): H9: 3.9%, H5: 0.3%; both H5 and H9: 0.4%, and 9.5% were non-subtypeable. 59.5% of LBMs had air samples positive for influenza A, 31% positive for both H5 and H9, 23.8% for H9, one for H5, and one was non-subtypeable. The winter season (Jan-March) (p=0.032) and LBMs selling ducks (p=0.044) were associated with influenza A positive respiratory specimens in workers.

No sera were seropositive for H5N1 or H9N2; 27 workers (3.9%, 95% CI 2.7-5.6%) had an H5N1 neutralizing antibody titer of 1:10. No exposures were associated with an H5N1 neutralizing antibody titer of 1:10 except for working in a stall where ducks or geese were sold (aOR=3.77, 95% CI 1.09-12.10). 4.5% (4/89) of workers with follow-up sera had an H5N1 neutralizing antibody titer of 1:10; of these 4 workers, 3 had the same titer and one had no detectable antibodies in their initial serum specimens.

Conclusion

LBM workers had extensive exposures to H5N1 and H9N2 viruses based on work activities, testing of upper respiratory tract specimens, and air sampling. However, no workers had serologic evidence of infection with H5N1 or H9N2 viruses circulating among poultry at the time. Ongoing surveillance and monitoring of AIVs in LBMs and poultry workers are needed to assess zoonotic risk.

Bitrus Inuwa - AOXI0501

Emergence of Highly Pathogenic H5N1/H9N2 Reassortant Influenza Virus in Poultry in Hotspot Nigeria

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Background

Nigerian poultry faces current challenges amidst the COVID-19 pandemic and global food insecurity. In the last two decades, there have been multiple intercontinental epidemic waves of the highly pathogenic avian influenza (HPAI) viruses of the H5 subtype, descendent of the H5N1 A/goose/Guangdong/1/1996 (Gs/GD) virus, which have dramatically impacted on the poultry production in Nigeria. In January 2021, a new HPAI H5Nx incursion was reported to have caused multiple outbreaks across the country. These new HPAIVs introductions in a territory where the H9N2 subtype is also entrenched in the poultry population are a matter of great concern. Herein, we report the results obtained after characterizing the pathogen which had caused high mortality in a commercial mixed-species poultry farm in Toro, Bauchi State Nigeria in 2021.

Method

Total RNA was extracted from tracheal sample and analysed for avian influenza viruses (H5, H7, H9, and Nx) subtypes by real-time RT-PCR using Qiagen QuantiTect® Multiplex RT-PCR Kit and virus isolation was carried out in embryonated chicken eggs. Whole genome data were generated by an Illumina Miseq platform. Sequences were aligned using MAFFT v. 7 and Maximum Likelihood (ML) phylogenetic trees were obtained by using IQtree v1.6.6.

Result

Influenza A virus of the H5N2 subtype was identified in the mixed-species poultry farm by molecular investigations and virus isolation. The sample tested negative for IBV and NDV. Phylogenetic analysis of the HA gene confirmed the virus belongs to clade 2.3.4.4b and is highly related to the HPAI H5Nx viruses which have been circulating in poultry in Nigeria since early 2021. The NA (N2) and M genes showed the highest similarity to the respective genes of the H9N2 viruses (G1 lineage) identified in Nigeria in 2019 while the PB2, PB1, PA, NP, and NS gene segments were clustering with the gene sequences of the H5N1 subtype previously identified in Nigeria.

Conclusion

Based on these results, it can be suggested that the H5N2 virus is a new reassortant strain containing two genes of H9N2 origin (NA and M segments), with the remaining six genes of H5N1 origin. Further pathogenicity and transmission studies in poultry and mammalian models will be essential to evaluate the potential animal and public health threat posed by this novel H5N1/H9N2 reassortant virus.

Keywords: Highly Pathogenic Avian Influenza, H5N1/H9N2 Reassortment, H5N2 virus, Poultry, Nigeria

Thomas Fabrizio - AOXI0515

Pandemic Risk Assessment of Avian Influenza A(H5Nx) Clade 2.3.4.4b viruses Using the WHO TIPRA

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Background

To better assess pandemic risk of animal derived influenza viruses, the World Health Organization (WHO) developed the Tool for Pandemic Risk Assessment (TIPRA). TIPRA was designed to assess pandemic risk and identify knowledge gaps of assessed viruses to inform and direct government and public health agencies to better prepare for pandemic influenza viruses.

The H5Nx clade 2.3.4.4b viruses were most recently assessed by TIPRA due to an outbreak of human infections of H5N8 clade 2.3.4.4b in the Russian Federation in February of 2021. At the time there were a total of 8 human infections reported to WHO. Since the TIPRA assessment, there have been additional human infections reported in China, Nigeria, UK, and USA. Additionally, the H5Nx clade 2.3.4.4b viruses have become more geographically widespread in birds.

Method

The primary questions addressed by TIPRA are what is the likelihood of sustained human-to-human transmission of the assessed virus and what would be the impact on the human population if the virus were to transmit from human-to-human? A literature review was conducted to provide participating technical experts with a comprehensive overview. The technical experts then scored the virus for 10 different risk elements covering the virus properties (4 elements), attributes in the human population (3 elements), and virus ecology and epidemiology (2 elements). Following the virus scoring, the technical experts discussed and justified scores for each element. The scores were then used in a multi-attribute additive model with rank order centroid weights based on the elements' importance to either the likelihood or impact of sustained human-to-human transmission to calculate the overall risk score.

Result

The assessed likelihood of Influenza A(H5Nx) clade 2.3.4.4b viruses to develop sustained human-to-human transmission resulted in a moderate score of 4.53 while the impact if human-to-human transmission were to occur had a lower moderate score of 4.18. Three risk elements were scored as lower risk while 3 additional elements were scored as lower risk but had upper ranges into moderate risk (Figure 1). Only 1 element was scored in the moderate risk range while 3 risk elements were scored in the higher risk range (Figure 1).

Conclusion

Influenza A(H5Nx) clade 2.3.4.4b viruses were considered to have low risk of becoming transmissible within the human population and have low potential impact should they develop this capacity. TIPRA provides a scientific approach to systematically assess the likelihood and impact of sustained human-to-human transmission of zoonotic influenza viruses.

Antonia Ho - AOXI0464

A Novel Syndromic Surveillance of Influenza and SARS-CoV-2 Infections among Patients with Hospitalised Severe Acute Respiratory Illness in Glasgow, Scotland, November 2021 to May 2022

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Background

Before SARS-CoV-2 emerged, respiratory viral surveillance largely focused on influenza viruses in adults. With relaxation of COVID-19 mitigation measures, influenza and SARS-CoV-2 are anticipated to co-circulate in years to come. We report the preliminary findings of a novel syndromic surveillance aimed to characterise the incidence and evolving epidemiology of influenza- and SARS-CoV-2-associated severe acute respiratory illness (SARI) in the 2021/2022 winter season.

Method

Adults aged >16 years admitted to the Queen Elizabeth University Hospital, Glasgow, with an acute respiratory presentation clinically suspected to be due to influenza or SARS-CoV-2 were recruited. Patient demographics, presenting symptoms, COVID-19 and influenza vaccination history, patient journey (including critical care admission), and outcome were recorded using the SARI Turas Clinical Assessment tool. All patients underwent point-of-care multiplex respiratory viral PCR (cobas® Liat® SARS-CoV-2 & Influenza A/B). A dashboard (Microsoft Power BI) illustrating patient demographics and weekly influenza A/B and SARS-CoV-2 PCR positivity was available to Public Health Scotland (PHS) and hospital clinicians in real time. Routine healthcare data linkage will provide supplemental

Result

Between 23 November 2021 and 22 May 2022, 1,263 patients with 1,294 hospitalised SARI episodes were recruited. Median age of SARI cases was 71.7 years (IQR 59.3-81.7) and 55.7% (n=704) were female. The proportion of SARI cases that had received 3 doses of COVID-19 vaccines increased from 56.5% in Dec 2021 to 74.7% in May 2022. Weekly number of SARI admissions ranged from 22 (29 Nov-5 Dec 2021) to 72 (20-26 Dec 2021). Overall, 289 (22.3%), 40 (3.1%) and 1 (0.1%) SARI episodes were PCR positive for SARS-CoV-2, influenza A and influenza B, respectively. Weekly proportion of cases with a positive SARS-CoV-2 PCR ranged from 4.4% (2/44; 6-12 Dec 2021) to 49.1% (27/55; 27 Dec 2021-2 Jan 2022). Influenza A activity peaked at 13.6% (9/66; 14-20 March 2022). Two patients had influenza-SARS-CoV-2 co-infection. Although cough and breathlessness remain the most commonly reported symptoms, fatigue, headache, myalgia, diarrhoea, loss of smell and loss of taste were predictive of SARS-CoV-2 PCR positivity among SARI cases.

Conclusion

Our novel syndromic surveillance provided near real-time data on hospitalised SARI to hospital clinicians and PHS. It highlighted a significant contribution of SARS-CoV-2 to hospitalised SARI in the 2021/22 season, and differing clinical presentation to non-COVID-19 SARI. Linkage to patient journey and outcome data are ongoing.

Dong Kyu Kim - AOXI0471

Burden of hospitalization due to laboratory-confirmed influenza in adults aged 50-64 years, 2010/11 to 2016/17

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Background

We describe the epidemiology of laboratory-confirmed influenza resulting in hospitalization among 50-64 year-old residents of Toronto/Peel Region, Canada (pop'n 4.5M) during the 2010/11 to 2016/17 influenza seasons.

Method

Prospective population-based surveillance for hospitalization associated with lab-confirmed influenza was conducted from 9/2010-8/2017. Death within 30 days of diagnosis was considered attributable to influenza. Population data were from Statistics Canada. Conditions increasing the risk of influenza complications were as defined by Canada's National Advisory Committee on Immunization; age-specific prevalence of medical conditions was estimated using data from ICES (formerly the Institute of Clinical and Evaluative Sciences).

Result

Over 7 seasons, 1,228 patients aged 50-64 years were hospitalized. Average annual rates of influenza-associated hospitalization and mortality were 22.4 and 0.9 per 100,000, respectively; the ICU admission rate was 3.9/100,000. The hospitalization rate was 15.6, 20.9 and 33.2/100,000 in 50-54, 55-59, and 60-64 year-olds, respectively. 40% of infections were A(H3N2), 30% A(H1N1), 22% influenza B.

Of 1,125 patients with detailed clinical data, 33% had received current season influenza vaccine and 27% both current and previous season vaccines. Overall, 930 (83%) had ≥1 underlying condition increasing the risk of influenza complications; this compares to 40% of 50-64 year-olds with such conditions in the overall population. The most common underlying medical conditions were chronic lung disease (38%), diabetes mellitus (31%),and cardiac disease (27%); 25% of patients were immunocompromised. Rates of influenza-associated hospitalization and mortality in persons with different underlying condition are shown in the table. The case fatality rate in hospitalized patients was 4.4% and median length of stay was 4 days (IQR 2-8). Overall, 128 (11%) had at least one in-hospital complication: most commonly cardiac (e.g. MI; 8%), secondary bacterial/fungal infections (8%), and renal failure (3%).

Conclusion

We describe the burden of hospitalization due to lab-confirmed influenza in adults aged 50-64 years, and quantify the increased risk of hospitalization and death due to influenza conferred by common underlying illnesses in this age group.

Vennila Gopal - AOXI0490

Possible viral interference leading to protection from subsequent respiratory viral infections: results of an observational study at a Singapore teaching hospital.

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Background

The global disappearance of influenza during the COVID-19 pandemic despite resurgences in other respiratory viruses has not been completely explained. A previous Singapore analysis showed that prior influenza or adenovirus infection conferred cross-protection against subsequent febrile respiratory incidents compared with other respiratory viruses. The reasons for this are unclear and this has not been well defined in other populations.

Method

We conducted a retrospective review of the hospital epidemiology database of clinical laboratory reports in our 1200-bed teaching hospital. We did a preliminary analysis of patients who were positive by respiratory immunofluorescence assay (IF) from April 2017 to June 2018. Testing is based on clinical grounds for symptomatic patients using primarily the D3 Ultra™ DFA Respiratory Virus Screening and Identification Kit (Diagnostic Hybrids, Inc., USA). We compared the frequency and clinical characteristics of patients infected with the four main viruses identified by IF as well as prior viral infections and subsequent respiratory viral infections detected by IF and other PCR based assays. Data were compiled and analysed in Microsoft EXCEL and using SPSS.

