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The economic impact of prenatal varicella immunity among pregnant women in Alberta

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ABSTRACT

In light of the changing epidemiology of varicella, we sought to examine varicella antibody levels in the prenatal population in the Canadian province of Alberta. All prenatal varicella screening tests performed between August 1, 2002 and February 2, 2014 (454,592) were included in this study. Test results, demographics and vaccination status were examined to identify varicella seroprevalence and correlates for being seronegative. An overall seroprevalence for varicella of 95.8% was found across all pregnancy screenings. Significant independent correlates of seronegativity included younger age (AOR: 4.72 (95% CI: 3.87–5.77) for <20 years of age vs. >40 years of age) and having immigrated to Alberta from Africa or Asia (AOR: 4.55 (95% CI: 4.10–5.05) and AOR: 5.83 (95%CI; 5.48–6.19), respectively). Women who were initially seronegative for varicella antibodies and who received both postnatal vaccination and post-vaccination prenatal screening (2566) were examined to assess seroconversion. 66.3% of women who were tested up to six months post-vaccination were seropositive, however only 36.9% of women tested after 36 months were seropositive. Finally, 40.9% of all prenatal varicella specimens tested were deemed redundant, i.e. women had either a history of (1) ⩾2 doses of varicella vaccine, (2) varicella infection, or (3) a previous positive varicella serology. Eliminating this redundant screening could provide an estimated $96,000 in savings annually in laboratory and Public Health follow-up costs alone. As the number of women with vaccine-derived immunity through universal childhood vaccination increase in the prenatal population, screening methods may need to adapt to ensure varicella immunity is accurately conducted and assessed.

1. Introduction

Varicella infection is generally regarded as a mild, self-limiting illness when it affects young healthy children. If a pregnant woman becomes infected with Varicella Zoster Virus (VZV) however, the neonate is at risk for developing neonatal varicella or congenital varicella syndrome (CVS) [1]. While the incidence of CRS is low in Canada (estimated to occur in 1–2% of women who contract VZV during pregnancy or roughly 4 cases in Canada per year [2]), neonatal mortality can approach 20% in these cases [3]. To reduce the incidence of neonatal varicella and CVS, Alberta Provincial Public Health Guidelines recommend prenatal varicella screening be performed during the first trimester for all pregnant women who have not had (1) previous varicella infection, (2) two doses varicella vaccination, or (3) positive varicella immunoglobulin G (IgG) antibody serology [4]. In Alberta, a universal one-dose childhood vaccination schedule was implemented (measles, mumps, rubella and varicella; MMRV) for all children 12 months of age in 2001. The vaccine schedule was updated in 2012 to include a second dose for children 4–6 years of age [5].

As the majority of pregnant women in the study population were not eligible for universal varicella childhood vaccination, women who test negative for varicella IgG during their prenatal screen are recommended to receive one dose of a

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varicella-containing vaccine one-week post-partum and a second dose at least 6 weeks after the first [6]. Active public health intervention is therefore required for all women who are considered susceptible to varicella infection, which includes sending a letter explaining varicella infection, and the importance of post-partum vaccination, offering free vaccine, and providing nurses to administer vaccinations.

Here we report varicella IgG antibody levels, and correlates of seronegativity, among pregnant women in the Canadian province of Alberta. The proportion of women who lack vaccine-induced seroconversion was evaluated for women who received postnatal vaccination. Finally, potential cost savings were identified for the laboratory and Public Health teams based on the number of redundant varicella screening tests performed in Alberta, current laboratory reagent and labor costs, and the cost to provide postpartum vaccination to women who are susceptible to infection.

2. Material and methods

2.1. Varicella antibody testing

A comprehensive prenatal program to screen for select communicable diseases (Syphilis, Hepatitis B, Varicella, Rubella and HIV) was implemented in Alberta in 2002. Varicella screening is an 'opt-out' program, where the physician assesses the need for prenatal screening based on (1) history of receiving two doses of a varicella containing vaccine, (2) history of varicella infection, or (3) a previous positive laboratory result for varicella IgG [4]. Prenatal varicella screening was performed using the Enzygnost anti-VZV/IgG assay (Siemens, Germany) as per manufacturer's instructions [7]. Absorbance values <0.100 were reported as negative and values >0.200 as positive. Absorbance readings $\geqslant$0.100 but $\leqslant$0.200 were run in duplicate, if results were repeatedly equivocal, the result was reported as indeterminate. If duplicate runs were either negative or positive, they were reported as such [7].

