

Rates of Rubella Immunity Among Immigrant and Non-immigrant Pregnant Women

Roisin McElroy, MD, CCFP,¹ Matthew Laskin, MD,² Depeng Jiang, PhD,³ Rajiv Shah, MD, MSc, FRCSC,⁴ Joel G. Ray, MD, MSc, FRCPC^{4,5,6}

¹Emergency Department, Humber River Regional Hospital, Toronto ON

²Department of Obstetrics and Gynaecology, University of Toronto, Toronto ON

³Li Ka Shing Knowledge Institute, St. Michael's Hospital, University of Toronto, Toronto ON

⁴Department of Obstetrics and Gynecology, St. Michael's Hospital, University of Toronto, Toronto ON

⁵Department of Medicine, St. Michael's Hospital, University of Toronto, Toronto ON

⁶Department of Health Policy Management and Evaluation, St. Michael's Hospital, University of Toronto, Toronto ON

Abstract

Objective: Elimination of congenital rubella syndrome depends not only on effective childhood immunization but also on the identification and immunization of susceptible women of childbearing age. Since many countries do not immunize against rubella, it is possible that some immigrant women may not be immune. Moreover, contemporary estimates of rubella immunity among Canadian-born mothers are lacking. Accordingly, we sought to compare the immunity status in pregnancy of a large number of immigrant and Canadian-born women in Toronto.

Methods: We examined data among 5783 consecutive pregnant women who gave birth at an inner city hospital in downtown Toronto between 2002 and 2007. Antenatal maternal rubella immunity status was recorded at the time of delivery, and assessed according to the mother's birthplace. Odds ratios (OR) for rubella immunity were adjusted for maternal age, gravidity and duration of residency in Canada.

Results: Relative to a rate of 93.2% among Canadian-born mothers, the adjusted risk of being rubella immune was lowest among women from Northern Africa and the Middle East (OR 0.54, 95% CI 0.31–0.94) and China and the South Pacific (OR 0.78, 95% CI 0.59–1.03).

Conclusion: Rates of rubella immunity are lower than desired among Canadian-born and, especially, new immigrant pregnant women. Under-immunized populations might be identified at the time of the immigration medical examination, while consideration should be given to screening for rubella immunity among all young Canadian women before puberty.

Résumé

Objectif : L'éradication de l'embryopathie rubéolique dépend non seulement d'une immunisation efficace pendant l'enfance, mais également de l'identification et de l'immunisation des femmes sensibles en âge de procréer. Puisque bon nombre de pays ne procèdent pas à l'immunisation contre la rubéole, il est possible

que certaines immigrantes ne soient pas immunisées. De surcroît, nous ne disposons pas d'estimations contemporaines quant à l'immunité contre la rubéole chez les mères nées au Canada. Par conséquent, nous avons cherché à comparer l'état immunitaire pendant la grossesse d'un grand nombre d'immigrantes et de Canadiennes de naissance à Toronto.

Méthodes : Nous avons examiné les données propres à 5 783 femmes enceintes consécutives ayant accouché au sein d'un hôpital du centre-ville de Toronto entre 2002 et 2007. L'état immunitaire prénatal de la mère quant à la rubéole a été consigné au moment de l'accouchement et évalué en fonction du lieu de naissance de la mère. L'effet de l'âge maternel, de la gravidité et de la durée de résidence au Canada a été neutralisé en ce qui concerne les rapports de cotes (RC) quant à l'immunité contre la rubéole.

Résultats : Par comparaison avec un taux de 93,2 % chez les mères nées au Canada, le risque corrigé d'être immunisée contre la rubéole atteignait son niveau le plus bas chez les femmes d'Afrique du Nord et du Moyen-Orient (RC, 0,54, IC à 95 %, 0,31–0,94), ainsi que chez les femmes de Chine et du Pacifique Sud (RC, 0,78, IC à 95 %, 0,59–1,03).

Conclusion : Les taux d'immunisation contre la rubéole sont plus faibles que ce qui serait souhaitable chez les Canadiennes de naissance et, particulièrement, chez les nouvelles immigrantes enceintes. Les populations sous-immunisées pourraient être identifiées au moment de l'examen médical d'immigration, tandis qu'une attention devrait être portée au dépistage avant la puberté de l'immunisation contre la rubéole chez toutes les jeunes Canadiennes.