Result

A total of 589 patients were IF positive during the study period. The majority were children, with a slight male predominance, 332 (56.4%) vs 257 (43.6%). Comorbidities were present in 176 (29.9%) patients predominantly asthma, 60 (10.2%) and other chronic respiratory diseases, 52 (8.8%). The most common virus identified was RSV, 299 (50.8%), Influenza, 194 (32.9%), Parainfluenza, 62 (10.5%) and Adenovirus, with 34 (5.8%) cases during the current study period. Fever occurred in 521 (88.5%) cases; respiratory symptoms were also common including cough, 533 (90.5%), rhinorrhoea, 460 (78.1%) or sore throat, 190 (32.3%). Chest x-rays were abnormal in 112 (19%) patients but only 8 (1.4%) needed ICU care. Thirty-four patients had subsequent respiratory viral infections identified up to Jan 2022. These included RSV, (22), Influenza, (14), EV/RV, (11), Parainfluenza, (8) and SARS CoV2 (7) occuring a median of 336 (11-1731) days after the first infection. Patients infected with adenovirus (6.2%), RSV (8.6%) and influenza (4.8%) virus were less likely to be infected with another respiratory virus in the subsequent five-year period than patients infected with parainfluenza virus (17%, OR: 0.41, 95% CI 0.2-0.9, p=0.03).

Conclusion

It is possible that prior infection with certain viruses protects individuals against subsequent respiratory viral infections. Larger prospective studies which incorporate host immune responses are needed to better understand if viral interference can explain the epidemiology of various respiratory pathogens over time.

Alyona Zheltukhina - AOXI0502

Antigenic characterization of the deletion variants of influenza viruses B of Victoria lineage isolated in Russia in the last 5 years

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Background

Up from 2017, influenza B (Victoria lineage) viruses holding double or triple deletions in the HA molecule became widespread. The first deletion variants in Russia were registered in 2018 and later on, they completely ousted Brisbane-like strains, which circulated earlier during ten years. During the last 5 years, the circulation of different variants was completely substituted by a domination of the strains holding the triple deletion in HA.

Method

Virus isolation, identification, antigenic analysis in HI-test using a set of rat polyclonal- and ferret post-infection antisera, antigenic cartography

Result

In the season 2018-2019 we observed a mismatch of the vaccine strain (B/Brisbane/60/2008) and the actual strains - a circulation of deletion variants became already evident. In 2019-2020, influenza B/Washington/02/2019 started to spread worldwide. The same picture was evident also in Russia. However in that season the strain B/Colorado/07/2017 was admitted as a component B of influenza vaccines and it was a double deletion variant. Meanwhile the strain B/Washington had a triple deletion that is why we could observe a partial mismatch of the vaccine and epidemic strains. Interestingly, some triple deletion variants were registered earlier (B/Hong Kong/269/2017 and B/Cote d'Ivoire/1662/2018) but later they disappeared.

In the season 2020-2021, on the background of the SARS-CoV-2 pandemic influenza viruses in Russia practically were not registered. However we revealed two cases of influenza B and isolated the appropriate strains - both were B/Washington/02/2019-like (which was the vaccine strain in that season). However, both isolates were closer in HI-test to the reference strain B/Rhode Island/01/2019. The characteristic feature of this strain is the substitution N150K in HA and particularly these deletion variants are ubiquitous worldwide in the present time.

Nowadays we observe the division of the influenza B vic into several genetic groups and the prevailing group became B/Austria/1359417/2021-like which is actually included in the composition of influenza vaccines and is registered worldwide.

Conclusion

The growing heterogeneity of influenza B viruses of the Victoria lineage requires an improvement of the serological methods for more precise analysis of the variants selected as the candidates for the vaccine composition.

Alyona Zheltukhina - AOXI0503

Application of the murine monoclonal antibodies in the antigenic analysis of influenza viruses B, Victoria lineage

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Background

High heterogeneity of influenza B vic viruses that became evident last years, significantly complicated the choice of candidates of this component into seasonal vaccines. The traditional antigenic analysis with the application of polyclonal antisera can give only general assessment of the match/mismatch to the strains for which antisera were generated, so the need for more sensitive and refined techniques in the antigenic analysis is evident. One of such methods is the antigenic analysis with the application of monoclonal antibodies (MCA) directed to a specific epitope of HA-molecule. It can indicate which particular antigenic sites could be responsible for the changes of antigenic properties.

Method

Influenza virus isolation, HI-test with the application of polyclonal rat and post-infectious ferret antisera, HI-test with the murine MCA obtained using the hybridoma technology.

Result

We obtained 23 escape-mutants to the different epitopes of the HA. All MCA were generated against the reference strain B/Brisbane/46/2015. These MCAs were used for the antigenic analysis of some influenza B strains isolated in Russia during past 10 years and the reference strains, which had triple deletion in the loop 160 and representing four different genetic groups. Some MCAs were able to differ the viruses of the genetic group V1A of the deletion variants attributed to the other groups. Two MCAs (10B6 and 10D9) were able to reveal conservative sites in the HA, the other three (7G9, 10F1 and 7C8) did not differ in their results. They probably were directed to the 120-loop which is the most conservative HA antigenic site. On the other hand, MCA 8A8 revealed the substitution T121I and poorly interacted with the earlier strains of Victoria lineage, while modern reference strains B/Cote d'Ivoire/948/2020 and B/Paris/9878/2020 demonstrate a good interaction with this MCA.

The obtained data showed the divergence of B vic into several groups which is consistent with the data of antigenic analysis. Some MCAs allow to clearly differing the representatives of the clade V1A.3a.2. B/Austria/1359417/2021-like strains poorly interacted to the MCAs 10B6 and 7H8 (directed to the sites in the α-helix area 190) comparing to the representatives of the other clades including the strains of previous seasons.

Conclusion

We obtained the murine hybridoma MCAs to the different B vic influenza strains and studied their affinity to the specific epitopes. Application of such MCAs allows studying the evolutionary variability of new appearing strains according the specific antigenic sites. It may improve the process of strain selection for seasonal influenza vaccines.

Angie Lackenby - AOXI0512

Summary Analysis of the 2021 WHO GISRS External Quality Assessment Programme for Detection of Severe Acute Respiratory Syndrome Coronavirus 2 by reverse transcription polymerase chain reaction

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Background

WHO is leveraging the Global Influenza Surveillance and Response System (GISRS) network of over 150 national public health laboratories for surveillance of SARS-CoV-2. The WHO GISRS External Quality Assessment Project incorporated a panel for SARS-CoV-2 detection by reverse transcription polymerase chain reaction (RT-PCR) in 2020, to assess testing proficiency of nationally recognized SARS-CoV-2 molecular testing laboratories.

Method

The panel comprised five samples; three SARS-CoV-2 varying viral concentrations including a variant of concern (VOC); one human coronavirus OC43 (hCoV) and one SARS-CoV-2 negative (influenza A(H1N1)pdm09 virus). Panel samples were heat inactivated and blind passaged for sterility, followed by vacuum-drying for dispatch. Of 224 participating laboratories, 218 (97.3%) received the EQAP samples, 211 (96.8%) returned results, and 181 (83.0%) reported results before the closing date for analysis. Reporting of VOC or other hCoV was optional.

Result

Overall, 149/181 participants (82.3%) returned correct results for all 5 samples; 20/181 (11.0%) returned one incorrect result; 12 (6.6%) returned more than one incorrect result. Thirty-one false negative results were reported for SARS-CoV-2 positive samples. Some participants reported correct PCR results but incorrect final interpretation caused by transcription errors. Sixty participants (33.1%) returned influenza results for the SARS-CoV-2 negative sample (unscored) with 98% (59/60) reporting a correct result.

To detect emerging SARS-CoV-2 variants, 97/176 (55.1%) of participants screened for mutations of concern (N501Y; E484K and L452R) by molecular methods including real-time PCR and sequencing.

Numerous molecular methods were reportedly used by the participants. Comparable numbers of participants achieved 100% score using in-house 83/97 (85.6%) versus those using commercial methods 105/129 (81.4%). One hundred participants (55.2%) employed more than one detection method and a greater proportion achieved a 100% score (86.0%) than those using only one method (77.8%).

The proportion of participants with 100% correct results was lower in 2021 [149/181 (82.3%)] compared to 2020 [203/214 (94.9%)].

Conclusion

The detection SARS-CoV-2 is critical in the response to the COVID-19 pandemic. Two factors are likely to have contributed to the differences in proportions of correct results in 2020 and 2021; viral concentrations were 1-2 logs lower in panel 2021 than in panel 2020 and RNA extraction was required in 2021, while samples were sent as RNA in 2020.

Results show good laboratory capacities for detection of SARS-CoV-2 by RT-PCR. Future influenza EQAP will focus on laboratory proficiency to detect SARS-CoV-2 and characterize contemporary variant viruses.

Angie Lackenby - AOXI0513

Summary Analysis of the 2021 WHO GISRS External Quality Assessment Programme for Detection of Influenza viruses by Reverse Transcription Polymerase Chain Reaction

Angie Lackenby[7], Rickjason Chan[2], Arunkumar GOVINDAKARNAVAR[10], Alina GUSEINOVA[9], Belinda Herring[8], Francis Yesurajan Inbanathan[5], Juliana LEITE[1], Marie-jo Medina[4], Karen Nahapetyan[6], Dmitriy PEREYASLOV[3], Magdi SAMAAN[3], Sun Wong[2], Wenqing Zhang[3]

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Background

Influenza virus surveillance has been conducted through the WHO GIobal Influenza Surveillance and Response System (GISRS) for 70 years. Regular assurance of laboratory testing quality and capability is essential due the continuous evolution of the virus and the potential emergence of a pandemic strain. The WHO external quality assessment programme (EQAP) for the detection of influenza viruses by reverse transcription polymerase chain reaction (RT-PCR) started in 2007. We summarize here the results for panel 20 distributed in2021.

Method

The panel, shipped to 197 national influenza laboratories, consisted of 10 samples; seven influenza A viruses [A(H1N1)pdm09, A(H3N2), A(H7N9) two A(H5N6) (genetic clade 2.3.4.4) and two A(H9N2)] at differing virus titres; two influenza B viruses (Victoria lineage and Yamagata lineage) and an influenza negative (SARS-CoV-2 wild-type).

Influenza viruses (grown in Madin-Darby canine kidney cells and inactivated with Triton X-100) and SARS-CoV-2 (grown in Vero E6 and heat-inactivated) were vacuum-dried before distribution. Participants had four weeks to return results. Detection of influenza A and B viruses and subtyping of seasonal A(H1N1)pdm09 and A(H3N2) viruses were mandatory. Reporting of non-seasonal subtypes and other types was optional.

Result

Included in the analysis were 162 laboratories that reported results on time. A total of 125/162 (77.2%) participants scored 100%, with 23/162 (14.2%) participants returning one incorrect result and 14/162 (8.6%) returning more than one incorrect result. The number of participants scoring 100% for the seasonal and the non-seasonal influenza panel components (7 samples) was 150/162 (92.6%) and 131/162 (80.9%) respectively. Reported PCR protocols had no effect on overall panel performance. Eleven new laboratories participated in comparison to 2020.

Conclusion

Results show good laboratory capacities for detection of influenza viruses by RT-PCR and provides incentive for continuous improvement even during the COVID-19 pandemic. Reporting of influenza B detection was mandatory for the first time in this panel, and inclusion of SARS-CoV-2 as the influenza negative sample enabled laboratories with influenza+/-SARS-CoV-2 multiplex PCR capacity to evaluate assay performance. Future influenza EQAP will continue to focus on laboratory proficiency to detect non-seasonal influenza A viruses for pandemic preparedness, characterize influenza A subtypes, and incorporate contemporary influenza viruses.

Angie Lackenby - AOXI0514

Summary Analysis of the 2021 WHO GISRS External Quality Assessment Programme for Genotypic and Phenotypic Testing of Influenza Virus Neuraminidase Inhibitor Susceptibility

Angie Lackenby[8], Rickjason Chan[2], Arunkumar GOVINDAKARNAVAR[11], Alina GUSEINOVA[10], Belinda [9], Francis Yesurajan Inbanathan[6], Juliana LEITE[1], Marie-jo Medina[5], Karen Nahapetyan[7], Dmitriy PEREYASLOV[4], Magdi [4], Wong[3], Wenqing Zhang[4]

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Background

Neuraminidase Inhibitors (NAI) and a polymerase inhibitor (baloxavir marboxil) are marketed for use against seasonal influenza viruses. Emerging viruses that are resistant to there therapeutics could pose a threat to the treatment and control of influenza. Many Global Influenza Surveillance and Response Systems (GISRS) have laboratories implemented susceptibility testing since 2007. The WHO external quality assessment programme (EQAP) for influenza virus detection has incorporated an NAI susceptibility testing panel since 2013. Here we summarize the antiviral susceptibility results for panel 20 dispatched to participating laboratories in 2021.

