



Screening for Infections in Pregnancy - What Tests Should We Offer?

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Infections in pregnancy may cause significant morbidity and mortality through various different mechanisms in pregnancy. Concerns with congenital infections are focused on the possible vertical transmission of these infections to the foetus, which may lead to various forms of malformations, neuro-developmental delay and long term childhood consequences (such infections include syphilis, varicella, rubella, cytomegalovirus, toxoplasmosis, parvovirus B19, human immunodeficiency virus). Other maternal infections may adversely affect the course of the pregnancy, leading to increased risks for miscarriage or preterm delivery (such infections include listeriosis, asymptomatic bacteriuria, vaginal bacteriosis), or are associated with possible severe neonatal sepsis (examples include Gp B streptococcus infection or colonisation, and genital herpes). The more common infections in the antenatal period and recommendations for screening are briefly discussed in this article.

Rubella

The aim of screening for rubella in pregnancy is to identify susceptible women so that postpartum vaccination may protect future pregnancies against rubella infection and its consequences. Hence, rubella screening does not attempt to identify current affected pregnancies. There is also no treatment to prevent or reduce mother-to-child transmission of rubella for the current pregnancy. Vaccination during pregnancy is contraindicated because of fears that the vaccine could be teratogenic. However, in an evaluation of surveillance data from the USA, UK, Sweden and Germany of 680 live births to susceptible women who were inadvertently vaccinated during or within 3 months of pregnancy, none of the children was born with congenital rubella syndrome¹.

Recommendation - Rubella susceptibility screening should be offered early in antenatal care to identify women at risk of contracting rubella infection and to enable vaccination in the postnatal period for the protection of future pregnancies.

Syphilis

The prevalence of syphilis in pregnant women is very low in Hong Kong, but there were trends of a higher incidence in new immigrants and non-resident mothers. In pregnant women with early untreated syphilis, 70% to 100% of infants will be infected and one-third will be

stillborn. The risk of congenital transmission declines with increasing duration of maternal syphilis prior to pregnancy. Full and timely treatment of syphilis in pregnancy with penicillin has shown pregnancy outcomes when comparable with untreated seronegative women. Although erythromycin is useful in the treatment of syphilis for non-pregnant women who are allergic to penicillin, treatment of pregnant women with erythromycin has been shown to be ineffective in some cases².

Recommendations - Screening for syphilis should be offered to all pregnant women at an early stage in antenatal care because treatment of syphilis is beneficial to the mother and foetus.

Toxoplasmosis

No data specific to Hong Kong were available, but in the UK, approximately 75% to 90% of pregnant women are estimated to be susceptible to toxoplasmosis infection. The prevalence of congenital toxoplasma infection was reported to be approximately 0.3/1000 live births in Denmark. A study in six European centres identified undercooked meat and cured meat products as the principal factor contributing to toxoplasma infection in pregnant women³. The reported overall risk of congenital toxoplasmosis with primary infection with *T. gondii* increases from 6% to 26% from 7 to 15 weeks of gestation and rising to 32% to 93% at 29 to 34 weeks of gestation. Clinical manifestations of congenital toxoplasmosis include inflammatory lesions in the brain and retina and choroids that may lead to permanent neurological damage or visual impairment. In contrast to the risk of transmission, the risk of an infected infant developing clinical signs of disease (hydrocephalus, intracranial calcification, retinochoroiditis) is highest when infection occurs early in pregnancy, declining from an estimated 61% at 13 weeks to 9% at 36 weeks⁴.

Available screening tests to determine sero-conversion cannot distinguish between infection acquired during pregnancy or up to 12 months beforehand and women who have acquired the infection before conception are not at risk of foetal infection. For pregnant women with a diagnosis of primary toxoplasma infection, it is possible to multiply the risk of congenital infection by the risk of signs among congenitally infected children to estimate the risk to the foetus and to arrive at an informed decision. Primary prevention of toxoplasmosis with the provision of information about how to avoid toxoplasma infection before or early in



pregnancy should be given. Systematic reviews on the effects of antiparasitic treatment (spiramycin alone, pyrimethamine sulphonamides or their combination) on women who acquire primary toxoplasmosis infection during pregnancy showed inconsistent treatment effects. The drugs are reported to be well tolerated and non-teratogenic, although sulpha drugs may carry a risk of kernicterus in infants and also of bone marrow suppression in the mother and infant. Although universal screening with antenatal treatment reduced the number of cases of congenital toxoplasmosis, an additional 18.5 pregnancies were lost for each case avoided⁵. Other costs include the unnecessary treatment or termination of uninfected or unaffected fetuses. As an alternative, neonatal screening aims to identify neonates with congenital toxoplasmosis in order to offer treatment and clinical follow up. The vast majority of congenitally infected infants are asymptomatic in early infancy and would be missed by routine paediatric examinations. Neonatal screening is based on the detection of toxoplasma-specific IgM and has been found to detect 85% of infected infants. There are no published studies that have determined the effect of postnatal treatment.

Recommendation - Routine antenatal serological screening for toxoplasmosis should not be offered because the harms of screening may outweigh the potential benefits. Pregnant women should be informed of primary prevention measures to avoid toxoplasmosis infection such as washing hands before handling food; thoroughly washing all fruit and vegetables, including ready-prepared salads, before eating; thoroughly cooking raw meats and ready-prepared chilled meals; wearing gloves and thoroughly washing hands after handling soil and gardening; and avoiding cat faeces in cat litter or in soil.

Cytomegalovirus

Congenital infection is thought to occur in 3/1000 live births⁶, and a small proportion of these babies would be expected to have severe neuro-developmental problems as a result. At present, antenatal screening for this condition is thought to be inappropriate, as it is not currently possible accurately to determine which pregnancies are likely to result in the birth of an infected infant, and which infected infants will have serious sequelae. There is no currently available vaccine or prophylactic therapy for the prevention of transmission and no way to determine whether intrauterine transmission has occurred.