J Obstet Gynaecol Can 2009;31(5):409–413

INTRODUCTION

A cute rubella infection manifests as a mild self-limiting condition in children and adults. While up to 50% of cases are asymptomatic, others manifest with fever, scarlatiniform rash, conjunctivitis, coryza, pharyngitis, and polyarthriti.¹ Importantly, maternal rubella infection prior to 16 weeks' gestation may result in the congenital rubella syndrome (CRS), characterized by congenital hearing loss, heart defects, cataracts, glaucoma, chorioretinitis, neuro-

Key Words: Rubella, immunity, immunization, pregnancy, immigration, congenital rubella syndrome

Competing Interests: None declared.

Received on August 19, 2008

Accepted on October 31, 2008

logic disorders, hepatosplenomegaly, intrauterine growth restriction, thrombocytopenia, and radiolucent bone disease. Affected infants are highly contagious in their first year, as they shed the virus through nasopharyngeal secretions.² Although a measles, mumps, and rubella (MMR) immunization program for all infants was introduced in Canada in April 1983,³ only 25% of the world's nations routinely vaccinate children against rubella.⁴ Prior to routine rubella vaccination among Canadian infants, the incidence rate of rubella infection was 109 per 100 000 persons. After routine vaccination, the rate of infection declined to 4 per 100 000 persons, and the incidence rate of CRS declined to 0.6 per 100 000 live births.⁵

Elimination of the CRS depends not only on effective childhood immunization but also on the identification and immunization of susceptible women of childbearing age.⁵ Despite current antenatal screening recommendations, there are no contemporary Canadian studies of rubella immunity among foreign-born or Canadian-born women living in Canada. Because Toronto has the largest number and greatest diversity of immigrants to Canada,⁶ we sought to compare the rubella immunity status in pregnancy of a large number of immigrant and Canadian-born women in that city.

METHODS

We conducted a retrospective cohort study of all women who delivered at St. Michael's Hospital, an inner city hospital in downtown Toronto, between 2002 and 2007, using the obstetrical database. As described elsewhere,⁷ as a routine part of each woman's care, maternal and obstetrical data are recorded on a standardized form, which is completed by her obstetrician and intrapartum nurse. Rubella immunity status is based on a woman's first trimester screening results, as recorded on her standard antenatal care forms or from the hospital laboratory database when the former is not available. Women who are not immune are vaccinated postpartum, prior to discharge from hospital.

The obstetrical database form also contains information about a woman's country of birth and her duration of residency in Canada. For each woman, her first delivery was considered, and her country of birth was categorized according to global regions defined by the Organisation for Economic Co-operation and Development,⁸ and described in the footnote of Table 1.

The prevalence of rubella immunity was determined for each global region of maternal birth, and the odds of immunity expressed as a crude odds ratio (OR) with 95% confidence intervals (CI), using Canadian-born women as the reference group. Adjusted odds ratios were calculated by logistic regression analysis, with current maternal age

(continuous in years), gravidity (1, 2, 3, etc.), and duration of residency in Canada (0–5 or > 5 years) included in the model, a priori. We compared the characteristics of rubella immune and non-immune individuals in a post hoc analysis restricted to Canadian-born women. For the latter, we used a non-paired *t* test for continuous data and a chi-square test for bivariate data.

All *P*-values were two-sided, and significance was set at a value of 0.05. Statistical analyses were performed using SAS Version 9 (SAS Institute Inc., Cary, NC).

Permission to conduct the study was obtained from the St. Michael's Hospital Research Ethics Board, and all patient identifiers were removed from the dataset prior to analysis.

RESULTS

Among 7368 individual patients, information about maternal country of birth and rubella immunity status was available for 5783 women (78%). Over 65% of the study participants were immigrants to Canada, of whom the largest number were born in China and the South Pacific (29%), followed by Latin America and the Caribbean (24%), South Asia (16%), and Sub-Saharan Africa (10%) (Table 1).

Approximately 93% of Canadian-born women were rubella immune. The lowest rates of rubella immunity were among those born in Northern Africa and the Middle East (87.1%) (adjusted OR 0.54; 95% CI 0.31–0.94) as well as China and the South Pacific (91.5%) (adjusted OR 0.78; 95% CI 0.59–1.03) (Table 2). In a post hoc analysis restricted to Canadian-born women, comparing rubella non-immune and immune women, the former tended to be younger (28.5 vs. 31.9 years), and current smokers (8.2% vs. 2.1%) (Table 3).