Method

The panel comprised of two sets of vacuum-dried coded samples; one for phenotypic (triton X-100 inactivated) and one for genotypic testing (heat inactivated). Each set contained two A(H1N1)pdm09 viruses [NAI01G/P-2021; NAI normal inhibition (NI); baloxavir reduced inhibition (RI) (I38T)) and NAI02G/P-2021; H275H/Y oseltamivir RI, and one influenza B virus (NAI03G/P-2021; NAI normal inhibition (NI)]. Phenotypic or genotypic interpretation of each sample was assessed separately with equal weighting. Laboratories were to report the level of inhibition including highly reduced inhibition (HRI) and associated amino acid substitutions.

Result

Forty-six participating laboratories returned results within the deadline and 38/46 (82.6%) participants reported 100% correct interpretations. Overall performance varied for each virus; correct results were reported by 42/46 (91%); 44/46 (96%) and 38/42 (91%) participating laboratories for NAI01G/P-2021, NAI02G/P-2021 and NAI03G/P-2021 respectively.

Performance in the NAI susceptibility panel 20 was similar to or better than the 2020 panel 19 (all correct panel 20, genotypic 93%, phenotypic 97%; panel 19 genotypic 91%, phenotypic 97%). Laboratories performing phenotypic testing were more likely to achieve a 100% score than those performing genotypic testing 29/33 (87.9%) vs 35/42 (83.3%) respectively.

Conclusion

The most common phenotypic testing error was incorrect interpretation of IC50 fold change, most notable for influenza B which had a higher baseline IC50 value. Genotypic testing errors included incorrect interpretation of amino acid substitutions as relevant for NAI RI/HRI, detection of amino acid substitutions not present in the test virus, and not considering the consensus threshold of massive parallel sequence data. These errors could be easily addressed with training.

WHO will continue to provide the EQAP to GISRS laboratories for influenza antiviral susceptibility testing. Inclusion of viruses with varied amino acid substitutions associated with NAI or baloxavir RI will encourage laboratories to expand their methodology and detection capabilities.

Catherine Moore - AOXI0517

Early Implementation of Multiplex testing for Respiratory Viruses to Included SARS-CoV-2 in Wales, UK, Allowed for Ongoing Detection and Surveillance of Other Seasonal Viruses during the Pandemic

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Background

Laboratory efforts during the early pandemic period focused on the detection of SARS-CoV-2. This negatively affected detection and surveillance of other respiratory viruses including influenza. To mitigate against this, the Wales NHS laboratory network implemented early a minimum assay panel of SARS-CoV-2/RSV/influenza for all symptomatic patients admitted to hospital and a proportion of symptomatic community patients. We analysed the results from this testing to assess the impact of pandemic measures on other seasonal viruses and to understand how the co-circulation of SARS-CoV-2 might affect seasonality and severity of the other respiratory viruses.

Method

Comprehensive multiplex panels were used on samples received from children admitted to hospital, vulnerable adults and sentinel surveillance sites from the start of the pandemic. From late 2020, a further multiplex assay to include SARS-CoV-2/RSV/Influenza was implemented to increase multiplex capacity. This combined with the ongoing capability to run comprehensive testing strengthened the detection of other respiratory viruses from samples received from sentinel, non-sentinel and SARI surveillance sources. Data from the laboratory network was downloaded weekly by the respiratory virus surveillance team for analysis. Reports were generated for the general population, patients in intensive care and also children under 5 years old.

Result

Over the pandemic period in Wales, >100000 multiplex tests have been performed. The data generated supports the global picture, that the mitigations used to prevent SARS-CoV-2 transmission, impacted the circulation of other respiratory viruses. Notable exceptions to this was rhinovirus and adenovirus with circulation observed throughout the period analysed. As mitigations eased, significant epidemics of parainfluenza and enterovirus D68 were detected, followed by a summer RSV season. Influenza was notable by its absence until winter 2021, with widespread low level circulation occurring across Wales, and whilst failing to reach epidemic threshold levels, it still contributed to hospital and ITU admissions.

Conclusion

The mitigations used during the pandemic displaced the epidemics of other respiratory viruses. In Wales throughout the pandemic, every effort was made to ensure ongoing testing for at least influenza and RSV, using multiplex assays. The data generated allowed for monitoring of all causes of viral respiratory infection in both community and hospital settings. Post-pandemic, we recommend that that multiplex panels for ARI cases in hospital and community settings are routinely deployed to further the understanding of the interplay that SARS-CoV-2 might have on the epidemic patterns of our seasonal viruses going forwards

Lynnette Brammer - AOXI0527

Influenza Surveillance Enhancements and Their Contributions to Pan-Respiratory Surveillance

Lynnette Brammer[1]

[1]CDC

Background

Influenza surveillance in the United States has historically relied on indirect measures of activity such as outpatient visits for influenza-like illness (ILI) and pneumonia- and influenza-associated (P&I) mortality. Indirect measures, paired with virologic surveillance data from clinical and public health laboratories, are sufficient to track trends in influenza activity and compare the relative severity of annual epidemics, but they do not produce population-based rates of influenza impact. These methods were focused solely on influenza and relied on influenza being the primary cause of increases in ILI and P&I mortality above the baseline of other respiratory illness activity and the seasonally expected proportion of all deaths due to pneumonia, respectively. During the COVID-19 pandemic, many of the assumptions under which influenza surveillance worked were no longer valid and even more direct measures of influenza activity such as virologic data became difficult to interpret.

Method

We examined existing influenza surveillance systems for opportunities to modify data analysis and identify more useful data subsets and new data sources to improve our ability to track influenza during the COVID-19 pandemic.

Result

During the COVID-19 pandemic, syndromic surveillance data for influenza was difficult to interpret and communicate due to changes in health care seeking behavior, clinical presentation, and inconsistent application of syndrome definitions. Addition of COVID-19 coded deaths to existing P&I mortality tracking was useful for visualization of mortality burden relative to previous influenza seasons but tracking of influenza coded deaths specifically was needed to understand the contribution of influenza to mortality estimates. The use of multiplex diagnostic assays testing for both SARS-CoV-2 and influenza virus were valuable in maintaining influenza surveillance during the pandemic. The subset of virologic data with links to epidemiologic data, including reason for testing, and that included testing for multiple respiratory pathogens was optimal. Population-based rates of laboratory confirmed influenza-associated hospitalization were less impacted by the pandemic and provided data that could be compared to previous influenza seasons.

Conclusion

Going forward, the approach to influenza surveillance will need to adjust to account for continuing circulation of SARS-CoV-2. Correct interpretation of syndromic surveillance data will require tighter linking of [what??] to laboratory test results, preferable for a panel of respiratory viruses. Surveillance using laboratory-confirmed outcomes, particularly systems that produce population-base rates, is needed for reliable season-to-season comparisons.

Gisela Barrera - AOXI0538

Impact of the COVID-19 pandemic on the circulation of influenza and other respiratory viruses in Mexico

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Background

In Mexico, the first case of COVID-19 occurred on February 27, 2020, and to date, 5.76 million and 325,000 deaths have been reported. The circulation of the SARS-CoV-2 virus has not only had a major impact on global public health, but also on the transmission patterns of influenza and other respiratory viruses. In Mexico, a large decrease in the circulation of influenza and other respiratory viruses was observed from week 21 of 2020 to week 39 of 2021.Likewise, the percentage of other respiratory viruses decreased considerably during 2020 and 2021 compared to the previous decade.

Method

In this study, we compared the circulation of influenza and other respiratory viruses one decade before the pandemic (2010-2019) and during the pandemic (2020-2022). Since 2009, the diagnosis of influenza is performed by real-time RT-PCR and the diagnosis of other respiratory viruses by multiplex RT-PCR (NxTAG® Respiratory Pathogen Panel with Luminex/MAGPIX System).

Result

From 2010 to 2019, 194,768 samples were processed for influenza diagnosis nationwide, on average 24,346 samples were processed per year with 24% positivity. From 2020 to 2022, 116,367 samples were processed, on average 38,789 samples were processed per year with 8% positivity.

Regarding the circulation of other respiratory viruses from 2010 to 2019, 7,606 samples were processed, the average of the percentage of positivity was 42%, while for 2020 to 2022, 7,564 samples were processed on average of percentage of positivity was 20%.

Conclusion

Analysis of the circulation of influenza and other respiratory viruses a decade before the COVID-19 pandemic and during the pandemic shows that the percentage of positivity for respiratory viruses other than SARS-CoV-2 decreased considerably during 2020 and 2021 compared to the percentage of positivity observed from 2010 to 2019. It is considered that the prevention measures adopted during the COVID-19 pandemic, such as mandatory social isolation, healthy distance, use of masks, hand hygiene and use of alcohol gel, played an important role in the transmission pattern of other respiratory pathogens, not only in Mexico, but also worldwide.

Wey Wen Lim - AOXI0540

Surveillance for Influenza Including Joint Surveillance and Impact of COVID-19 on Other Respiratory Virus Diseases

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Background

COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a contagious and potentially fatal acute respiratory disease that has exacted great health and economic impact worldwide. Even though a vaccine is now available, protecting health care workers (HCWs), especially those who are exposed to potential COVID-19 cases is crucial on humanitarian grounds as well as patient safety and the maintenance of a working healthcare system during a pandemic. An accurate assessment of the risk of infection in the community and healthcare settings and its accompanying risk factors is also needed to support policy decisions surrounding public health measures in the community as well as infection control measures in healthcare settings.

Method

We conducted a longitudinal cohort study with continuous follow-up and sequential blood samples collected at six-month intervals from June 2020 through to April 2021. Seroprevalence of COVID-19 every six months (Round 1 = May - November 2020, Round 2 = December - May 2021) was calculated as a percentage of samples that tested positive for anti-SARS-CoV-2 neutralising antibodies by plaque reduction neutralisation test (PRNT) collected during that period.

Result

Overall seroprevalence (PRNT50 antibody titer >10) in Round 1 was estimated to be 0% with a 95% confidence interval of 0% to 0.50% despite heavy exposure to COVID-19 patients in our healthcare worker cohort. Among the 761 participating healthcare workers in round 1, 318 (42%) report having at least one occupational exposure to patients known to have COVID-19 since January 1, 2020, with 101 (32%) reporting exposure to 20 or more confirmed COVID-19 cases during the period. Of those who reported occupational exposure to confirmed COVID-19 cases, 208 (65%) reported spending at least 15 minutes or more with each COVID-19 case with which they have come into contact. In Round 2 there was an increase in overall seroprevalence (PRNT50 antibody titer >10), but the estimated overall seroprevalence of 0.52% (95% CI 0.14, 1.32) is still very low among this healthcare worker cohort with similar exposure to COVID-19 patients and potentially contaminated environments.

Conclusion

The seroprevalence of COVID-19 in healthcare workers in Hong Kong was low during the first 1.5 years into the COVID-19 pandemic. Surveillance of emerging infectious diseases such as COVID-19 among longitudinal cohorts of healthcare workers can be used to monitor the impact of evolving pandemics on healthcare workers and health systems. Further applications of such surveillance include the detection of emerging infectious diseases in the community and the estimation of vaccine effectiveness among healthcare workers.

Mairead Whelan - AOXI0541

SeroTracker: Lessons learned to optimize serosurveillance platforms and methodology for influenza and other respiratory viruses

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Background

Serosurveys, which sample and test for antibodies against influenza and other respiratory viruses using serology, are crucial tools to answer key questions during outbreak prevention and control: How many people have actually been infected beyond what has been captured by surveillance and routine viral testing, and how many people have acquired some level of humoral immunity against the virus in question? The SARS-CoV-2 pandemic has been a useful example of how serosurveys have been mobilized during an emergency respiratory disease response, how they could be improved for future pandemics and other respiratory viruses including influenza, and the growing and crucial role of such data from LMICs.

Method

We present SeroTracker, a living systematic review and open-access data and dashboard platform, as a case study of data centralization tool for respiratory disease surveillance and its associated challenges and strengths. We describe lessons from serosurvey studies we collected during the pandemic to be applied in future influenza and multi-pathogen 'joint' surveillance models.

