Antepartum Screening for Maternal Infection and Immune Status: Is it Time to Broaden Our Routine?

Vanessa Poliquin, MD, FRCSC,[1] Mark H. Yudin, MD, MSc, FRCSC,[2,3] Kellie E. Murphy, MD, MSc, FRCSC, FACOG,[3,4] Nan Okun, MD, FRCSC[4]

[1]Department of Obstetrics and Gynecology, University of Manitoba, Winnipeg MB

[2]Department of Obstetrics and Gynecology, St. Michael's Hospital, Toronto ON

[3]Department of Obstetrics and Gynecology, University of Toronto, Toronto ON

[4]Department of Obstetrics and Gynecology, Mt. Sinai Hospital, Toronto ON

INTRODUCTION

In Canada, it is routine to offer all pregnant women testing early in pregnancy for rubella immunity, hepatitis B virus, syphilis, chlamydia, gonorrhea, and asymptomatic bacteriuria.[1–3] For each of these infections, there is demonstrable advantage to knowledge of the infection antepartum and proven interventions that, if applied, can improve maternal, fetal and/or neonatal outcomes in the index or subsequent pregnancies.[1,3,4] In this commentary, we consider whether we should also screen for hepatitis C infection, parovirus B19 and cytomegalovirus seroconversion, as well as whether we should recommend national adoption of an "opt-out" policy for HIV screening (i.e., whether HIV screening should be routine unless directed otherwise by the woman).[5]

HEPATITIS C VIRUS SCREENING

The national prevalence of HCV in Canada remains low at 0.8%,[6] but the prevalence among women of reproductive age is increasing. Given the overall low seroprevalence, current Canadian recommendations advise that screening for HCV in pregnancy be limited to women with risk factors.[7] Some experts argue for universal screening because of evidence that 15% to 50% of individuals infected with HCV have no identifiable risk factor.[8–10]

Key Words: Screening, human immune deficiency virus, hepatitis C virus, cytomegalovirus, parvovirus, antepartum

Competing Interests: None declared.

Received on January 29, 2015

Accepted on March 16, 2015

HCV is an infection that has relevance for obstetric care providers, because vertical transmission rates are 3% to 5%.[7,11] Invasive monitoring during the intrapartum period is typically avoided in women infected with HCV with the aim of minimizing the risk of vertical transmission.[7] However, we have no effective way of reliably preventing vertical transmission, and, while treatment for HCV is available for the general population, the usual treatments (including pegylated interferon and ribavirin) are contraindicated in pregnancy due to teratogenicity.[12]

To date, cost-effectiveness studies have not been able to demonstrate that universal screening for HCV is tenable in a low seroprevalence setting.[8,9,13] Given all these considerations, while pregnancy is a time during which women are more likely to access care and Canadian women would generally accept universal screening,[10] there is insufficient evidence to change current national recommendations for screening based on risk factors. Importantly, new and effective direct-acting antiviral drugs for HCV are in development and may prompt new recommendations for screening if their use is financially feasible and appropriate during pregnancy or the immediate postpartum period.

PARVOVIRUS B19 SCREENING

Maternal PVB19 infection during pregnancy can produce fetal infection and associated fetal anemia, non-immune hydrops, and/or fetal demise.[14–16] It is estimated that 30% to 50% of pregnant women are susceptible to PVB19.[17,18] Acute maternal infection occurs in 1% to 3%

J Obstet Gynaecol Can 2015;37(12):1118–1121

of susceptible pregnancies; however, if there is a known exposure (particularly a household contact), the risk is 20% to 50%.[19,20] Serious fetal sequelae occur in 4% to 10% of acute maternal infections.[14–16] Current technology provides accurate detection of acute PVB19 infection.[21,22] In addition, significant improvements in fetal monitoring allow accurate, non-invasive methods of detecting fetal sequelae by sonographic measurement of the middle cerebral artery peak systolic velocity; this provides high sensitivity and specificity for the diagnosis of fetal anemia related to PVB19 infection.[23,24] Furthermore, intrauterine fetal transfusion produces dramatic benefit (although not without a small procedural risk), reducing fetal mortality from 30% to 6%.[25]

Tests for acute maternal PVB19 infection are limited by the need for serial testing because serum markers for acute infection wane over time, and the timing of fetal sequelae is only predictable within a 10- to 12-week window.

