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Effectiveness of seasonal trivalent influenza vaccination against hospital-attended acute respiratory infections in pregnant women: A retrospective cohort study

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ABSTRACT

Background: Pregnant women are at risk of serious influenza infection. Although previous studies indicate maternal influenza vaccination can prevent hospitalisation in young infants, there is limited evidence of the effect in mothers.
Methods: A cohort of 34,701 pregnant women delivering between 1 April 2012 and 31 December 2013 was created using birth records. Principal diagnosis codes from hospital emergency department (ED) and inpatient records were used to identify episodes of acute respiratory illness (ARI) during the 2012 and 2013 southern hemisphere influenza seasons. Cox regression models were used to calculate adjusted hazard ratios (aHRs) by maternal vaccination status, controlling for Indigenous status, socioeconomic level, medical conditions, and week of delivery.
Results: 3,007 (8.7%) women received a seasonal influenza vaccine during pregnancy. Vaccinated women were less likely to visit an ED during pregnancy for an ARI (9.7 visits per 10,000 person-days vs. 35.5 visits per 10,000 person-days; aHR: 0.19, 95% CI: 0.05–0.68). Vaccinated women were also less likely to be hospitalised with an ARI compared to unvaccinated women (16.2 hospitalisations per 10,000 person-days vs. 34.0 hospitalisations per 10,000 person-days; aHR: 0.35, 95% CI: 0.13–0.97).
Conclusions: Influenza vaccination during pregnancy was associated with significantly fewer hospital attendances for ARI in pregnant women.

1. Background

Seasonal influenza causes serious morbidity and mortality during annual epidemics, leading to nearly five million cases of severe illness and 500,000 deaths every year worldwide [1]. Severe complications resulting in hospitalisation mainly occur in high-risk groups, including pregnant women [2–5]. Pregnant women are three times as likely as non-pregnant women to be hospitalised as a result of influenza infection and are at twice the risk of influenza-associated mortality [6]. The risk of hospitalisation following influenza infection has been shown to increase with each trimester of pregnancy [2]. Severe infections can pose serious risk to the unborn infant. For example, analyses from the 2009 A/H1N1 pandemic found the risk of fetal death was twice as high in women infected during pregnancy compared to uninfected [7].

Due to this increased risk, seasonal influenza vaccination is recommended for pregnant women at any stage of pregnancy in order to prevent infection in pregnant women and their newborns [8]. The existing evidence supporting the benefits of influenza vaccination during pregnancy has largely concentrated on the ability to protect young infants [9–11]. A number of previous studies have demonstrated the effectiveness of seasonal influenza vaccination during pregnancy in preventing severe illness in young infants [10–13]; however, there are limited data documenting protection against serious infection (e.g. resulting in hospitalisation) in pregnant women [14,15]. While one previous randomised controlled trial observed a 36% reduction in respiratory illness with

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fever in vaccinated women compared to unvaccinated women [13], population-based data supporting the effectiveness of seasonal influenza vaccination during pregnancy are limited. Two previous retrospective cohort studies failed to find a significant effect of seasonal influenza vaccine in pregnant women [16,17], and the only cohort studies which have demonstrated an effect evaluated the influenza A/H1N1 2009 monovalent vaccine during the 2009 influenza A/H1N1 pandemic [7,18]. To date, no cohort study has observed a reduction in hospital admissions in pregnant women who receive seasonal influenza vaccine.

The goal of this study was to: a) estimate the proportion of pregnant women presenting to and/or admitted to hospital during influenza season for an acute respiratory tract infection; and b) compare the incidence of emergency department visits and inpatient hospital admissions for acute respiratory illness in vaccinated and unvaccinated pregnant women in order to estimate the effectiveness of seasonal trivalent influenza vaccination during pregnancy.

2. Methods

2.1. Setting

Western Australia has a resident population of 2.6 million people, with 71% of the population residing in the metropolitan area [19]. There are approximately 33,000 births each year in Western Australia [20]. In Australia, seasonal trivalent influenza vaccine is offered at no cost to pregnant women under the National Immunisation Program [21]. The seasonal influenza vaccination program typically begins 15 March each year and vaccination activity ends by August. More than 70% of antenatal vaccinations are administered by general practitioners and another 20% are administered by nurses at public hospital antenatal clinics [22].