Result

SeroTracker provided a centralized platform for serosurvey results globally in a timely and accessible manner, including literature reports and an interactive dashboard. Some challenges we found with centralizing serosurveillance data were reporting issues in quality of serosurveys, for example: risk of bias was found to be high in 44% and 30% of studies in each of our recent systematic reviews, respectively. We also a delay between data collection and median time to serosurvey publication of 154 days (IQR: 64-255), impacting timeliness of results, and heterogeneity in immunoassays used and inconsistency in their performance validation. Other challenges included scattered reporting and representativeness of data from LMICs, redundancy between platforms, and unclear or unstandardized data sources.

Conclusion

Serosurvey studies are crucial for multi-pathogen 'joint' respiratory virus surveillance and control. We need to improve serosurvey standardization and quality on several dimensions: epidemiological protocols, validation of laboratory assays, and data and reporting methods. There is a need for a central data submission and accession platform to enable rapid global analysis of data from these studies, and continued rapid dissemination of these results to countries and public health stakeholders via WHO initiatives. Infrastructure for these areas must be prepared for existing endemic respiratory diseases that can be rapidly re-deployed for future influenza and respiratory virus global threats.

Katarina Prosenc - AOXI0547

Coinfection of SARS-CoV-2 with other respiratory viruses in Slovenia from October 2020 to May 2022

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Background

Coinfections of respiratory tract with two or more respiratory viruses are common, although it is not clear whether these infections are more severe than single virus infections. Coinfections of severe acute respiratory syndrome coronavirus 2 (SCV2) with other respiratory viruses were confirmed early in the pandemic with frequencies from less than 3% to 30%. Non-pharmaceutical measures implemented to control pandemic also influenced circulation of influenza and other respiratory viruses. In this study, we analysed frequency and seasonal distribution of SCV2 coinfections with common respiratory viruses including influenza from October 2020 to May 2022 in sentinel and non-sentinel samples analysed in Slovenian National Influenza Programme.

Method

Surveillance of COVID-19/SCV2 has been integrated in influenza surveillance system from season 2020/2021 on. Respiratory specimens collected from patients with influenza-like illness at sentinel sites (primary care) and from hospitalized patients (non-sentinel) were tested for influenza, RSV, adenoviruses(AD), enteroviruses(EV), rhinoviruses(RV), human metapneumoviruses(hMPV), parainfluenza(PIV), seasonal coronaviruses(CoV), human bocaviruses(BoV), human parechoviruses(Pev) and SCV2 with PCR. Percentages of coinfection of SCV2 positive specimens with other viruses was calculated and background circulation of this viruses estimated.

Result

In 2020/2021 (Oct 2020-Sep 2021) 325 sentinel and 3237 non-sentinel samples were tested and no influenza viruses detected. In sentinel SCV2 positive samples, 2.8% were coinfected with AD and 2.8 % with RV. In non-sentinel SCV2 positive samples there were 0.3% coinfections with AD, hMPV and CoV each and 2.4% with RV. Regardless coinfections, most abundant virus circulating in 2020/2021 was RV(14.2%), followed by CoV(4.7%), PIV(3.1%), RSV(2.6%) and AD(2.4%). Other viruses were detected in less than 1% of specimens.

In 2021/2022, 603 and 2069 sentinel and non-sentinel samples were tested. We detected 5.4% coinfections with influenza in SCV2 positive sentinel samples, 3.6% with AD, 1.8% with RSV, EV and PIV, each. In SCV2 positive non-sentinel samples, 3.9% samples were coinfected with RV, 1.9% with PIV, 1.6 with CoV and 0.6% with influenza, RSV and AD each. Regardless coinfections, the most abundant virus circulating in 2021/2022 (till end of May) was RV(16.9%), followed by RSV(8.9%), influenza (3.1%), RSV(8%), AD(6%), PIV(5.1%), CoV(3%), EV(1.6%), BoV(1%), and Pev(0.2%).

Conclusion

Spatiotemporal variation in viral epidemiology reflected the rate of coinfections for SCV2 with common respiratory viruses. Surprisingly, more coinfections were observed in sentinel, primary care samples than in non-sentinel hospital samples.

Vasiliy Leonenko - AOXI0509

Population heterogeneity and influenza dynamics in St. Petersburg, Russia: a hybrid modeling approach

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Background

Mathematical modeling is one of the useful tools in public health that helps to explain the retrospective disease dynamics and to plan control measures for the future outbreaks. One of the important questions that could be addressed using models is how changes in contact patterns caused by day-to-day activities (public transport usage, school attendance, working schedules) in different age groups may result in variation of epidemic dynamics in different urban settings throughout different epidemic seasons. In the presented work the author investigates the matter by applying a hybrid model of influenza dynamics to synthetic population of Saint Petersburg, Russia.

Method

The applied approach combines three interlinked components: (1) a synthetic population of Saint Petersburg, Russia; (2) a hybrid modeling framework which is comprised of an agent-based and a compartmental model of influenza dynamics; (3) the micro and macro data connected with influenza dynamics (namely, weekly incidence of acute respiratory infections) provided by Russian Influenza Research Institute. For comparison purposes, an age-structured compartmental influenza model calibrated to the same data is also employed.

Result

The simulation results demonstrate the ability of a hybrid model to reproduce the trends in influenza incidence dynamics in Saint Petersburg and demonstrate the influence of population heterogeneity on the simulation output. The obtained results show the benefits of using spatially explicit models to reproduce disease dynamics in St. Petersburg, compared to age-structured compartmental models, and how uncertainty in input data affects the quality of model fitting to disease incidence.

Conclusion

In this work, it is demonstrated that a hybrid modeling approach combined with synthetic populations makes it possible to fully consider the influence of spatial heterogeneity of the population and variations in contact patterns, caused by day-to-day activities of individuals, on influenza dynamics in urban settings, using St. Petersburg as a case study. Also the research shows the limitations of the hybrid approach connected with its demand in detailed data. In case of influenza modeling with scarce input data, an age-structured compartmental model proves itself more useful for planning targeted influenza control measures, because the level of uncertainty of an output generated by a hybrid model becomes too high which results in low plausibility of the influenza dynamics assessment.

Verna Welch - AOXI0456

The impact of county-level deprivation on influenza vaccine uptake

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Background

Influenza vaccination is thought to avert 1.4 to 7.5 million cases of influenza, 39,000 to 105,000 influenza-related hospitalizations, and 3,500 to 12,000 deaths in the United States each year since 2010. Although health disparities have been documented among various groups concerning influenza vaccine uptake, disparate uptake has not been evaluated since the start of the COVID-19 pandemic. Here, we sought to assess county-level disparities in influenza vaccine uptake in 2021/2022 in the continental United States (US).

Method

This was an ecological study evaluating US county-level (administratively defined geographic boundaries) influenza vaccine and socioeconomic condition data. County-level data on influenza vaccine uptake was obtained from the US Centers for Disease Control and Prevention for the 2021/2022 influenza season. Disparities were measured using the 2019 Area Deprivation Index (ADI), a multidimensional measure of a county's socioeconomic conditions which has been used to evaluate disparities for various health outcomes. To assess associations between socioeconomic disparities and vaccine uptake, we used bivariate mapping and least-squares regression with US Census Division clustered standard errors to evaluate the association between ADI and county-level vaccine uptake as well as vaccine uptake by race and ethnicity after adjusting for the population per land area and the percent of the Black or White population in each county.

Result

Bivariate maps indicated that many counties in the Northeast and upper Midwest regions of the US had high vaccine uptake with low deprivation. In contrast, many Southern and Western counties had high deprivation with low uptake (Figure 1). The multivariable regression models suggested that for each 10 percent increase in deprivation, influenza vaccine uptake decreased by 1.5 percentage points (B = -1.5, 95% CI: -1.83 to -1.12). Stratifying by percent uptake for Blacks versus Whites suggested that county-level deprivation impacted uptake among Blacks slightly less than for Whites (B = -1.03, 95% CI: -1.24 to -0.18 for uptake among Blacks; B = -1.7, 95% CI: -1.96 to -1.35 for uptake among Whites).

Conclusion

Our study showed that US counties with high levels of social deprivation had lower uptake of influenza vaccine during the COVID-19 pandemic. These findings suggest that disparities in US influenza vaccination persisted despite a nationwide focus on vaccination.

Erik Karlsson - AOXI0552

Utility and comparison of multiplex assays for simultaneous detection of SARS-CoV-2, Influenza, and Respiratory Syncytial Virus

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Background

The COVID-19 pandemic significantly altered known patterns of respiratory infections (VRI) worldwide. As human seasonal infections with influenza virus (Flu), Respiratory Syncytial Virus (RSV), and spillovers of novel avian influenza viruses (AIV) resurge with the relaxation of sanitary measures, it is critical to maintain surveillance of SARS-CoV-2 along with other viruses. Manufacturers have modified their existing assays to detect simultaneously SARS-CoV-2, Flu, and RSV in a single test. While these assays present an attractive option to reduce diagnostic burden, clinical evaluation of these kits is critical to determine performance and limitations for informed choice before their routine use.

Method

TaqPathTM COVID-19, Flu A/B, RSV Combo Kit (Thermo Fisher) (TaqPath) was evaluated in comparison with individual standard of care (SOC) WHO/US-CDC assays, currently used at the National Influenza Center and WHO H5 and Global COVID-19 Referral Laboratory in Cambodia. Xpert® Xpress SARS-CoV-2/Flu/RSV assay (Cepheid, Sunnyvale, CA, USA) resolved discordant results. We first assessed sensitivity (limit of detection; LoD) using isolates of SARS-CoV-2 (Wuhan, Alpha, Omicron variants), human seasonal influenza (A/H1N1, A/H3N2 and A/H5N1, B/Victoria and B/Yamagata) and AIV (A/H5N1, A/H5N8, A/H7N4, and A/H9N2). Subsequently, we selected 300 residual clinical specimens collected under Flu/RSV surveillance and COVID-19 public health response for comparison.

Result

Overall, TaqPath accurately identifies all of the viruses, and LoD was comparable to SOC and Xpert Xpress. Viral detection in clinical samples was similar to SOC with 100% positive percent agreement and 99.2%, 99.21%, and 97.67% negative percent agreement for SARS-CoV-2, Flu, and RSV, respectively. Results were comparable for influenza on throat versus nasopharyngeal samples. Differences in assay costs and testing burden could influence test choice.

Conclusion

TaqPath offers a viable solution to quickly monitor influenza activity, COVID-19 trends, and RSV outbreaks, as well as spare and optimize human resources. Multiplex testing presents an attractive option to expand sustainable capacities for viral respiratory infection surveillance, as well as to perform large-scale screening. Multiplex assays also results in faster time to diagnosis and treatment decisions, minimizing isolation times, and reducing transmission.

Jurre Siegers - AOXI0568

Detection of A/H14 in domestic ducks in Southeast Asia

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Background

Avian influenza virus (AIV) is endemic in domestic poultry in the Greater Mekong Subregion, but little is known about AIV in the natural reservoir. Hemagglutinin (HA) subtypes H1-H16 are detected in wild birds, but some subtypes are common than others and some are rarely observed in domestic poultry. First detected in 1982 and recognized as A/H14 in 1990, only 50 sequences are available in global databases to date, all from wild Anseriformes. A/H14 viruses typically cause subclinical infection in birds, but experiments indicate support for a multi-basic cleavage site with high pathogenicity index, and grow productively in ferrets indicating zoonotic potential. To date, A/H14Nx viruses have not been detected in wild birds in Southeast Asia and in domestic birds globally.

Method

Active, longitudinal surveillance at the wild bird-poultry interface conducted between 2021-2022 in Cambodia were screened for AIV using standard RT-PCR and any positive samples (M gene Ct <25) were immediately sequenced using a barcoded, multi-segment amplification on Oxford Nanopore Technology. Maximum-likelihood and Bayesian phylogenetic analysis were used to infer the origins and genomic evolution in relation to all known AIV genomes.

Result

A/H14N2 (n=5) was detected in domestic ducks near the Boeung Sne Bird Sanctuary, Prey Veng province in February 2022, however no A/H14 was detected in wild birds. Their HA genes were similar to each other, and most closely related to previous A/H14 detections in Eurasia, including A/Sandpiper/Tomsk/112/2019/H14N7 in Russia and A/Goose/Karachi/NARC-13N-969/2014/H14N3 in Pakistan; however, sequences from Asia form a distinct geographic cluster. Sequence of the N2 NA suggests possible reassortment with A/H6N2 and A/H4N2 from wild birds in Turkey or Mongolia, respectively. Phylogeny of the internal genes is consistent with extensive reassortment events and interhemispheric movement via wild birds.

