Journal of Clinical Virology 83 (2016) 43–47

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Economic impact of switching rubella IgG methodologies to the prenatal public health program in Alberta

Florence Y. Lai[a,1], Douglas C. Dover[a], Carmen L. Charlton[b,c,*]

[a] Surveillance and Assessment, Alberta Ministry of Health, Edmonton, Alberta, Canada
[b] Provincial Laboratory for Public Health (ProvLab), Edmonton, Alberta, Canada
[c] Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada

ARTICLE INFO

Article history:
Received 8 February 2016
Received in revised form 1 July 2016
Accepted 12 August 2016

Keywords:
Rubella antibody positive
Prenatal immunity testing
Rubella antibody levels
Rubella cut-off
Public health care cost
Rubella vaccine

ABSTRACT

Background: Despite widespread use of a universal rubella standard, variability in rubella antibody titre can be observed between assays, particularly at the low end of the linear range.
Objectives: Here, we investigate the impact of a methodology change for rubella IgG from the Abbott AXSYM to the Abbott Architect in a comprehensive prenatal screening program in the Canadian province of Alberta.
Study design: 51,815 specimens (21,399 tested by AxSYM and 30,416 tested by Architect) submitted for routine prenatal screening between January 2006 and December 2012 from women who lived in Alberta after the universal childhood immunization programme for rubella was implemented, and whose immunization records were available, were included in the study.
Results: Prenatal samples tested by AxSYM for rubella IgG were approximately 30% higher than those reported by Architect. Among individuals who had tests across multiple pregnancies, the change in test platform led to an additional 7% of women who initially tested positive, becoming non-positive (i.e. negative or indeterminate) in their subsequent tests. The tendency of the Architect IgG assay to report lower quantitative values was demonstrated across all birth cohorts and vaccination status, and resulted in an additional 2800 women requiring vaccination between 2010 and 2012 with an estimated cost of $38,500.
Conclusion: The change in rubella IgG screening assay resulted in a significant increase in the number of women who required post partum vaccination and Public Health follow-up.

1. Background

Rubella virus infection during early pregnancy can lead to congenital rubella syndrome (CRS), causing miscarriage, stillbirth, and/or congenital defects [1]. The risk of congenital defects has been reported to be as high as 90% when maternal infection occurs during the first 10-weeks of gestation [2]. Although CRS is rare, it continues to occur in Canada [3]. Public health initiatives emphasize prevention of CRS, and rely on routine immunization of children in the population, and the identification and subsequent immunization of susceptible women of childbearing age. In Alberta (population 3,645,257, in 2011), the rubella vaccination program was started in 1971, as a single-dose vaccine for female adolescents. The program changed to a single dose of measles, mumps and rubella (MMR) vaccine for all children aged 12–15 months in 1982, with the inclusion of the second dose of MMR for children aged four to six years in 1996. A comprehensive testing panel (including testing for hepatitis B virus, syphilis, varicella, HIV and rubella) has been offered to all women in their first trimester since 2002. Women who lack serologic evidence of rubella antibodies are followed up by the community public-health-team and offered postnatal vaccination.

The prenatal program is publicly funded and has been highly successful, capturing >97% of all women giving birth in Alberta (approximately 50,000 in 2012). Beginning in 2002, all rubella antibody tests were performed on the AxSYM platform (Abbott Laboratories, Illinois, USA). In October 2009, the testing platform was switched to the Architect (Abbott Laboratories, Saint-Laurent, Québec). The proportion of women who were rubella IgG positive (>15 IU/mL) decreased from 80% during the first nine months in

Abbreviations: ANOVA, Analysis of Variance; CRS, Congenital Rubella Syndrome; IQR, Interquartile Range; MMR, Measles Mumps and Rubella.

* Corresponding author at: Provincial Laboratory for Public Health (ProvLab), 2B1.04 WMC, University of Alberta Hospitals, 8440-112 Street, Edmonton, Alberta, T6G 2J2, Canada.
E-mail address: Carmen.Charlton@albertahealthservices.ca (C.L. Charlton).
[1] Present address: Department of Cardiovascular Sciences, University of Leicester, United Kingdom.

http://dx.doi.org/10.1016/j.jcv.2016.08.294
1386-6532/

2009 to 73 during the last three months in 2009 following the platform switch. During this 12-month period there were no other changes in prenatal rubella screening recommendations or vaccine uptake. We therefore sought to investigate whether this decrease was indicative of a true increase in rubella susceptibility among pregnant women in Alberta, or a result of the assay change.

Here, we compared the rubella antibody levels in two ways – (1) comparing independent samples tested by AxSYM and Architect with adjustment for subjects' characteristics including birth cohort and vaccination status prior to prenatal screening; and (2) examining dependent samples from women with prenatal tests from different pregnancies classified into three categories: (a) those with the initial test by AxSYM and subsequent test by Architect, (b) those tested only by AxSYM, and (c) those tested only by Architect.

2. Objective

The aim of this study was to determine the clinical and economic impact of switching platforms for rubella IgG testing in the prenatal population in Alberta.

