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Influenza vaccine effectiveness in hospitalised Hong Kong children: Feasibility of estimates from routine surveillance data

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ABSTRACT

Background: Hong Kong has a high burden of influenza hospitalisation. This study estimated influenza vaccine effectiveness in hospitalised Hong Kong children aged 6 months to below 6 years using data potentially obtainable from routine surveillance sources.
Methods: This 'test-negative' case-control study was conducted over two summer and one winter influenza seasons in five public Hong Kong hospitals during 2015 and 2016. Patients admitted for febrile and/or respiratory-associated illnesses who met inclusion criteria were invited to participate. Case-patients were respiratory-associated admissions with nasopharyngeal aspirate or nasopharyngeal swab specimens obtained during the first 48 h of hospitalisation that tested positive for influenza A or B, whereas control-patients were those with specimens that tested negative for both influenza A and B. Reliability of a routinely collected influenza immunisation status form was evaluated. Vaccine effectiveness for administration of full or partial series of influenza vaccination was calculated as 1 minus the odds ratio for influenza vaccination history for case-patients versus control-patients.
Results: 2900 eligible subjects had influenza vaccination status available. A simple record form, designed to collect upon admission information on influenza vaccination status, was found to be reliable when compared to confirmed vaccination status from immunisation records and guardians' self-reports. Influenza vaccine effectiveness for preventing influenza A or B hospitalisation in children aged from 6 months to below 6 years during the period June 2015 to November 2016 was 68% (95% confidence interval [CI]: 55%, 77%) from unconditional analyses and 64% (95% CI: 46%, 75%) from conditional analyses.
Conclusions: Seasonal influenza vaccine was effective in preventing hospitalisation from influenza A or B in young Hong Kong children during 2015 and 2016. As influenza vaccination status is not currently routinely recorded, implementation of an influenza immunisation status form in all paediatric wards, and centralising the data in Hong Kong's central computerised database, could provide real-time monitoring of influenza vaccine effectiveness.

1. Introduction

Influenza is a leading cause of hospitalisation among children and the elderly in Hong Kong. All admissions to public hospitals (Hospital Authority, HA) in Hong Kong have discharge diagnoses recorded in a central computerised database (Clinical Management System, CMS). An analysis of the CMS database for April 2005 through March 2011 showed an unadjusted incidence rate of influenza of 1295–2906 per 100,000 person-years in children aged

Abbreviations: CDARS, Clinical Data Analysis and Reporting System; CHP, Centre for Health Protection; CI, confidence interval; CMS, Clinical Management System; HA, Hospital Authority; IF, immunofluorescence; NPA, nasopharyngeal aspirate; NPS, nasopharyngeal swab; OR, odds ratio; RT-PCR, reverse-transcriptase-polymerase chain reaction.

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below 5 years [1]. This study also indicated that the CMS discharge diagnoses under-estimated the influenza disease burden when compared to laboratory results.

Influenza vaccine effectiveness is increasingly being evaluated with studies using test-negative design [2]. In these 'test-negative' studies, patients with respiratory-associated illnesses are investigated and those testing positive for influenza are included in the case group and those with specimens testing negative for influenza in the control group. A recent 'test-negative' case-control study in Hong Kong showed overall influenza vaccine effectiveness against hospitalisation, with laboratory-confirmed influenza A or B, was 62% (95% confidence interval [CI]: 43%, 74%) during 2009 to 2013 [3].

Hong Kong has two influenza peaks each year, a small summer peak and a larger winter peak [4]. It uses the Northern Hemisphere influenza vaccine prior to the winter peak. The seasonality and variability of influenza vaccine effectiveness makes it desirable to have a system using routine surveillance data to monitor influenza vaccine effectiveness. The CMS currently collects discharge diagnoses and laboratory results for hospitalised patients, but not influenza immunisation status. This study aimed to determine whether data on influenza immunisation status could be routinely collected and used with laboratory data to monitor influenza vaccine effectiveness in hospitalised Hong Kong children aged 6 months to below 6 years.

2. Methodology

2.1. Subjects

A 'test-negative' case-control study was conducted over three periods of increased influenza activity in Hong Kong during 2015 and 2016 (2014/2015 summer influenza season and 2015/2016 winter and summer influenza seasons), to assess the effectiveness of influenza vaccine in children aged 6 months to below 6 years who were admitted to Hong Kong public hospitals with respiratory-associated illnesses. Hong Kong's HA manages 12 government funded hospitals, grouped into 7 geographical clusters, that provide general paediatric services. Hong Kong residents from all socioeconomic backgrounds can use these public hospitals that provide approximately 71% of all inpatient care [5]. This study was conducted in five public hospitals located in five clusters: Kwong Wah Hospital, Prince of Wales Hospital, Queen Elizabeth Hospital, Tuen Mun Hospital and United Christian Hospital.