2.2. Study design

A retrospective, population-based cohort of 34,701 pregnant women was established using linkage of administrative health records. Data from the state perinatal data collection were used to identify pregnancies with a date of delivery between 1 April 2012 and 31 December 2013. The Midwives Notification System is a legally-mandated perinatal data collection in Western Australia for births ≥20 weeks gestation, which has been in place since 1975 [23] and is estimated to include 99% of all births in Western Australia [24]. Midwives Notification System data include information on the mother, including the woman's full name, date of birth, demographics, health, and obstetric history, as well as information on the baby, including the date of delivery, estimated gestation, and birth weight. Gestation and date of delivery were used estimate a date of conception. The full name and date of birth of pregnant women were probabilistically matched to vaccination, emergency department, and hospital discharge records in order to measure vaccination status and severe respiratory illness during the 2012 and 2013 influenza seasons.

2.3. Exposure measurement

The vaccination status of pregnant women in the cohort was derived from the Western Australia Antenatal Influenza Vaccination Database, a Western Australia Department of Health database summarising reports of vaccines administered to pregnant women [25]. Reports are submitted to the Western Australia Department of Health directly by the immunisation provider. Data include date of administration, vaccine brand, and estimated gestation at time of vaccination. Pregnant women with a vaccination record identified in the state database with a date of vaccination during pregnancy were considered 'vaccinated.' Pregnant women with no vaccination record or with a vaccination record with a date of vaccination before or after pregnancy were considered 'unvaccinated.' Women who attended hospital and were vaccinated <14 days prior to presentation or admission were excluded from the analysis.

2.4. Outcome measurement

Emergency department visits and inpatient hospital admissions were identified using the Emergency Department Data Collection and the Hospital Morbidity Data Collection, respectively. The Emergency Department Data Collection includes emergency department activity in the state's metropolitan area public and private hospitals [26]. Information related to the episode of care included date of presentation, principal diagnosis (International statistical classification of diseases and health related problems, 10th revision, Australian modification; ICD-10-AM), method of arrival (e.g. referral or presentation), triage code, and disposal code. The Hospital Morbidity Data Collection is a state-wide data collection which summarises information related to inpatient discharge summaries in all public and private hospitals in Western Australia and is used to determine state hospital statistics [27]. Hospital inpatient records include a date of admission, ICD-10-AM coded discharge diagnoses, length of stay, and admission and length of stay in intensive care unit (ICU).

Acute respiratory illnesses were defined based on the principal diagnosis code of the emergency department or hospital inpatient record. An inpatient hospital admission for an acute respiratory infection was defined as an inpatient record with a principal diagnosis code consistent with an acute respiratory illness (croup [J05], upper respiratory tract infection [J06], influenza [J09-J11], pneumonia [J12-J18], bronchitis [J20], bronchiolitis [J21], or an unspecified acute lower respiratory tract infection [J22]). Similarly, an emergency department visit for an acute respiratory infection during pregnancy was defined as an emergency department record with a principal diagnosis code consistent with an acute respiratory illness. To ensure emergency department visits and hospital admissions were mutually exclusive, only emergency department records with a disposal code indicating the woman was not admitted to hospital were included in the analysis.

Laboratory-confirmed influenza is a reportable condition in Australia [28]. Emergency department visits and hospital admissions due to laboratory-confirmed influenza were identified based on data from the Western Australia Notifiable Infectious Disease Database, the state's notifiable infectious diseases register. Hospital admissions or emergency department visits which linked to a notification record for laboratory-confirmed influenza with a specimen collection date within 14 days of the admission or presentation date were considered to be associated with laboratory-confirmed influenza.

2.5. Eligibility criteria

Pregnancies eligible for inclusion in the final cohort were identified based on date of birth and estimated date of conception. State notification data were used to determine seasonal influenza virus activity. The final cohort was restricted to women who were pregnant during the 2012 or 2013 southern hemisphere influenza season, and the final analysis was restricted to emergency department presentations and admissions to hospital which occurred during the southern hemisphere influenza season (1 June 2012–30 September 2012; 1 July 2013–30 September 2013) (Fig. 1). Because the Emergency Department Data Collection is largely restricted to the Perth metropolitan area, all analyses were confined to women

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