2.2. Prenatal testing data

All prenatal specimens screened for varicella IgG between August 1, 2002 and February 2, 2014 were included in the study. Demographic data including personal healthcare number (PHN), date of birth, gravidity, and varicella IgG results were extracted from the laboratory information system (LIS). These data were merged with data from (1) the Alberta Health Care Insurance Plan (ACHIP) to obtain information on immigration status, year of immigration, country of origin, and First Nations status, (2) the Alberta Health Claims database (spanning from 1983 to 2013) to obtain varicella infection history and (3) the Alberta Immunization/Adverse Reaction to Immunization (IMM/ARI) Registry (spanning from August 1, 2002 to December 31, 2013) for vaccination dose and immunization schedule. Data management was performed using SAS version 9.2 (SAS Institute).

2.3. Definitions and analysis criteria

Immigrants were defined as individuals who had immigrated to Alberta after 1983 (as captured by the ACHIP). Immigrants described as "other" were from countries of origin not including countries in Africa, Asia, Europe or the USA. Immigrants described as "unknown" were individuals who are not Canadian but whose country of origin was not captured by the ACHIP. Interprovincial immigrants were defined as individuals living in another province before coming to Alberta, however, previous migrations and country of origin cannot be assessed for this category, as these data were not captured by ACHIP. First Nations were defined as aboriginal peoples who hold active treaty registration status under the Indian Act of Canada.

Postal code was used to determine geographical areas. Geographic boundaries were based on local planning aggregates, and consider both population and population density. Metropolitan centers were defined as those areas with populations >100,000 and population density >30,000 km^2; urban areas as populations between 50,000–100,000 and population-density >20,000 per km^2; rural areas as those with populations <10,000 and population-density between 100–10,000 per km^2; and rural remote as areas with population-densities <100 per km^2 that are >200 km from a regional centre.

Specimens submitted to the laboratory within 300 days from the same woman were considered to represent a single pregnancy. If multiple prenatal screens were performed within a 300-day period, the first specimen result was used to define the serology for that pregnancy. Seroprevalence was calculated at the pregnancy level to account for change in an individual's seroreactivity over time. Seroprevalence was defined as the number of positive serological results divided by the total number of serological results for that population.

Categorical variables were compared using the Chi-square test, while continuous variables were compared with *t*-tests. Multivariable logistic regressions were performed to identify independent correlates of seronegativity and to estimate odds ratios (OR), adjusted odds ratios (AOR), and 95% confidence intervals (95% C.I.). For multivariable analysis, the population was restricted to the first varicella IgG result in the database for each woman (292,858).

Seroconversion was defined as a change from a negative or indeterminate varicella IgG to a positive IgG in a subsequent sample from the same individual. Patients receiving postpartum vaccination, whose initial samples were IgG indeterminate or negative, were examined in subsequent pregnancies for seroconversion. Seroconversion was calculated based on the available laboratory data, and does not control for timing of vaccination and subsequent serological testing. The proportion of seroconversion for individuals who received one or two doses of vaccine was compared by Chi-square test. Multivariable logistic regression was used to identify independent correlates for non-seroconverters following post-partum vaccination.

Redundant varicella screening was defined as any test performed after one of the opt-out criterions was met. The number of redundant tests was stratified per opt-out-criterion. Calculations were performed at an individual level (including those submitted in the same pregnancy) to account for all possible redundant screening performed.

All statistical analyses were performed using Stata version 14 (StataCorps, College Station, TX, USA).

2.4. Study ethics

Research ethics approval for this study was obtained from the University of Alberta Health Research Ethics Board.

3. Results

3.1. Characteristics of study demographics

Between August 1, 2002 and February 2, 2014, a total of 454,592 specimens from 292,889 women were screened for varicella IgG. The majority of women had only one specimen submitted per pregnancy, however 25,244 (5.9%) women had two specimens, and 1007 (0.2%) had $\geqslant$ 3 specimens tested for varicella IgG. A total of 427,283 pregnancies were analyzed for varicella IgG

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