Conclusion

It is unclear if A/H14 has recently been introduced into Southeast Asia; however, lack of detection for over 10 years of live bird market surveillance in Cambodia indicates very low levels or lack of widespread circulation in the region. Detection, efficient replication in domestic poultry, and extensive reassortment does suggest the possibility that A/H14 is maintained in domestic poultry in Southeast Asia. Further explorations into the role domestic species play in the ecology and epidemiology of rare AIV subtypes, and the zoonotic risk of these novel A/H14s are warranted. Overall, vigilance in longitudinal, active surveillance of domestic poultry for all AIVs subtypes, not just those currently associated with high pathogenicity and economic damage.

Jacqueline Nolting - AOXI0610

Zoonotic influenza A virus and SARS-CoV-2 infections of youth swine exhibitors at agricultural exhibitions

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Background

The introduction of novel influenza A virus (IAV) to the human population from the vast pool of viral diversity maintained in animals is a constant pandemic threat. Since 2011, over 400 humans have been infected with IAVs of swine origin in the United States, with the vast majority of these zoonotic IAV transmissions occurring at swine exhibitions during agricultural fairs. These unique animal-human interfaces are the most active for zoonotic transmission of IAV in the United States. Risk factors for infection include close contact with swine at agricultural fairs, as well as age (most infections in children). However, there is substantial unexplained year-to-year variation in the number of human infections. A better understanding of the frequency in which swine-to-human IAV transmission events occur and the impact these exposures have on the human's immunological profile is greatly needed.

Method

To this end, we enrolled 700 youth swine exhibitors from twenty states in the US to test for active IAV infections at swine exhibitions. Since samples were being collected during the onset of the COVID-19 pandemic, we tested these nasal swabs for both IAV and SARS-CoV-2 to determine if the congregation of people at these livestock show events may represent significant transmission points for rural populations, as these individuals likely have fewer SARS-CoV-2 exposure opportunities due to residence in less-populated areas.

Result

The 99 samples collected in 2019 were all negative for both pathogens. In 2020, 1 of 246 (0.4%) all collected samples was positive for H1N1 IAV and all samples were negative for SARS-CoV-2. In 2021, 355 collected samples were negative for IAV and 2 (0.56%) were positive for SARS-CoV-2.

Conclusion

Although active infections were not detected in a majority of study participants at the time of sampling, regular exposure to pigs likely increases the risk of infection and may provide unique immunity to zoonotic pathogens.

Punam Mangtani - AOXI0618

Examining Influenza and Avian Influenza Seasonality in Bangladesh, 2010-2019

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Background

Seasonal and avian influenza viruses circulate among human and poultry populations in Bangladesh. Greater than 90% of poultry products are marketed through live bird markets (LBMs) in Bangladesh, and over half of the urban population regularly visit these LBMs. Therefore, LBMs are an important source of exposure to avian influenzas and for potential viral reassortment if seasonal influenza is concurrently circulating in humans. However, the epidemiology of influenza in humans and animals is not well-defined in this setting. In this study, we aimed to characterize influenza seasonality in humans, examine regional heterogeneity in transmission, and evaluate co-seasonality between circulating influenza viruses in humans and poultry in Bangladesh.

Method

In this retrospective time-series study, we used aggregated patient data collected between 2010 and 2019 from 32 hospital-based influenza sentinel surveillance sites across Bangladesh. We applied wavelet analysis to determine influenza periodicity in humans and estimated influenza peak timing and intensity in 10 regions using negative binomial harmonic regression models. We applied meta-analytic methods to determine whether influenza seasonality differed across regions. Using environmental surveillance data from 110 LBMs in Dhaka, Bangladesh, we then estimated avian influenza peak timing and intensity and examined whether there was co-seasonality between human and avian influenza viruses.

Result

Over the 10-year period, we included 8,790 human influenza cases and identified a distinct annual influenza season with an epidemic peak in June-July each year (peak calendar-week: 27.6, 95% CI: 26.7-28.6). Epidemic timing varied by region ($I2=93.9\%$, $p<0.001$), with metropolitan regions peaking earlier and epidemic spread following a spatial diffusion pattern based on geographic proximity. Comparatively, avian influenza displayed weak seasonal intensity, with moderate year-round transmission and a small epidemic peak in April (peak calendar-week: 14.9, 95% CI: 13.2-17.0) that was out of phase with influenza peaks in humans.

Conclusion

In Bangladesh, influenza prevention and control activities could be timed with annual seasonality and regional heterogeneity should be considered in health resource planning. Although human and avian influenza peaks are out of phase, year-round avian influenza transmission poses a risk for viral spillover. Our results support the need for more quantitative risk assessments of viral reassortment in urban Bangladesh and could be used to inform the future timing of sequencing-based surveillance. Targeted efforts will continue to be crucial for mitigating potential reassortment and future pandemic threats.

Mathilde Richard - AOXI0624

Mapping the global antigenic diversity of avian H7 influenza A viruses to aid the design of broadly reactive vaccines

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Background

Avian influenza viruses (AIVs) are frequently transmitted from wild waterfowl - their original reservoir - to poultry, resulting in outbreaks with significant socioeconomical impact and zoonotic risks. AIVs carrying the H7 hemagglutinin (HA) glycoprotein have caused the highest number of reported cases of human infection, highlighting their pandemic potential. Evidence of antigenic diversification within H7 AIVs has led to the selection by the WHO of 12 vaccine candidates. Nevertheless, a comprehensive global characterization of antigenic variation in H7 AIVs is missing. Here, we used antigenic cartography to visualize the global antigenic diversity of H7 HAs and to determine the molecular basis of antigenic change in H7N9 viruses, which have caused 1567 reported cases of human infection over five epidemic waves.

Method

A representative set of fifty-two H7 sequences was selected based on an H7 phylogenetic tree constructed with all publicly available sequences. Genetic outliers were specifically included to recapitulate the whole potential antigenic diversity of H7 AIVs. Recombinant viruses carrying synthetic HA genes of the respective strains were generated, a subset of which was used to generate 17 post-infection antisera in ferrets. Hemagglutination inhibition (HI) assay data were used to compute an antigenic map using multidimensional scaling algorithms and the molecular basis of antigenic change between H7N9 prototypes was determined by mutagenesis studies.

Result

The global antigenic diversity of H7 viruses from 1994 to 2021 was visualized by generating a two-dimensional antigenic map. Interestingly, cross-reactivity between antigens and sera from the divergent North American and Eurasian lineages was observed. More antigenic diversity was observed in the Eurasian lineage as compared to the North American lineage, especially between H7N9 strains, whose antigenic properties changed over the course of the five infection waves. One to four amino acid changes mediated antigenic differences as measured by HI and virus neutralization assays between selected H7N9 prototypes.

Conclusion

This study provides insights into the H7 antigenic evolution, which could aid the control of H7 AIVs, in particular with regards to developing and evaluating universal vaccination strategies for pandemic preparedness.

Vanessa Cozza - AOXI0564

Country approaches for integrating influenza and SARS-CoV-2 sentinel surveillance

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Background

The Global Influenza Surveillance and Response System (GISRS) initiated the integration of SARS-CoV-2 into the influenza sentinel surveillance early in the COVID-19 pandemic. Disruptions in health systems, altered clinical care pathways, changes in health care-seeking behaviours, repurposing of national influenza laboratories and sentinel surveillance hospitals as COVID-19 diagnostic and treatment centres, resulted in significant challenges and even cessation of influenza sentinel surveillance in some countries. This paper documents the various strategies adapted by countries to maintain and integrate influenza and SARS-CoV-2 sentinel surveillance and contribute to informing the COVID-19 response at the global and national levels.

Method

The consistency and timely reporting of influenza and SARS-CoV-2 testing of specimens sourced from sentinel sites was monitored on a weekly basis since March 2020. Information on the main reasons of disruptions in sentinel surveillance practices was collected through consultations and surveys with countries, to inform and update the WHO interim guidance on maintenance and the end-to-end integration of influenza and SARS-CoV-2 sentinel surveillance. In August 2021, the GISRS entities in countries were invited to share qualitatively, their experiences in addressing challenges in sourcing adequate specimens from sentinel sites, laboratory testing and sequencing, and epidemiological, clinical and virological data management. These experiences were reviewed by an expert committee and enriched with contextual information as required.

Result

Of the 30 received, 27 submissions were critically evaluated to summarize the lessons learnt from the COVID-19 pandemic, the various approaches adapted by countries to maintain and integrate influenza and SARS-CoV-2 sentinel surveillance. The expansion of the number of sentinel sites, the decentralization of laboratory testing, updating operating procedures and laboratory testing algorithms, systematic sourcing from non-sentinel sites, training, adapting data collection and reporting systems were recurrent practices implemented in countries.

Conclusion

Despite significant challenges posed by the COVID-19 pandemic, countries leveraged opportunities provided by the investment in the COVID-19 pandemic response, to maintain and integrate influenza and SARS-CoV-2 sentinel surveillance. Though contextual, these country experiences are lessons learnt and serve to build resilient and sustainable surveillance systems for influenza, SARS-CoV-2 and other respiratory viruses with pandemic potential for the globe to be better prepared for the next pandemic.

Yiu-Chung Lau - AOXI0580

Forecasting of influenza activity and estimating the impact of COVID-19 pandemic in Hong Kong

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Background

Various public health and social measures (PHSMs) have been implemented worldwide to fight against COVID-19 pandemic since early 2020. These measures, including mask wearing and social gathering restrictions, would also prevent virus transmission in general, thus affected the transmission dynamics of influenza viruses. This study was to assess the impact of COVID-19 PHSMs on the activity of influenza viruses in Hong Kong in 2020.

Method

We developed a statistical regression based forecasting framework by using surveillance and virological data on influenza virus activity, meteorological data, and school holiday/closure data in Hong Kong. We performed short-term (1-4 weeks ahead) and long-term (1-52 weeks ahead) forecasts for influenza virus activity in 2020 seasons. Cross-validation was used for model selection based on the forecast performance. We evaluated the impact of COVID-19 PHSMs on influenza activity by comparing counterfactual and observed attack rate during 2019-20 seasons.

Result

Influenza activity dropped to a negligible level since February 2020 in Hong Kong. Absolute humidity and ozone concentration were found to be potential predictors. The short-term forecast could reach the coefficient of determination of >0.5. We estimated the overall attack rate of 27.2% in 2019-20 season with two peaks. The estimated reduction in attack rate was 79% for the winter peak during the period of December 2019 - March 2020, and 87.7% overall for the 2019/20 season.

Conclusion

Our results suggest substantial reduction in influenza infection given the PHSMs against COVID-19 in Hong Kong. However, this may imply low level of herd immunity against influenza infection in the community and the possibility of the surge in influenza activity after PHSMs relaxation cannot be ruled out.

Gisela Barrera - AOXI0605

Co-infections of SARS-CoV-2, Influenza and other respiratory viruses during 2021 and 2022 in Mexico

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Background

The SARS-CoV-2 virus has been characterized by its constant genetic changes, which have forced manufacturers to constantly update diagnostic methods according to the different epidemiological situations. That is to say, at the beginning of the pandemic there were only kits to identify SARS-CoV-2, due to the fact that influenza and other respiratory viruses changed their transmission pattern. Later, with the concern of influenza circulation, kits were designed to simultaneously identify SARS-CoV-2 and Influenza, which has allowed us to integrate and strengthen the surveillance of SARS-CoV-2, influenza and other respiratory viruses and to detect co-infections in a timely manner that can hinder the treatment and evolution of patients.

Method

In Mexico, since August 2021, the simultaneous detection of SARS-CoV-2 and Influenza A/B has been performed by real-time RT-PCR, and the diagnosis of other respiratory viruses has been performed since 2009 by multiplex RT-PCR (NxTAG® Respiratory Pathogen Panel with Luminex/MAGPIX System) on a small percentage of SARS-CoV-2 and Influenza negative samples from severe cases and deaths. Surveillance is performed on specimens that meet the operational definition of Viral Respiratory Disease and Severe Acute Respiratory Infection (SARI).

Result

From August 2021 to May 2022, 1,386,777 samples were processed for the simultaneous diagnosis of SARS-CoV-2 and Influenza A/B within the sentinel surveillance system. During this period, 679 co-infections were identified, 180/679 with other non-SARS-CoV-2 respiratory viruses, 499/679 were SARS-CoV-2/other respiratory viruses, of which 324/499 SARS-CoV-2/Influenza, 102/499 SARS-CoV-2/VSR, 41/499 SARS-CoV-2/HEV/HRV, 32/499 SARS-CoV-2/other respiratory viruses.