3. Study design

3.1. Study subjects

Prenatal specimens from non-First Nations Alberta residents who were either born in Alberta, or who immigrated to Alberta and were eligible for universal childhood vaccination were included. Exclusion of all other prenatal results, resulted in a study size of 51,815 specimens, with 21,399 tested by AxSYM (January 2006–October 2009) and 30,416 tested by Architect (October 2009–December 2012). This study population was chosen because women lived in Alberta after the universal childhood immunization programme for rubella was implemented, and their immunization records were recorded. Multiple specimens submitted within a 365-day period from the same women were considered as related to the same pregnancy. The first rubella serology test per pregnancy was included; any repeat tests within one year of the initial test were excluded.

All testing was performed by a single laboratory, and was performed as per manufacturers' instructions. Reporting range was 0–500 IU/mL, with a recommended cut-off of 10 IU/mL for both assays. For public health follow-up purposes, a modified reporting structure was employed; specimens with antibodies <10 IU/mL were reported as negative, 10–15 IU/mL as indeterminate, and >15 IU/mL as positive. Indeterminate results were not repeated, and were reported directly to the physician with a comment to provide postpartum vaccination.

3.2. Comparison between AxSYM and Architect

Quantitative IgG levels were compared between AxSYM and Architect from independent specimens and stratified by year of test, and birth cohort. Vaccination status was stratified by the number of doses received, and the time since last vaccination (<10, 10+ years), to differentiate between childhood and adulthood vaccination.

Individual woman's antibodies across multiple pregnancies were used to monitor the quantitative changes between platforms. Women who had specimens submitted from pregnancies no more than two years apart, and who did not receive rubella vaccination between specimen submissions were included in the analysis. The difference in antibody levels when first tested by AxSYM and then tested by Architect (AxSYM-Arch) was compared against women whose specimens were both tested by AxSYM (AxSYM-AxSYM) or both tested by Architect (Arch-Arch).

3.3. Statistical analysis

Descriptive statistics were reported as proportions for categorical variables, and as median and interquartile range (IQR) for continuous variables. Subject characteristics were compared using Chi-square test and Wilcoxon test. Quantitative antibody data were natural-log transformed for statistical analyses, and estimates from the analysis were exponentiated and reported as geometric means. Group differences were reported as the ratio of geometric means. Analysis of variance (ANOVA) analysis was performed to compare IgG levels between assays. ANOVA analysis compared the change in IgG for women with test results across multiple pregnancies. The change in antibody was expressed as a ratio, where >1 indicates an increase, and <1 indicates a decrease in antibody levels. Post hoc analyses included adjustment of p-values by the Bonferroni method to account for multiple testing. All analyses and statistical tests were conducted with SAS version 9.2. A p-value of <0.05 was considered statistically significant.

4. Results

The geometric mean IgG levels showed a significant decrease after switching test platform (Fig. 1A) from 21.2 IU/mL (95% CI 20.7–21.7) in those tested by AxSYM in 2009 to 16.4 IU/mL (95% CI 15.6–17.2) ($p < 0.001$) in those tested by Architect in 2009. The Architect had a higher proportion of samples with lower quantitative values, particularly in the range between 1 and 20 IU/mL (Fig. 1B).

Among those tested by AxSYM, 19.9% were reported to have IgG levels <10 IU/mL and 14.7% to have IgG levels 10–15 IU/mL, compared to 24.0% and 17.2% reported by Architect (Table 1). The median IgG levels were 22 IU/mL for AxSYM, compared to 18 IU/mL for Architect ($p < 0.001$). The tendency of the Architect to report lower quantitative values was demonstrated across all birth cohorts and vaccination status (Table 1). The ANOVA analysis showed that AxSYM values were on average 1.3 times ($p < 0.001$) that of Architect values, which remained similar across birth cohorts and vaccination status (Table 2).

We identified 4780 women with multiple screening results within two years and no rubella vaccination between their screenings: 1389 had AxSYM-AxSYM, 1900 had Arch-Arch, and 1491 had AxSYM-Arch testing (Table 3). Of those whose initial results were positive (>15 IU/mL), 86.0% in AxSYM-AxSYM group and 89.5% in Arch-Arch group remained positive in their subsequent tests, compared to 79.1% in the AxSYM-Arch group ($p < 0.001$). In those who showed 10–15 IU/mL in their initial tests, 38.5% in AxSYM-AxSYM and 29.4% in Arch-Arch group showed negative results (<10 IU/mL) in their subsequent tests, and 44.3% and 57.6% remained between 10–15 IU/mL. This proportion increased to 55.6% in the AxSYM-Arch group ($p < 0.001$).

In those who had AxSYM-AxSYM, their IgG was 11% lower (ratio of change = 0.89, 95% CI 0.82–0.97) in subsequent compared to initial tests, which was not significantly different from those who had Arch-Arch testing (ratio of change = 0.91, 95% CI 0.88-0.93). However, in those tested by AxSYM-Arch, their antibody levels decreased by 29% (ratio of change = 0.71, 95% CI 0.67-0.74), which was significantly lower than the groups with AxSYM-AxSYM or Arch-Arch testing ($p < 0.001$). Women showed decline in their antibody levels over time. While the extent of decline as demonstrated by either AxSYM or Architect was similar (0.89 (0.82–0.97) for AXSYM compared to 0.91 (0.88–0.93) for Architect), there was a larger decline in the group with AxSYM-Arch testing (0.71 (0.67–0.74)). This observation was consistent across maternal birth cohorts and vaccination status (Table 4).