Routine antepartum screening for PVB19 immunity is not currently recommended because there is insufficient evidence to support this policy change, even among women at increased risk (teachers, day care workers, or women with children in the home). As demonstrated above, however, PVB19 is a clinical infection for which the at-risk population can be well defined (IgG negative at outset of pregnancy), testing for acute infection is possible (serial monitoring for seroconversion and appearance of IgM), monitoring for adverse fetal outcome can be undertaken non-invasively, and effective management is available. As such, while a change in national recommendations would be premature, current evidence indicates a need for a large-scale prospective study of a routine screening protocol for PVB19 susceptibility and seroconversion during pregnancy. Such a study should consider feasibility, acceptability, and cost-effectiveness of this strategy for all pregnant women and women at increased risk of exposure to PVB19.

CYTOMEGALOVIRUS SCREENING

Acute infection with CMV occurs in 1% to 4% of all pregnancies and has an intrauterine transmission rate of up to 30% to 40%; the highest risk of transmission is during a primary infection and not during a reactivation.[26,27] Distinguishing a primary CMV infection from a reactivation is complex. CMV IgM is present in both of these, and the distinction requires either serial maternal serum samples or avidity testing for CMV IgG present in maternal serum at the time of acute infection.[28] If acute primary maternal infection is identified, use of the polymerase chain reaction to detect CMV DNA in amniotic fluid allows for the accurate diagnosis of intrauterine infection. While this diagnostic test has excellent negative predictive value for absence of fetal and infant sequelae, amniocentesis is an invasive procedure, and cannot be performed until at least seven weeks after acute maternal CMV infection and after 21 weeks' gestation for optimal sensitivity.[26,29] Predicting the minority of fetuses who will suffer consequences from CMV infection (15% to 25%) is extremely challenging, given that the most common neurologic sequela is sensorineural hearing loss, for which we have no antepartum test.[26,30] Potentially beneficial interventions such as antepartum administration of hyperimmune globulin and postnatal administration of ganciclovir have been reported to reduce the rate and severity of sequelae for fetuses and infants, but current evidence is inconsistent and includes only small studies[31–34]; to date, the evidence regarding their effectiveness is insufficient. There is no question that acute antepartum CMV infection is an important infection for pregnant women across Canada and is a significant cause of sensorineural hearing loss. However, because of the challenge of identifying women at highest risk of intrauterine transmission, our inability to identify which fetuses will have significant sequelae from intrauterine CMV infection, and the lack of robust evidence for beneficial interventions, routine screening for CMV infection in pregnant women cannot be recommended.

HIV SCREENING: OPT-IN OR OPT-OUT?

In contrast to the viral infections discussed to this point, the benefits of screening for HIV during the antepartum period have been clearly established. Appropriate management of known HIV infection during pregnancy successfully reduces the risk of vertical transmission from over 20% to less than 2%.[35] In accordance with national guidelines, all Canadian provinces and territories offer universal antepartum screening for HIV by means of one of two screening strategies: opt-in or opt-out screening. Opt-out screening (in which a clinician routinely performs an HIV screening test after notifying the patient that the test will be performed and that the patient may elect to decline or defer testing) has been recommended by both the Centers for Disease Control in the United States and the American College of Obstetricians and Gynecologists.[36,37] Arguments in favour of opt-out screening have included higher rates of HIV screening and less patient anxiety

ABBREVIATIONS

CMV	cytomegalovirus
HCV	hepatitis C virus
PVB19	parvovirus B19