Conclusion

In this study it was observed that 0.05% of the samples presented co-infection. This percentage is low compared to other countries. However, it is important to take into account that we start from the same operational definitions and that the evolution days for the reception of the samples is 10 days, due to the fact that the request for medical attention is late, which hinders the timely identification of influenza and other respiratory viruses in which the first three days after the onset of symptoms are crucial for their detection. The results show that co-infections between SARS-CoV-2 and influenza are more frequent because they are searched simultaneously, while co-infections with other respiratory viruses are only searched for in a small percentage of negative samples.

AnnaSara Carnahan - AOXI0629

Double influenza epidemics in Sweden 2021-22 and high vaccination coverage

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Background

The current pandemic and related restrictions have affected influenza transmission and testing. Through early 2022, community testing for COVID-19 was widely available. After Feb. 9, 2022, COVID-19 testing was restricted to patients and staff within medical and elderly care. These changes also affected influenza testing.

Seasonal influenza vaccination is recommended for individuals 65 years and older, pregnant women, and those with risk factors. The 21 Swedish regions provide free vaccination each fall. During the 2021-22 season, co-administration was recommended for those eligible for influenza vaccination and a COVID-19 booster dose.

Method

We analysed national surveillance data on laboratory-confirmed influenza cases, cases in ICU, and testing levels. We described the season's transmission patterns, also taking into account COVID-19 transmission. Regional influenza vaccination coverage data were collected.

Result

Influenza transmission in Sweden started in late Nov., with a rapid increase in reported cases that peaked in week 50 (Fig 1). Data on patients in ICU reflected a low to medium activity level. Age groups not often tested for influenza were more prevalent among cases than previous seasons (Fig 2). Cases were mainly reported from Stockholm and nearby regions.

The Omicron variant of SARS-CoV-2 was first detected in late Nov. and COVID-19 cases increased rapidly starting in late Dec. to a peak in weeks 4-5 2022. Concurrently, influenza case counts decreased precipitously and remained very low until an increase during the late spring, when a second, smaller wave was seen. The rapid increase in and high level of Omicron transmission, in combination with COVID-19 restrictions, coincided with the extinction of Sweden's first influenza wave. Changed testing patterns meant that those 65 years an older had the highest incidence in the second wave. Cases were mainly reported from regions with low first wave transmission.

Influenza vaccination coverage increased from 60 percent to over 70 percent [preliminary data] among those 65 years and older, a group which also has high COVID-19 vaccination coverage.

Conclusion

The 2021-22 influenza season in Sweden had an unusual pattern with two epidemic waves, separated by a period of very low activity. The first and second waves showed differences in geography and age distribution. The arrival of the Omicron variant at the end of Dec. coincided with a rapid decrease in influenza circulation. Efforts to provide COVID-19 vaccination in Sweden had a positive effect on influenza vaccination coverage.

David Muscatello - AOXI0652

The PEARL project - pandemic and epidemic assessment of risk using linked data

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Background

The COVID-19 pandemic has highlighted the limitations of existing disease surveillance systems. With ever-increasing growth of electronic health and related records, there is a need to unify previously independent sources of information for surveillance of acute respiratory infections.

This project aims to create the 'PEARL' database as a respiratory epidemic research resource, identify early epidemic severity characteristics for severe influenza and COVID-19 epidemics for use in risk assessment, develop analytic approaches for locally-specific epidemic risk assessments using temporospatial methods, and estimate the added short-term burden placed on health services due to both recognised and unrecognised influenza, COVID-19 and other respiratory infections.

Method

The study setting is the state of New South Wales (NSW), Australia, with a population of >8 million in 2020 comprising metropolitan, urban, rural and remote populations.

Currently the PEARL database comprises a population-based cohort of all persons presenting to any public hospital in NSW that participates in the statewide Emergency Department (ED) Data Collection, and who were assigned an ED diagnosis of any respiratory infection, other unspecified infection, fever or cough during the period January 2005 through September 2021.

Each person's ED record is matched to contemporaneous COVID-19 and influenza detections, emergency services (ambulance), and hospital admission and death records. Intensive care admission status and associated respiratory interventions such as ventilation and extra-corporeal membrane oxygenation (ECMO) can also be extracted.

Result

Currently, the database contains >3.3 million emergency department presentations by >1.9 million people to 177 health facilities. These match to at least 350,000 emergency services events, 1.5 million hospital admission records, 60,000 deaths, 61,000 influenza detections and 1,000 COVID-19 detections (as at December 2020).

Conclusion

The PEARL database can be used to emulate real-time public health surveillance of persons presenting to hospitals with an acute respiratory infection. Through record linkage, we aim to demonstrate how future surveillance systems using integrated, electronic medical and other records could provide a much richer and more useful source of surveillance information and epidemic risk assessment. The inclusion of emergency service records will fill an important knowledge gap in the role of emergency services in pandemic health service use.

Catalina Pardo-Roa - AOXI0655

SARS-CoV-2 Genomic Surveillance in Chile: contributing from academia to a countrywide response

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Background

COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic in March 2020. To date, the virus continues to spread globally and has caused over 530 million cases and 6 million deaths. SARS-CoV-2 has shown high mutation rates. While most changes do not appear to provide a functional value, some mutations can alter the viral fitness, host-pathogen interactions, and antigenic properties. To prioritize the global surveillance, the WHO defined specific SARS-CoV-2 lineages as Variants of Concern (VOCs; e.g., B.1.617/Delta, B.1.1.529/Omicron); VOC Lineages Under Monitoring (VOC-LUM: e.g., BA.4, BA.5, BA.2.12.1) Variants of Interest and Variants Under Monitoring (not currently circulating). This classification system is continuously adjusted according to the global impact of each variant.

Method

To increase the real-time surveillance in Chile, we leverage clinical and surveillance infrastructure built through the Centre for Research on Influenza Pathogenesis (CRIP). Hence, in close collaboration with the UC-Christus Health network and the sequencing core at the Icahn School of Medicine at Mount Sinai in New York, we rapidly obtained 751 whole viral genomes utilizing the ILLUMINA platform. With support from the "SARS-CoV-2 Genomic Acceleration Plan", a public-private alliance led by the Ministry of Science, we also established an in-house whole-genome amplicon-based sequencing pipeline using the Oxford Nanopore Technology and designed a long-term surveillance program to generate high-quality sequences to rapidly elucidate the variants circulating at the community level in Santiago.

Result

This allowed us to sequence 1,735 samples in-house between March 2020 to March 2021, which resulted in 1466 (84.5%) whole genomes of SARS-CoV-2 uploaded to GISAID. Until now, our laboratory has generated more than 7% of all Chilean SARS-CoV-2 sequences, being the second largest contributor of sequences in the country. This work has allowed us to track the introduction and community transmission dynamics of the original pandemic outbreak and to rapidly identify and report to the authorities the community introduction of C.37/Lambda (February 2021), B.1.621/Mu (April 2021), and BA.1/Omicron (December 2021) SARS-CoV-2 variants in the Metropolitan Region.

Conclusion

Our efforts demonstrate the contribution of academia and research laboratories to expanding the capacity to monitor seasonal and emerging viruses of public health relevance, especially in developing countries. We highlight the value of having additional Centers capable of generating viral genomic data to complement the efforts of Public Health systems and monitor the emergence of variants and the need to update vaccine and diagnostic tools.

Mahesh Moorthy - AOXI0662

Dynamics of seasonal influenza at a tertiary hospital in South India

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Background

Globally, Influenza A and B viruses (IAV and IBV) are responsible for high disease burden, hospitalization and mortality. IAV(A/H1N1, A/H3N2) and IBV(Victoria and Yamagata lineage) cause influenza-like illness(ILI) and severe acute respiratory infection(SARI). IAV and IBV cause yearly epidemics of variable timing, intensity and time span. In lower-middle income countries (LMICs) like India, burden of severe disease is many fold higher than the developed world. Epidemiology (temporal trends, age distribution) and clinical outcomes of IAV and IBV infection can inform influenza vaccine implementation in the country (at-risk populations, vaccine composition and timing of vaccination). The onset of the COVID pandemic in early 2020, has resulted in 43 million cases and 524,000 reported deaths in India to-date. Community-level mitigation measures (universal mask usage, social distancing, and reduction of gatherings) and international air travel restriction during the pandemic resulted in a dramatic reduction in respiratory virus transmission and possible eradication of influenza B/ Yamagata lineage. We report the dynamics of influenza among ILI/SARI cases at a tertiary care hospital in India (South) over a 13-year period (2009-2021).

Method

Respiratory samples from patients presenting at Christian Medical College, Vellore between 2009 and 2021 with ILI and SARI, were tested for influenza viruses and IAV subtype (A/H1N1 or A/H3N2) by real time RT-PCR. The date and location of sampling (outpatient, ward or ICU admission) were captured from the diagnostic request.

Result

A total of 31208 samples received between 2009-2021 and influenza viruses were detected in 7045 (22%). IAV and IBV were detected in 5147 (16%) and 1832 (6%)cases, respectively with co-infections among 66 (0.2). Seasonal peaks of detection were seen with both subtypes of IAV (A/H1N1 and A/H3N2) and IBV with A/H1N1 was the predominant subtype overall (63%). Influenza viruses were detected in 26%, 21% and 15% of outpatients, ward admitted and ICU-admitted patients, respectively, with detection rates similar among age-groups. Due to the COVID-19 pandemic, the detection rate of influenza viruses in 2020 was <0.3% with a resurgence of A/H3N2 and influenza B (>2.5%) towards late-2021.

Conclusion

IAV and IBV caused a high burden of disease including severe disease during the period with seasonal peaks of varying intensity and timing. The onset of the COVID-19 pandemic caused a reduction in detection rates, with resurgence in late-2021 caused by A/H3N2 and influenza B.

Jessylene Ferreira - AOXI0593

GENETIC DIVERSITY AND SEASONAL PROFILE OF INFLUENZA A (H3N2) VIRUSES CIRCULATING IN NORTH AND NORTHEAST REGIONS OF BRAZIL

Wanderley Chagas Junior[1], Luana Barbagelata[1], Jessylene Ferreira[1], Amanda Mendes[1], Edivaldo Sousa Jr[1], Edna Filizzola[1], Wyller Mello[1], Rita Medeiros[2], Mirleide Santos[1]

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Background

The flu is a highly contagious disease and one of the main responsible for the cases of acute respiratory infections (ARI's), where it is estimated that 10% of the world population gets sick with influenza annually. The etiologic agent of influenza is the Influenza virus, which is subject to intense epidemiological surveillance due to epidemics and pandemics having a major impact on public health. Since its introduction into humans in 1968, Influenza A (H3N2) viruses have a high rate of genetic and antigenic variability, which has impacted the need to make 28 changes to the vaccine composition since then. Among the countless factors that may determine the circulation of these viruses, the climate is the one that stands out the most, since the occurrence of influenza is associated with colder seasons in countries with temperate climates and in rainy seasons in tropical regions. In light of this, this study aimed to describe the genetic diversity and seasonal pattern of Influenza A (H3N2) viruses in the North and Northeast regions of Brazil from January 2011 to December 2017.

Method

Thus, epidemiological analyzes were carried out from database and phylogenetic analyzes. The analysis of the gene encoding hemagglutinin (HA) was performed through the synthesis of complementary DNA (cDNA), amplification of the cDNA by polymerase chain reaction (PCR) and subsequent capillary electrophoresis based on the Sanger method. After obtaining the nucleotide sequences, phylogeographic analyzes were performed, in which the sequences used in this study were compared with sequences from other geographic regions.

Result

Of a total of 18,547 samples in the Evandro Chagas Institute's Respiratory Virus Laboratory 732 database, they were positive for influenza A (H3N2), indicating a detection rate of 3.95%. The year 2017 presented a higher frequency of detection with 8.01%. It was found that the period of greatest circulation was in the first months of the years analyzed, with the peak between the months of February to April, the period of greatest rainfall in the regions. The circulation of five phylogenetic clades 3C, 3C2A, 3C2A1, 3C2A2 and 3C3A was observed.

Conclusion

Therefore, it is confirmed that knowledge of the circulation profile and monitoring of phylogenetic variants of influenza viruses directly impact control and prevention measures, since the data obtained can support the best choice of vaccine strains, adequacy of the vaccine and auxiliary calendar in the adoption of prevention and control measures for this pathogen.

