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Epidemiology & Public Health

Article Type: Short Commentary

Volume 2 Issue 1 - 2024

Low Influenza Vaccine Uptake; What is the Impact in Hospitalised Children

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Abstract

Seasonal influenza is an RNA virus spread by droplets. The burden of disease is significant, particularly in children under five, and in those with underlying health conditions. Vaccination against influenza is effective and recommended for all children aged 2-16, and those from 6 months of age with underlying health conditions. We completed a retrospective study examining the notes of all patients presenting to a large tertiary children's hospital in the UK with confirmed seasonal influenza over the 2022/2023 season.

238 children were included in this study. 88/238 (37.0%) children in our cohort were under 2. 112/238 (47.1%) were discharged from ED. 41/238 (17.2%) were admitted for observation for 24 hours. 41/238(17.2%) stayed 3 days or longer. 1 child passed away. Overall 73/238 (30.6%) had a significant comorbidity, in those under 2 13/88 (14.8%) had a comorbidity. 13/238 (5.4%) were admitted to PICU or HDU. 30/238 (12.6%) received Oseltamivir, 114/238 (47.8%) children were given antibiotic therapy at presentation for a presumed secondary bacterial infection. 13/238 (5.4%) were vaccinated 14 days or more prior to presentation. 0 children admitted to HDU or PICU were vaccinated.

Due to delays and vaccine availability and hesitancy we had very low rates of vaccination. Our results show the impact of influenza on an unvaccinated cohort. Just under half of all children were given antibiotics for a presumed secondary bacterial infection. We highlight that a significant number did not have an underlying comorbidity. This is most notable in the under 2 cohort. This reinforces data supporting the importance of vaccination in children and raises the question of whether we should extend our vaccination program to cover all children over 6 months of age.

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Received: Jan 10, 2024

Accepted: Feb 12, 2024

Published: Feb 19, 2024

Epidemiology & Public Health - www.jpublichealth.org

Citation: Knappe F, Mather F, Tan LT, Stoate W, Pymont H, et al. Low Influenza Vaccine Uptake; what is the Impact in Hospitalised Children. Epidemiol Public Health. 2024; 2(1): 1031.

Keywords: Influenza; Viral infection; Respiratory infection.

Introduction

Seasonal influenza is a highly contagious RNA virus that can cause illnesses ranging from mild to severe. It is spread via large droplets and has a relatively short incubation period of 2 days. Influenza causes a substantial disease burden in children, particularly those under the age of five, with an estimated 109 million episodes per year worldwide [1]. Symptoms are initially non-specific with fever, headache and myalgia. While it is self-limiting in most patients it can lead to life-threatening lower respiratory tract complications such as Acute Respiratory Distress Syndrome (ARDS) and predispose to secondary bacterial infection particularly pneumonia. There are a range of non-infective complications such as febrile convulsions and myocarditis also rarely associated with influenza. Risk factors for serious infection include those under the age of 6 months,

patients with severe immunosuppression, those with diabetes and underlying neurological, pulmonary, hepatic and cardiac disease [2]. The severe complications however can also occur in healthy children [3].

Typically influenza causes annual outbreaks; these are greatest when antigenic shift occurs, although each year minor changes known as antigenic drift occur. It has been estimated that in 2018 there were 109 million cases globally and around 870,000 hospital admissions with influenza associated acute lower respiratory infection [1]. Children are considered a key driving group of influenza transmission in the community, especially those between 5 and 17 years of age [4].

Vaccination remains the most effective measure to protect against influenza. It also leads to a significant reduction in the morbidity and mortality risks associated with influenza infection in children and adults [5]. Vaccination can be given as either an inactivated vaccine or a Live Attenuated Vaccine (LAIV) which is given intranasally. The UK immunisation Green Book recommends all 2-16 year old receive the LAIV vaccine [2]. Data from 21/22 season showed vaccine uptake among 2 and 3 year olds was 50.1%. In primary school aged children (age 4 to 11 years old) uptake was 57.4% and in secondary school aged children (11 to 16 years old) it was 43.6% [6]. Those with underlying risk factors who cannot have the LAIV should be offered the inactivated vaccine. This can be given from 6 months of age [2]. Vaccine efficacy is greatest for the LAIV. It has been estimated that for every 7 children immunised 1 case of influenza will be prevented [5].

Antiviral drugs against influenza, are an important treatment option for many patients. These work by inhibiting the activity of viral neuraminidase which prevents viral replication. Neuraminidase inhibitors such as Oseltamivir or Zanamivir may reduce the risk lower respiratory tract complications, hospitalization, severe illness, or death compared with placebo or no treatment [7]. Therefore, guidance from UKHSA highlights that patients with complex infection (defined as those requiring hospitalisation and/or those with signs of lower respiratory tract infection, Central Nervous System (CNS) involvement or a significant exacerbation of an underlying medical condition) should be given Oseltamavir [8].

We describe the vaccination status, clinical characteristics, management, and outcomes of all children and adolescents under the age of 16 with laboratory confirmed influenza who presented to a tertiary children's hospital in the UK during the 2022/2023 influenza season.

Methods

We performed a retrospective study of all children and young people under the age of 16 who presented to the Bristol Royal Hospital for Children with the confirmed influenza during the 2022/2023 season. The Bristol Royal Hospital for Children is a tertiary referral centre in the UK with 190 beds.