DISCUSSION

We found that pregnant women originating from Northern Africa and the Middle East, as well as China and the South Pacific, had the lowest rates of rubella immunity. Even among Canadian-born women the rate of immunity was only 93%. This is the first North American study of a diverse sample of women to determine the rate of rubella immunity in pregnancy, especially among immigrant women. While our sample may not be reflective of some birthing centres, the data are likely generalizable to immigrant populations in major cities like our own.⁶ Nonetheless, we did not record the rubella immunization status or country of birth of some participants, since these fields are optional within the obstetrical database. Also, for some regions, the sample comprised fewer than 250 women, which may affect the generalizability and precision of our estimates of rubella immunity.

Table 1. Participant and index pregnancy characteristics in relation to OECD global region of birth (n = 5783)

Characteristic	Mother's region of birth*								
	Canada (n = 1987)	US and developed Oceania (n = 167)	Caribbean and Latin America (n = 918)	Northern, Western, and Southern Europe and UK (n = 210)	Eastern Europe and Central Asia (n = 285)	Sub-Sahara Africa (n = 366)	Northern Africa and Middle East (n = 124)	South Asia (n = 623)	China and the South Pacific (n = 1103)
Mean (SD) maternal age, years	31.7 (5.5)	33.3 (4.3)	30.2 (5.9)	32.8 (5.6)	31.0 (4.9)	30.7 (5.3)	31.2 (5.1)	30.0 (4.9)	32.5 (4.7)
Median (interquartile range) gravidity	2 (2)	2 (1)	2 (2)	2 (2)	2 (1)	2 (3)	2 (1)	2 (2)	2 (2)
Median (interquartile range) parity	0 (1)	0 (1)	1 (1)	0 (1)	0 (1)	1 (2)	0 (1)	1 (2)	0 (1)
Mean (SD) gestational age at delivery, weeks	39.0 (2.8)	39.2 (1.2)	39.0 (1.8)	39.4 (1.4)	39.1 (2.5)	39.2 (2.0)	38.8 (3.5)	38.9 (1.5)	38.9 (2.0)
No. (%) living in Canada < 5 years	23 (1.2)	33 (19.8)	156 (17.0)	22 (10.5)	35 (12.3)	45 (12.3)	38 (30.7)	119 (19.1)	181 (16.4)
No. (%) with diabetes mellitus before pregnancy	9 (0.5)	1 (0.6)	9 (1.0)	3 (1.4)	0 (0)	6 (1.6)	1 (0.8)	12 (1.9)	6 (0.5)
No. (%) with diabetes mellitus during pregnancy	20 (1.0)	2 (1.2)	14 (1.5)	5 (2.4)	0 (0)	9 (2.5)	1 (0.8)	31 (5.0)	27 (2.5)
No. (%) smoking during pregnancy	61 (3.1)	3 (1.8)	4 (0.4)	2 (1.0)	4 (1.4)	3 (0.8)	0 (0)	2 (0.3)	7 (0.6)
Mean (SD) infant birthweight, grams	3450 (512)	3350 (507)	3357 (517)	3497 (511)	3438 (478)	3415 (492)	3365 (529)	3216 (472)	3309 (444)

*Country groups by region. Paris: Organisation for Economic Co-operation and Development (OECD). 2008. <http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20421402~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html>
US and developed Oceania: United States, Australia, New Zealand, Japan, Hong Kong, South Korea, Macau, Singapore and Taiwan.
Caribbean and Latin America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Central America (not specified), Barbados, Cuba, Dominican Republic, Haiti, Jamaica, Netherlands Antilles, Saint Vincent and the Grenadines, Trinidad and Tobago, Caribbean (not specified), Argentina, Bolivia, Brazil, Chile, Columbia, Ecuador, French Guiana, Guyana, Paraguay, Peru, Uruguay, Venezuela, and South America (not specified).
Northern, Western, and Southern Europe and UK: Austria, France, Germany, Netherlands, Switzerland, Republic of Ireland, United Kingdom, Denmark, Finland, Sweden, Czech Republic, Greece, Italy, Malta, Portugal and Spain. Eastern Europe and Central Asia: Bulgaria, Lithuania, Poland, Romania, Slovakia, Belarus, Moldova, Russian Federation, Ukraine, Albania, Bosnia and Herzegovina, Croatia, Yugoslavia (former, not specified), Serbia and Montenegro and Turkey.
Sub-Sahara Africa: Burkina Faso, Ivory Coast, Ghana, Guinea, Mali, Nigeria, Sierra Leone, Togo, Burundi, Ethiopia, Kenya, Madagascar, Mauritius, Somalia, Tanzania, Uganda, Zimbabwe, Eastern Africa (not specified), Sudan, Angola, Cameroon, Chad, Democratic Republic of the Congo (Zaire), Congo, Botswana, South Africa and Africa (not specified).
Northern Africa and Middle East: Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, United Arab Emirates, Yemen, Armenia, Kazakhstan, Kyrgyzstan, Turkmenistan, Uzbekistan, Algeria, Egypt, Libya, Morocco and Tunisia.
South Asia: Afghanistan, Bangladesh, India, Pakistan and Sri Lanka.
China and the South Pacific: China (not specified), People's Republic of China, North Korea, Cambodia (Kampuchea), Indonesia, Laos, Malaysia, Philippines, Thailand, Vietnam, South East Asia (not specified), East Timor and Fiji.