Jessylene Ferreira - AOXI0606

GENETIC DIVERSITY OF INFLUENZA C VIRUS STRAINS CIRCULATING IN THE CITY OF BELÉM, PARÁ, BRAZIL, IN THE YEARS 2015 TO 2017

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Background

Influenza viruses belong to the Orthomyxoviridae family and are subdivided into three main genus that cause disease in humans, they are: Alphainfluenzavirus, Betainfluenzavirus and Gammainfluenzavirus. Currently, the attention of the responsible agency for health surveillance, when it comes to influenza, it is exclusively dedicated to influenza viruses of genus A and B, known for the greater severity symptoms and their epidemiological characteristics. However, more recent studies have revealed the importance of respiratory infections caused by influenza C viruses. Unlike influenza A and B viruses, the detection of this infectious agent is not included in the routine diagnosis of public health laboratories, so epidemiological and molecular information about influenza C virus circulating in Brazil is still unknown. Thus, the aim of the study was analyze the genetic diversity of influenza C virus strains circulating in Belém city, Pará, Brazil, in the years 2015 to 2017.

Method

For this, clinical specimens (nasopharyngeal aspirate or combined swab) were included in the study. 660 outpatients with Acute respiratory infection (ARI) treated at the School Health Center of UEPA. The analysis of the samples included three main steps: a) extraction of the viral genome with a commercial kit; b) detection by RT-qPCR according to standardized protocol; c) complete sequencing of the influenza C virus genome using the synthesis system through the Illumina platform.

Result

Among the analyzed samples, influenza C virus vRNA was detected in seven (1%) of the samples by RT-qPCR, with children between one and seven years old being the group that concentrated the largest number of cases. Although the detection occurred in several months of the year, there was a predominance of cases in the first four months. Rhinovirus was detected in two of the three cases of co-detection with other respiratory viruses. In three of seven samples detected by RT-qPCR, was possible obtain and analyze the sequences based on the HEF, NP, PB1, PB2 and P3 genes for the influenza C virus, where all the strains analyzed were grouped in the lineage C/São Paulo/378/82.

Conclusion

Thus, this study represents the first report of molecular epidemiological data about influenza C virus in the northern region of Brazil. However, complementary studies are needed to better assess clinical aspects, seasonality and molecular characterization of this agent.

Jessylene Ferreira - AOXI0607

CIRCULATION DYNAMICS AND GENETIC DIVERSITY OF INFLUENZA A AND B VIRUS STRAINS ISOLATED IN THE METROPOLITAN REGION OF BELÉM-PA

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Background

Due to the impact on public health, the genetic characterization of seasonal viruses - influenza A (H1N1) pdm09, A (H3N2) and influenza B, is crucial to monitor their genetic diversity, considering their importance in the dynamics of circulation, vaccine formulation and possible failure in treatment. However, there is a lack of knowledge of these viruses in equatorial regions of Brazil. In this regard, the objective was to demonstrate the dynamics of circulation and genetic diversity of strains of influenza A and B strains isolated in the Metropolitan Region of Belém-PA from January 2015 to December 2019.

Method

For this, we used the RNA library of the Respiratory Virus Laboratory of the Evandro Chagas Institute, to proceed with the synthesis steps of the complementary DNA strand (cDNA), amplification of the cDNA and sequencing of the Hemagglutinin (HA) and Neuraminidase genes (NA).

Result

Thus, 86 influenza virus RNAs were found, 18 (21%) belonged to the influenza B virus and 68 (2.22%) to the influenza A virus, with a subtype A (H3N2) predominance. The co-circulation of influenza A and B viruses was observed, as well as between subtypes A (H3N2) and A (H1N1) pdm09, where the period of greatest viral activity was concentrated in the rainiest months of the year (March and April). Phylogenetic inferences exposed that subtype A (H1N1) pdm09 grouped in subgroups 6b.1 and 6b.1A; subtype A (H3N2) in clades 3c3A and 3c2A (subclasses A1, A2 and A3); and influenza B viruses in the B/Yamagata strain. There was a genetic discrepancy between circulating strains and vaccine strains in most of the years analyzed, for both influenza A and B viruses. Amino acidic substitutions were also visualized in the four antigenic sites of HA - Cb, Ca, As and Sb of subtype A (H1N1) pdm09, in three of the five antigenic sites of subtype A (H3N2) they are: site A, B and E, and also in loop 120 of influenza B viruses. In addition, the S247N substitution was detected in A (H1N1) pdm09 and was associated with decreased susceptibility to NA inhibitors.

Conclusion

In general, the results described here demonstrate the importance of a sentinel surveillance network in Belém-PA, aiming to strengthen the monitoring of the circulation activity and the genetic profile of influenza viruses, in order to promote information to contribute to prevention and control strategies flu.

Monica Galiano - AOXI0612

Long-term genome evolution of influenza B viruses and the emergence of the Yamagata lineage

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Background

Around 40 years ago, influenza B viruses split into two genetic lineages named after prototypes B/Yamagata/16/88 and B/Victoria/2/87, which have since co-circulated worldwide until recently. However, little is known about the genetic characteristics of older viruses prior to detection of these prototype viruses. Here we present the results of the evolutionary analysis of >800 influenza B genomes spanning over 70 years of evolution from the 1940s to 2020, including 300 newly-sequenced viruses collected before 1987.

Method

Virus isolates and clinical samples from the UK were obtained as part of the Public Health England (PHE-UKHSA) laboratory surveillance system. Viruses from around the world, received at the Worldwide Influenza Centre (WIC) as part of its duties as WHO Collaborating Centre, were retrieved from its archive. Viral RNA was extracted from influenza B cell or egg isolates, freeze-dried egg-propagated viruses and original influenza B-positive clinical specimens. PCR amplification was performed using a multi-segment RT-PCR strategy (Zhou et al, 2014). Amplicons were sequenced by Illumina paired-ends methodology. Sequence data was processed using in-house pipelines both at PHE-UKHSA and WIC. Whole genome (WG) sequences were used together with sampling dates to estimate the evolutionary history using Bayesian methods. Reassortment analysis was carried out with tanglegrams.

Result

Phylogenetic and sequence analysis revealed the existence of different populations characterised by in-frame HA-gene insertions/deletions resulting in HA glycoproteins of different lengths, with some co-circulating during the 1940-60s. The earliest B/Yamagata viruses dated from the early 1970s and were characterised by a 2-amino acid deletion in their HA; after 1990 they "switched" to a 1-amino acid deletion. Lineage-specific insertion and deletion events also appeared in NA and NS genes. Phylogenetic analysis showed a major split event for all segments, suggesting that the emergence of B/Yamagata viruses was a genome-wide occurrence. We observed some events of reassortment involving PB2, PB1 and HA segments soon after the emergence of B/Yamagata, however those quickly died out; the evolution of these segments continued to have distinct evolutionary lineages. Since the early 2000s, viruses with HA of the B/Victoria lineage have acquired NA, PA, NP, M and NS genes from the B/Yamagata lineage, maintaining this genome constellation to the present.

Conclusion

Evolutionary analyses suggest that emergence of the B/Yamagata lineage was a major genome-wide event. Amino acid deletions and insertions, as well as reassortment events, play key roles in the evolution of influenza B viruses.

Jessylene Ferreira - AOXI0644

SEASONALITY AND PHYLOGEOGRAPHIC DISPERSION OF INFLUENZA A(H1N1)pdm09 VIRUSES ISOLATED IN THE NORTH AND NORTHEAST REGIONS OF BRAZIL

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Background

Influenza virus is the etiological agent of influenza, a highly contagious disease that affects the respiratory tract, Due to this, the pathogen is a major surveillance target and also because of its ability to cause epidemics and pandemics causing great impact on public health. In this context, occurred in 2009 the first pandemic of the 21st century caused by influenza A (H1N1) pdm09. The phylogeography has become an important epidemiological tool since it allows to predict the areas where the emergence and dissemination of infectious agents can occur through the analysis of phylogenetic data. In Brazil, little is known about the routes of dispersion of influenza A (H1N1) virus pdm09. Therefore, the objective of this study was to describe the seasonality, circulation of clades and phylogeographic dispersion of influenza A (H1N1) pdm09 strains circulating in the North and Northeast regions of Brazil, from 2011 to 2016.

Method

For this, epidemiological and genetic analyzis were performed. In the latter, the characterization of the gene coding for hemagglutinin (HA) through complementary DNA synthesis (cDNA), cDNA amplification by PCR and sequencing by the Sanger method. After obtaining the nucleotide sequences, phylogeographic analyzis were performed, in which the sequences of this study were compared with sequences from other geographical regions representative of each continent, for the same period.

Result

After such analyzis, it was verified that of the 16,248 samples collected in the period studied, 1,204 were positive for H1N1pdm09, with a detection rate of 7.41%. The year of 2016 presented the highest frequency of detection with 16%. In the evaluated regions the H1N1pdm09 virus circulated mainly in the first six months in most of the years. This period represents the months of greatest rainfall in these regions, and in the year of 2015 there was no detection of the H1N1pdm09 virus. In the period evaluated, it was possible to identify the circulation of six distinct phylogenetic groups: 4, 6, 6b, 6b.1, 6c and 7. The groups that circulated in the North and Northeast regions of Brazil were mainly from other regions of the world, with North America being the main source of influenza A (H1N1) pdm09 virus spread to the Northeast region of Brazil. Within Brazil, the largest flow occurred from the Northeast to the North.

Conclusion

Epidemiological surveillance and studies on the dynamics of circulation of influenza viruses in the North and Northeast regions of Brazil are fundamental for public health, since the data obtained can subsidize the best choice of vaccine strains, suitability of the vaccination schedule, and aid in the adoption of prevention and control measures of this pathogen.

Sheena Sullivan - AOXI0657

Post-pandemic re-emergence of influenza in Victoria, Australia

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Background

COVID-19 pandemic mitigation measures, including travel restrictions, effectively limited global circulation of influenza viruses for much of 2020 and 2021. In Australia, travel bans for non-residents and quarantine requirements for returned travellers were lifted in November 2021, contingent on COVID-19-vaccination. The reopening of borders and reinvigoration of international travel provided pathways for influenza viruses to recirculate. Here, we describe the reintroduction of influenza in the state of Victoria.

Method

Influenza is notifiable in Australia, with confirmed cases required to be reported by pathology services to the relevant public health authority. We attempted to contact the first 200 cases notified to the Victorian Department of Health after borders reopened on 1 November 2021. We collected travel history, exposure to agricultural settings, known exposures to influenza cases, vaccination status, pathway to testing, and risk factors for severe disease. Concurrently, pathology services were asked to forward all specimens positive for influenza to the WHO Collaborating Centre for Influenza in Melbourne for characterisation. These viruses were grown in cell culture and assessed genetically by whole genome sequencing.

Result

Between 1 November 2021 and 31 May 2022 >17,000 cases were notified to the Department of Health. The first 200 cases were tested between 7 December 2021 and 6 April 2022, of which 122 were interviewed. Most cases (n=101/122) reported testing for SARS-CoV-2 by rapid antigen test prior to influenza testing, which may delayed diagnosis. Nine had a history of international travel within 1 week of diagnosis, six of whom travelled in December (6/25 cases). Case numbers subsided in January (n=13) and February (n=3), coinciding with a SARS-CoV-2 Omicron epidemic. However, from late March 2022, a sharp increase in cases was observed, many of whom lived in residential colleges co-located around a single university campus. Initial sequencing data from March-April indicate circulation of a restricted virus population of influenza A(H3N2) suggesting an initial point-source outbreak.

Conclusion

Importations of influenza in December-February did not result in known influenza outbreaks in Victoria. However, an outbreak in March may have initiated widespread community transmission of A(H3N2). Updated data will be reported, including further genetic analysis, to identify emergence of heterogeneity in the virus population, and serological analyses to understand population susceptibility after nearly 2 years without exposure.

Kin On KWOK - AOXI0585

Development of SARIMA forecasting prediction model for pre-pandemic influenza preparedness using Influenza like illness (ILI) hospital episode data in Hong Kong

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Background

Seasonal and pandemic influenza both pose substantial challenges and burdens to health systems around the world. Near-term forecasting of incidence and the estimation of per-infection severity can be considered as two important measures to decide key intervention policy decisions. However, there is still uncertainty about both of these during seasonal epidemics and during pandemics. The availability of large-scale historic clinical episode data generated by Electronic Health Records (EHRs) combined with disease-dynamic models can shorten the time to characterize the severity of novel respiratory pathogens and also potentially provide real-time forecasts, thus reducing uncertainty at these crucial times. In light of this, we develop a validated suite of models to predict influenza incidence in the future.