All patients had a standardised sample collection on admission. Influenza was confirmed for using the Cepheid Xpert Xpress CoV-2/Flu/RSV plus. Bacterial cultures, extended respiratory viral panel PCRs and chest X-ray were recorded where they had been taken. All microbiology tests were performed according to the UK standards for microbiology investigations (UK SMI). Data on patient demographics, clinical symptoms, vaccination status, comorbidities and management was obtained via electronic patient records.

For statistical analysis data is expressed as descriptive statistics as number and percentage.

Results

Demographics

238 children were included in this study. Demographic data on age, comorbidities and ethnicity is displayed in Figure 1. 165/238 (69.3%) of patients did not have a significant comorbidity.

Outcome

112/238 (47.1%) were discharged from ED. 41/238 (17.2%) were admitted for observation for 24 hours. 41/238(17.2%) stayed 3 days or longer with the longest admission being 22 days. 1 child passed away. They were an out of hospital cardiac arrest transferred to PICU. They also tested positive for adenovirus. They had no known comorbidities and the cause of the arrest was unclear. 22/238 (9.2%) represented to ED in the subsequent 4 weeks of these 8/22(36.4%) were readmitted.

Admission to HDU/PICU

8/238 (3.4%) children were admitted to the Paediatric Intensive Care Unit(PICU). 1 patient was an out of hospital arrest who passed away, 1 had asthma and another metachromatic leucodystrophy. 6/8(75%) children did not have an underlying comorbidity. 6/8(75%) had evidence of lower respiratory tract infection (LRTI), 1 had an empyema which was drained, 1 had a normal CXR.

5/238 (2.1%) children went to the HDU (high dependency unit). 3/5 (60%) had no underlying comorbidities, 1 had mild learning difficulties and the other Friedreich's ataxia. One had concurrent RSV and another tested positive rhinovirus/enterovirus. Two children had a normal chest X-ray and did not require antibiotics. The remaining 3 had evidence of LRTI.

None of the children admitted to PICU or HDU were vaccinated at the time of admission.

Concurrent viral infection

46/238 (19%) had concurrent viral infection (Figure 1). No children had more than 1 virus present. Of note not all children had an extended respiratory panel sent.

Concurrent bacterial infection

41 children had a bacterial throat swab sent. 5 were positive for Group A strep. 1 child had a positive blood culture with Moraxella, another had a micrococcus that was felt to be a contaminant. 3 were positive for Bordetella pertussis on PCR. No children had a positive pneumococcal urinary antigen.

Management

30/238 (12.6%) received Oseltamivir. 110/238 (46.2%) children were given antibiotic therapy. The indication for this is summarised in Figure 1 with lower respiratory tract infection the most common cause 47/238 (19.7%). 30/238 (12.6%) were initially given Ceftriaxone, 26/30 (86%) had Ceftriaxone stopped after 48 hours indicating a large number of children were covered for sepsis at presentation. 8/238 (3.3%) were treated for tonsillitis.

Vaccination

106/238 (44.5%) weren't eligible for vaccination due to age.

Of the remaining 132 eligible, 88/132 (66.6%) were not vaccinated and 44/132 were vaccinated (33.3%). 5/44(11.3%) were given the inactivated flu vaccine, 39(88.6%) were given the live attenuated influenza vaccine.

19/44 (43%) were vaccinated after they presented with influenza. Of the 25 vaccinated before presentation and a further 12 were within 14 days of presentation suggesting antibody levels may not have been sufficient. In summary 13/238 (5.4%) patients in this cohort were vaccinated against influenza in a time frame that could have protected them against influenza. Given the low numbers we felt we could do a full subgroup analysis on the vaccinated group. It was however noted that the proportion of vaccinated children admitted was lower.

Discussion

Our results highlight the significant burden of influenza in children. Secondary bacterial infection is common following influenza and this was shown with the high numbers requiring antibiotics for LRTI, as well as other bacterial complications such as tracheitis, and empyema seen. A Group A streptococcal infection epidemic that peaked at week 49 (2 weeks prior to influenza) further added to this [9]. This put health systems under increased pressure with large numbers of children presenting to both ED and GP practices. The impact on otherwise healthy children was also notable. 69.9% of children presenting did not have an underlying comorbidity and 69.2% admitted to ITU or HDU did not having any underlying health conditions.

Vaccination uptake was particularly poor in our cohort. Issues with timing were marked showing that even those that were vaccinated were vaccinated late in the season. Usually the influenza season peaks after Christmas however this year influenza rates peaked at week 51. Nationally uptake was 43.7% for 2 and 3 year olds, and school uptake (4-14) was 51.9% [5]. This is higher than our cohort. The reasons behind vaccine hesitancy are complex, however it was concerning to find that even children with risk factors for disease such as asthma were not vaccinated. In our cohort 7/13 (53.8%) children with asthma eligible for vaccination were unvaccinated.

Reducing the age of routine vaccination to include children from 6 months is another potential area for research. 88/238 (37.0%) children in our cohort were under 2. While those with significant comorbidities will be offered the inactivated vaccine from 6 months, 75/88 (85.2%) did not have an underlying comorbidity and therefore would not have been offered vaccination.

If the UKHSA guidelines were implemented all patient's admitted or those with underlying comorbidities should have been provided with Oseltamivir. In our cohort only around 12.6% received Oseltamivir. Much reluctance comes from concerns around efficacy particularly if given late into illness and mild side effects such as vomiting [10]. More work is required to increase use in hospitalised patients.

This paper highlights the impact of influenza and provides key information on the morbidity seen in children and adolescents. Further research is required to improve vaccine uptake and evaluate vaccination in children under the age of 2.

Conflicts of interest: No conflicts or sources of support.

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