Our results are in keeping with a WHO survey published in 2003, which found that populations in Africa and South-East Asia had the lowest rates of rubella vaccinations.⁹ Other surveys have yielded comparable results to our own, despite differences in their use of regional ethnic groupings. For example, Tookey et al. analyzed data from London, England, and found that women from East Asia and the Pacific region, black women, and South Asian women had the lowest rates of rubella immunity.¹⁰ However, they did not distinguish between a woman's "ethnicity" and her country of birth. In a second study of 8000 pregnant women in two hospitals in Sydney, Australia, Asian-born women comprised the majority (65%) of

rubella-susceptible women.¹¹ In a Canadian study completed in Montreal, 1480 non-pregnant adult immigrants and refugees were examined for rubella serological status.¹² Compared with immigrant men, immigrant women were 1.7 times more likely to be non-immune, and women from Latin America and the Caribbean, Sub-Saharan Africa, and Asia had the highest rates of rubella susceptibility.¹²

All immigrants and certain categories of visitors who seek admission to Canada are required to have an immigration medical examination (IME). The IME does not routinely include a review of immunization status, such as that for rubella.¹³

Table 2. Rates of rubella immunity by maternal region of birth (n = 5783)

Mother's region of birth	Rubella immune during current pregnancy		
	N (%)	Crude OR (95% CI)	Adjusted OR (95% CI)*
Canada (n = 1987)	1852 (93.2)	1.00 (ref)	1.00 (ref)
US and developed Oceania (n = 167)	162 (97.0)	2.36 (0.95-5.85)	2.28 (0.92-5.68)
Caribbean and Latin America (n = 918)	845 (92.1)	0.84 (0.63-1.14)	0.94 (0.70-1.28)
Northern, Western, and Southern Europe and UK (n = 210)	199 (94.8)	1.32 (0.70-2.48)	1.30 (0.69-2.44)
Eastern Europe and Central Asia (n = 285)	272 (95.4)	1.53 (0.85-2.73)	1.61 (0.89-2.88)
Sub-Sahara Africa (n = 366)	353 (96.5)	1.98 (1.11-3.54)	2.16 (1.20-3.88)
Northern Africa and Middle East (n = 124)	108 (87.1)	0.49 (0.28-0.86)	0.54 (0.31-0.94)
South Asia (n = 623)	578 (92.8)	0.94 (0.66-1.33)	1.05 (0.73-1.50)
China and the South Pacific (n = 1103)	1009 (91.5)	0.78 (0.60-1.03)	0.78 (0.59-1.03)

*Adjusted for maternal age at onset of current pregnancy (continuous, in years), gravidity (1, 2, 3, etc.), and number of years living in Canada (0-5 or > 5)

Table 3. Post hoc analysis of characteristics of rubella immune versus non-immune Canadian born women

Characteristic	Canadian born, rubella immune (n = 1852)	Canadian born, not rubella immune (n = 135)	P*
Maternal age, years (SD)	31.9 (5.4)	28.5 (5.8)	< 0.001
Median (interquartile range) gravidity	2 (2)	2 (1)	0.86
Median (interquartile range) parity	0 (1)	0 (1)	0.57
Mean (SD) gestational age at delivery, weeks	39.0 (2.9)	39.3 (1.3)	0.03
No. (%) living in Canada less than 5 years†	21 (1.1)	2 (1.5)	0.67
No. (%) with diabetes mellitus before pregnancy	9 (0.5)	0	1.00
No. (%) with diabetes mellitus during pregnancy	18 (1.0)	2 (1.5)	0.65
No. (%) smoking during pregnancy	50 (2.7)	11 (8.2)	0.002
Mean (SD) infant birthweight, grams	3453 (513)	3414 (501)	0.39

*Evaluated by a non-paired t test for continuous data and a chi-square test for bivariate data.