Method

We developed a SARIMA forecasting model with weekly hospital records of influenza-like illness (ILI) episodes from all hospital clusters in Hong Kong from the first week of 2011 to February 2019 to predict the (ILI) hospital episodes in 2018/2019 influenza season from February 2019 to last week of April 2019. Two standards (loose and strict) based on the level of accuracy in predicting the epidemic onset, the duration of the epidemic, magnitude and timing of the peak were used to evaluate the goodness of fit of the predictive models. We also developed a null model using the moving average of ILI episodes within two days for comparison and assistance in modelling.

Result

Our SARIMA model (SARIMA(0,1,3,0,1,1)66) was able to forecast both the peaking timing and magnitude of influenza in 2018/2019. Average forecast accuracies were 90.06 and 100 respectively in terms of both peak timing and peaking magnitude at 4-5 week advances. Forecast accuracy varied by the start point of the forecast. Our SARIMA model had initially proved to be predicting peak outcome of the upcoming influenza events quite well, amid variation of the starting point and the period of the forecast.

Conclusion

This study will develop a calibrated transmission model using historic hospital episode data to provide world-leading severity knowledge for pandemic and seasonal influenza. With this validated model and input of new electronic health records, regular updates on the influenza episode as well as the timing of epidemics can be estimated. Therefore, there will possibly be an opportunity to characterize the next pandemic in Hong Kong.

Thomas Shin - AOXI0651

Investigating the Relationship between Canadian and Australian Influenza Trends

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Background

In preparation for every upcoming influenza season, Canadian public health officials may speculate about disease severity by observing Australia's preceding influenza season. Although viewed as a "moderate" litmus test in Canada, there is a lack of peer-reviewed evidence to support this. Given the current environment, incremental insights in disease forecasting could provide timely support to public health stakeholders. As such, this study will aim to investigate the relationship between Canada and Australia's influenza seasons.

Method

The WHO FluNet surveillance data (from 1996 to 2020) was retrieved for Canada, Australia, and Chile. Descriptive statistics and data visualizations were generated for both countries. Overall, three approaches were implemented: cross-correlation (CCF), logistic regression, and artificial neural networks (ANN). Each approach required preparation/adjustments to the data and provided insights regarding the temporal correlation, magnitude, and directionality of any existing relationship.

Result

Throughout 23 seasons, the circulating strain of influenza was matched for 15 seasons (n=12 H3N2, n=3 H1N1) between Canada and Australia. The CCF analysis with Granger Causality tests revealed temporally correlated weeks with strong directionality between Canada and Australia. The quasi-Poisson modelling for influenza activity in Australia indicated the incidence rate for influenza in Canada was approximately two times higher when there was an increase in total A strain case activity in Australia. Furthermore, the ANN illustrated the predictive relationship between Australia and Canada with 70% accuracy, 54% sensitivity, 71% specificity, and PPV/NPV of 9% and 97%.

Conclusion

The seasonality and nuances of influenza are unpredictable and complex. However, the current evidence suggests a moderate relationship between Canada and Australia's influenza seasons over 23 years. While this may provide additional support/insights for public health preparedness, additional comparators (i.e. countries) in the southern hemisphere may help improve the robustness of this analysis.

George Okoli - AOXI0595

Impact of the universal seasonal influenza vaccination policy in Manitoba, Canada: a population-based, province-wide record-linkage study

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Background

Manitoba, Canada introduced universal seasonal influenza vaccination policy (USIVP) in 2010, providing seasonal influenza vaccine (SIV) free-of-charge to registered residents (Manitobans) at least, six months of age. Despite the USIVP and availability of SIV in Manitoba, SIV uptake (receipt of vaccine) remained suboptimal even among the high-risk individuals for whom seasonal influenza vaccination is highly recommended. Impact of the USIVP on SIV uptake remains unclear, as there is a lack of published evaluations.

Method

We conducted an ecological study utilizing the Manitoba immunization registry linked with other Manitoba administrative health databases. The study period was from 2000/01 to 2019/20 influenza seasons. The primary exposure was USIVP (five influenza seasons pre-policy [2005/06 to 2009/10] compared with post-policy [2010/1 to 2014/15]). The outcome was SIV uptake. We conducted pre-post logistic regression analysis stratified by age groups (<5, 5-17, 18-44, 45-64, ≥65 year-olds) and certain population socioeconomic and health-related characteristics. We presented results as adjusted odds ratios with 95% confidence intervals (CI).

Result

The adjusted odds of SIV uptake post-policy relative to pre-policy was significantly increased among all age groups except for ≥65 year-olds. The odds ratios ranged from 0.76 (95%CI 0.75-0.76) among ≥65 year-olds to 2.15 (95%CI 2.13-2.18) among 5-17 year-olds, but were largely homogeneous within age groups across sex, income quintile, and region of residence, and across categories of number of visits to primary care physician/hospitalization one year prior to an influenza season, except among <5 and 5-17 year-olds. Within age groups, the odds ratios were higher for not having a chronic disease compared with having, except for ≥65 year-olds among whom we observed homogeneity. These findings were mostly consistent irrespective of sex and region of residence although there was variability across income quintiles in Northern Manitoba.

Conclusion

USIVP possibly led to increased SIV uptake among age groups <65 years in Manitoba and may have had similar impact on SIV uptake across important population characteristics within age groups. The variation across income quintiles in predominantly indigenous Northern Manitoba requires attention.

Almiro Tivane - AOXI0641

Varying influenza seasonality in Maputo: implications on control strategies

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Background

Influenza characteristics and circulation patterns is crucial for the effective control measures. This study aimed to analyze the seasonal behavior of influenza viruses in Maputo and discuss possible challenges for the control.

Method

Influenza seasonality during eight consecutive epidemic seasons (2015-2022) in Maputo, Mozambique was analyzed and compared to global patterns. Antigenic and genetic characteristics of Maputo isolates were also compared to vaccine and global strains.

Result

With exception to 2017 that higher influenza activity peaked at year-end, all the analyzed seasons exhibited at least on peak at the year beginning, with varying start points (January to March); seconds peaks were observed at the mid-year in 2015, and year-end in 2018 seasons. Although varying seasonality, these patterns were more likely to coincide with northern hemisphere than southern season; with few exceptions, genetic strains are more likely to be detected first in Maputo, before are isolated in South Africa and after NH countries. From 2015 to 2017 seasons, Mozambique isolates were antigenically similar to vaccine strains recommended for both hemispheres, but the 2018 influenza A(H3N2) and all 2019 influenza isolates were different from SH vaccine strains. Vaccination strategies for northern hemisphere countries should be considered for Mozambique.

Conclusion

Mozambique influenza seasonality is variable but seems to be more influenced seasonally, antigenically, and genetically by northern hemisphere patterns. Further monitoring and analysis are required for precise conclusions

Susanne Oberle - AOXI0597

The burden of influenza in the Swiss adult population during the 2018/19 season

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Background

Although influenza and its complications are known to pose a heavy burden on patients and payers, evidence on the burden of influenza and its determinants is still scarce in Switzerland. Standard-dose quadrivalent vaccines are the current standard of care in Switzerland but vaccination rates are low. The objective of this study was to assess influenza-related resource utilization, excess mortality and associated health care expenditures in Switzerland during the Influenza A dominant 2018/19 season.

Method

The study population included Swiss residents aged 18+ years. Subgroup analyses were performed for age groups 18 - 49, 50 - 64 and 65+ years. The observation period was one year between week 26 2018 and week 25 2019. We estimated the number of general practitioner (GP) visits for influenza-like illness (ILI) using data from a sentinel monitoring system covering 1.8% of the population and the number of inpatient stays with influenza primary diagnoses (ICD-10-GM J10, J11) in a complete registry of all inpatient cases in the country. Excess mortality was estimated using a negative binomial regression of weekly nation-wide all-cause mortality rates on weekly influenza incidence and temperature over the period 2011 - 2019. Resource use in the 2018/19 season was valued using 2022 tariff rates.

Result

A projection from the sentinel monitoring system suggested 176,439 GP visits for ILI in the Swiss adult population (2.52% incidence rate). 5,303 cases were hospitalized with influenza as the primary diagnosis of which 97% were laboratory-confirmed. 93.2% of hospitalized cases were admitted through the emergency department, 4.8% received intensive care, 6.7% were discharged to inpatient rehabilitation, 37.3% received a recommendation for post-discharge outpatient care and 2.4% died in the hospital. We estimated 1,120 (16 per 100,000) excess deaths due to influenza in the Swiss adult population.

Patients aged 65+ were less likely to see a GP for ILI than patients of age 18 - 49 or 50 - 64 years (1,595 vs. 2,902 or 2,537 visits per 100,000) but were more likely to get hospitalized (250.3 vs. 14.6 or 45.9 admissions per 100,000) or die due to influenza in- and outside hospitals (63.8 vs. 1.4 or 3.5 deaths per 100,000).

Total inpatient care costs amounted to more than EUR 51 Mio. At an average life expectancy of 12.71 years at premature death, 16,726 life- years were lost due to influenza in the Swiss adult population.

Conclusion

The burden of influenza on patients and payers is significant and particularly high in the elderly population. Policy interventions to increase vaccination rates as well as uptake of more effective vaccines among the elderly are needed to reduce the burden of influenza in Switzerland.

Haya Hayek - AOXI0636

Influenza detection at academic hospital before and during COVID-19 pandemic

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Background

The seasonality of influenza was altered after community mitigation measures were implemented during the SARS-CoV-2 pandemic. Since restrictions have been relaxed, reports of influenza circulation are limited. We aimed to describe the circulation of influenza before and during the COVID-19 pandemic in Nashville, TN.

Method

We conducted a retrospective cohort study of clinician-ordered multiplex molecular testing using the BioFire® FilmArray Respiratory Pathogen Panel (RPP) 2.0 from April 2018 to April 2022 at Vanderbilt University Medical Center (Nashville, TN). The RPP includes 21 common respiratory pathogens, including influenza A and B. Overall and age-specific detection frequencies were analyzed for influenza A and B. Descriptive statistics were reported for these groups.

Result

A total of 49,780 samples were tested, and 1,281 (2.6%) were influenza positive: 72.9% and 27.1% were influenza A and B, respectively. Demographic characteristics are shown in Table 1, with higher influenza B detection in children (66.2%). Frequency of influenza detection over time is shown in Figure 1. Influenza reached peak circulation during the pre-pandemic winter months; however, after the introduction of SARS-CoV-2 in March 2020 and the initiation of community mitigation measures, influenza circulation abruptly ceased but then reappeared in November 2021 (Figures 1 and 2).

Conclusion

Influenza circulation markedly decreased after community mitigation measures were implemented in March 2020 and resurgence was not observed until the winter following the relaxation of community measures. Our study suggests infection control practices, such as wearing a mask, handwashing, and social distancing, may effectively limit community transmission of influenza.

Nicolas Noulin - AOXI0664

Initial characteristics of respiratory viruses in symptomatic subjects during the pandemic, a cohort study

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Background

During the most intense waves of the recent pandemic, we have witnessed an intense and almost complete wipe-out of many respiratory viruses routinely circulating in the community over the north-hemisphere winter. As such situation never happened in the past, hVIVO team, based in the United Kingdom and more precisely in the London area, launched an active surveillance with the intent to assess the circulation and co-circulation of virus over the 2021-2022 winter.

Method

hVIVO employees, their relatives and friends were provided with collection kits and kindly asked to contribute to this research. When becoming symptomatic for respiratory virus-like infection, subjects were swabbing themselves and posted their samples by mails. kits were processed and tested by multiplex qualitative PCR. Adenovirus, Coronavirus 229E, HKU1, NL63, OC43, SARS-CoV-2, HMPV, Human Rhinovirus / Enterovirus, Flu A, Flu B, Parainfluenza Virus 1, 2, 3, 4 and RSV were tested. Symptomatic subjects also captured their clinical signs of infection and provided informed consent for the testing of their sample.

Result

Out of 349 samples collected to date, 217 (62.2%) tested positive for at least one of the viruses tested. Interestingly we observed 16 (4.6%) and 1 (0.3%) cases of double and triple infection respectively. The predominant viruses were enterovirus/rhinovirus, SARS-CoV-2 and coronavirus OC43 with 38.0 %, 24.8% and 12.8%. Remarkably, only 8 samples were positive for RSV and just 6 were found positive for influenza (5 type A and 1 type B). Further sample processing and data analysis are still ongoing and will be presented and discussed, linking especially to field surveillance programs.

Conclusion

Our results confirm the general observation that, over the past two winter seasons, the usual pattern of circulating respiratory viruses and their intensity were almost completely disrupted. Such testing program and analysis may contribute to predict which family of virus is most relevant for efficient public health preparedness.