All consecutive febrile or respiratory-associated admissions were considered for enrolment. Febrile illness was defined as having a body temperature of more than or equal to 38 °C. Respiratory-associated illness included, but was not limited to, fever, runny nose, cough and respiratory distress. Families were invited to participate if their children met the inclusion criteria: (1) admitted to one of the study hospitals for treatment of a febrile or respiratory-associated illness during the study period; (2) aged from 6 months to below 6 years; (3) onset of symptoms started less than 7 days before admission; and (4) normally received vaccination and/or medical care in Hong Kong. Patients with parents or guardians unable to speak Chinese (Cantonese or Mandarin) or English were excluded.

Since the admission records at recruitment may not reflect the actual diagnoses of patients, subsequently some recruited subjects were found not to be admitted for respiratory-associated illnesses. Final diagnoses or discharge summaries of recruited subjects were reviewed independently by two authors (EASN and KCCC), and non-respiratory-associated patients were excluded from the analyses. Subjects who were hospitalised for more than 6 months during the recruitment period or without any nasopharyngeal aspirate (NPA) or nasopharyngeal swab (NPS) specimens collected and tested for influenza within the first 48 h of hospitalisation, were also excluded.

Recruitment was started before Hong Kong entered anticipated influenza seasons during 2015 and 2016. Subject recruitment concluded when peak influenza activity was reported by the Department of Health to have ended. Potential respiratory-associated patients were identified from admission records. As part of standard hospital practice, influenza virus testing is performed routinely on NPA or NPS specimens collected from all those patients admitted for respiratory-associated illnesses at the five study hospitals. Specimens are tested for influenza virus by immunofluorescence (IF) test, conventional virus culture or rapid antigen test. Specimens may also undergo reverse-transcriptase-polymerase chain reaction (RT-PCR) by the hospital laboratory and/or the Department of Health. RT-PCR is regarded as a gold standard for influenza virus detection with higher sensitivity [6]. All patient information, including laboratory test results for every clinical admission, is routinely entered into the CMS and included in the Clinical Data Analysis and Reporting System (CDARS). CDARS has been implemented in the HA since 2002 and facilitates the retrieval of clinical data [7]. In this study, laboratory results on influenza virus detection were obtained from CDARS.

A case-patient was defined as a respiratory-associated recruited subject with NPA or NPS specimen(s) obtained during the first 48 h of hospitalisation that tested positive for influenza A or B, while a control-patient was defined as a respiratory-associated recruited subject with specimens that tested negative for both influenza A and B.

2.2. Data collection

A standardised questionnaire [8], modified for respiratory-associated hospitalisation, collected demographic information, birth and medical history from parents or guardians. Patients' admission details, disease severity, treatments, discharge diagnoses and laboratory results were obtained from the medical records. Copies of subjects' immunisation records were collected after the interviews but if not available, verbal reports of vaccination history were obtained and copies of immunisation records were requested to be sent by text message, e-mail, fax or post. Since influenza vaccination history is not routinely collected and entered into the CMS or CDARS, the same set of questions for verbal influenza vaccination history was asked by ward staff (usually nurses or ward clerks on duty) on admission in four of the five study hospitals. An initial more detailed record form was used in 2014/2015 summer influenza season (version 1, Appendix) but this had a low completion rate and was not well understood by ward staff. Hence, two versions of a simplified record form, that did not ask about the types of influenza vaccines received, were piloted before the start of the 2015/2016 winter influenza season (versions 2 and 3, Appendix). After gathering feedback from ward staff and guardians of patients, the simplest influenza immunisation status form (version 3, Appendix) was adopted for use in the 2015/2016 winter and summer influenza seasons in four of the five study hospitals.

2.3. Influenza vaccination status

A subject was considered as vaccinated for an influenza season if he/she had received at least one dose of influenza vaccine for that season. Subjects were regarded as partially vaccinated if vaccinated for the first time and received only one dose of influenza vaccine in that season. Otherwise, they were considered to be fully vaccinated. A dose of vaccine was considered as relevant if administered at least 14 days before admission, when the date of last

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