†Refers to women born in Canada who moved away for a period of time and have been back in the country for less than five years.

Our results show that some immigrant women who become pregnant are susceptible to rubella infection. There are two main approaches in Canada for the prevention of CRS. The first entails screening for rubella immunity in the periodic health examination of all women of childbearing age, with subsequent vaccination of susceptible individuals.¹⁴ The second involves routine vaccination of all women of childbearing age without assessing their immune status, which would then avoid the problem of non-compliance with return clinic visits. The decision of which strategy to adopt should be tailored to each individual clinician's practice setting.¹⁴ We feel that the IME program should consider adopting a similar strategy of either testing for rubella

immunity at the time of the IME or directly vaccinating all new immigrants.

It is troubling that as many as 7 in 100 Canadian-born women may be susceptible to rubella infection in pregnancy. These women appeared to be younger than immune mothers and were more likely to be smokers. We expected their rate of immunity to be higher. Rubella testing is optimally performed using the hemagglutination inhibition test, with a serologic titre of IgG = 10 or = 15 IU/mL indicating immunity, depending on the selected population threshold¹⁵; nonetheless, results are reported to clinicians only as "immune" or "non-immune." Therefore, it is unclear if some "rubella susceptible" women in our study were never

vaccinated, or if their antibody levels may have waned over time, falling below the protective threshold.

ACKNOWLEDGEMENT

Dr Ray is supported by a Canadian Institutes for Health Research New Investigator Award. The study itself was not directly funded.

REFERENCES

1. Dontigny L, Arsenault MY, Martel MJ. Rubella in pregnancy. *J Obstet Gynaecol Can* 2008;203:152–8.
2. Burrow GN, Duffy TP, Copel JA. *Medical complications in pregnancy*. 6th ed. Philadelphia: Elsevier Saunders;2004.
3. Canadian Immunization Guide. Ottawa: Public Health Agency of Canada;2006. Available at: <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-rube-eng.php>. Accessed May 5, 2008.
4. Best JM. Rubella. *Semin Fetal Neonatal Med* 2007;12:182–92.
5. Public Health Agency of Canada. Surveillance of congenital rubella syndrome and other rubella-associated adverse pregnancy outcomes. Ottawa: *CCDR*;1996:22–05.
6. Recent immigrants in metropolitan areas—a comparative portrait based on the 2001 census. Ottawa: Citizenship and Immigration Canada;2005. Available at: <http://www.cic.gc.ca/english/pdf/research-stats/2001-toronto.pdf>. Accessed July 5, 2007.
7. Little M, Shah R, Vermeulen MJ, Gorman A, Dzendoletas AG, Ray JG. Adverse perinatal outcomes associated with homelessness and substance use in pregnancy. *CMAJ* 2005;173:615–8.
8. Country groups by region. Paris: Organisation for Economic Co-operation and Development (OECD);2008. Available at: <http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20421402~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html>. Accessed April 9, 2008.
9. Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: global update. *Pan Am J Public Health* 2003;14:306–15.
10. Tookey PA, Cortina-Borja M, Peckham CS. Rubella susceptibility among pregnant women in North London, 1996–1999. *J Public Health Med* 2002;24:211–6.
11. Sathanandan D, Gupta L, Liu B, Rutherford A, Lane J. Factors associated with low immunity to rubella infection on antenatal screening. *Aust NZ J Obstet Gynaecol* 2005;45:435–8.
12. Greenaway C, Dongier P, Boivin JF, Tapiero B, Miller M, Schwartzman K. Susceptibility to measles, mumps, and rubella in newly arrived adult immigrants and refugees. *Ann Intern Med* 2007;146:20–4.
13. Canadian Immunization Guide. Ottawa: Public Health Agency of Canada;2006. Available at: <http://www.phac-aspc.gc.ca/publicat/cig-gci/p03-11-eng.php>. Accessed May 5, 2008.
14. Beaulieu M-D. Screening and vaccinating adolescents and adults to prevent congenital rubella syndrome. Canadian Task Force on Preventive Health Care;1998. Available at: http://www.ctfphc.org/Full_Text/Ch12full.htm. Accessed July 5, 2007.
15. Field PR, Ho DW, Cunningham AL. Evaluation of rubella immune status by three commercial enzyme-linked immunosorbent assays. *J Clin Microbiol* 1988;26:990–4.