Recommendation - The available evidence does not support routine cytomegalovirus screening in pregnant women and it should not be offered.

Asymptomatic Bacteriuria

Local data on the incidence of asymptomatic bacteriuria are not available, but it occurs in around 2-5% of pregnant women in the UK. Evidence from randomised controlled trials designed to verify the benefits of treatment amongst women with ASB indicates an increased risk of preterm labour and pyelonephritis in women with ASB⁷. Midstream urine culture has been

used as the reference standard for diagnosis of ASB. This has been shown to be superior to rapid tests such as reagent strips, microscopic urinalysis, Gram staining, urinary interleukin or enzymatic tests. A Cochrane systematic review of 14 RCTs has shown that antibiotic treatment reduced persistent bacteriuria during pregnancy, reduced preterm delivery or low birthweight babies, and reduced the development of pyelonephritis⁸. Economic considerations also supported the use of urine culture as a cost effective means to prevent the wider cost consequences of ASB.

Recommendation - Pregnant women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture in pregnancy. The identification and treatment of the condition reduces the risks of preterm birth.

Hepatitis B and C Virus

The prevalence of hepatitis B surface antigen (HBsAg) in pregnant women in HK has been found to range from 6-10%. As many as 85% of babies born to mothers who are positive for the hepatitis e antigen (eAg) will become HBsAg carriers and subsequently become chronic carriers, compared with 31% of babies who are born to mothers who are eAg negative (RR 2.8)⁹. Mother-to-child transmission of the hepatitis B virus is approximately 95% preventable through administration of vaccine and immunoglobulin to the baby at birth¹⁰. To prevent mother-to-child transmission, all pregnant women who are carriers of hepatitis B virus need to be identified by antenatal screening for screening for HBsAg, HCV prevalence observed in most antenatal populations ranges from 0.1 to 0.8%. The risk of mother-to-child transmission is estimated to lie between 3% and 5%¹¹. Although there is consistent evidence that the risk of mother-to-child transmission of HCV increases with increasing maternal viral load, whether caesarean delivery could reduce perinatal transmission as compared to vaginal delivery is uncertain. The clinical course of HCV in infants who have acquired the disease through mother-to-child transmission is also unclear, and some infected children could subsequently become HCV-RNA negative. Nevertheless, it is possible that infected children may develop long-term clinical outcomes. Upon confirmation of a positive screening test, a woman should be offered post-test counselling and referral to a hepatologist for management and treatment of her infection.

Recommendation - Serological screening for hepatitis B virus should be offered to pregnant women so that effective postnatal intervention can be offered to infected women to decrease the risk of mother-to-child transmission.

Pregnant women should not be offered routine screening for hepatitis C virus because there is insufficient evidence on its effectiveness and cost effectiveness.

Human Immunodeficiency Virus

HIV infection in HK pregnant population is reported to be less than 1: 4200. Currently available HIV tests are more than 99% sensitive and specific for the detection of HIV antibodies. Available tests for HIV diagnosis in



pregnant women include the EIA and Western blot protocol, which is at least 99% and 99.99% sensitive and specific. Interventions to reduce mother-to-child transmission of HIV during the antenatal period include antiretroviral therapy, elective caesarean section delivery and advice on avoidance of breast feeding after delivery. The risk of infant mortality and maternal death was found to be reduced with zidovudine treatment compared with treatment with placebo (infant mortality: OR 0.57, maternal death: OR 0.30). In the absence of intervention, mother-to-child transmission was reported to occur in 25.5% of deliveries and was reduced to 8% with antiretroviral treatment with zidovudine¹². The combination of interventions (i.e. combination antiretroviral therapy, caesarean section and avoidance of breast feeding) can further reduce the risk of transmission to 1%¹³. The use of anti-retrovirals to reduce mother-to-child transmission has resulted in resistant mutations, and has raised concerns about the efficacy of anti-retroviral treatment decreasing with time.

Recommendations - Pregnant women should be offered screening for HIV infection early in antenatal care because appropriate antenatal interventions can reduce mother-to-child transmission of HIV infection. A system of clear referral paths should be established in each unit or department so that pregnant women who are diagnosed with an HIV infection are managed and treated by the appropriate specialist teams.

Group B Streptococcus

There is little organised antenatal screening for maternal GBS carriage in Hong Kong and its prevalence in Hong Kong is uncertain. The estimated incidence of GBS carriage varied from 6.6% to 20% of mothers in the USA. Maternal intrapartum GBS colonisation is a risk factor for early onset disease in infants. The collection of cultures between 35 and 37 weeks of gestation appears to achieve the best sensitivity and specificity for detection of women who are colonised at the time of delivery, with swabs of both the vagina and rectum provide the highest predictive value for identification¹⁴. A comparison of screening methods (obtaining cultures from all pregnant women versus identifying women for intrapartum treatment through clinical risk factor assessment) in a large study in the US found that the risk of early-onset disease was more than 50% lower in the universally screened group compared with those screened by assessment of clinical risk factors to identify candidates for intrapartum antibiotics¹⁵. However, a systematic review of RCTs of intrapartum antibiotics for the reduction of perinatal GBS infection has not yet demonstrated an effect on neonatal deaths from infection (Peto OR 0.12), although a reduction in infant colonisation rate (Peto OR 0.10), as well as a reduction in early-onset neonatal infection with GBS, was observed¹⁶. With an assumption of 80% effectiveness for the prevention of early-onset GBS disease in infants with intrapartum antibiotics, for every 1000 women or more treated with intrapartum antibiotics for GBS, 1.4 cases of early-onset disease may be prevented.

Recommendations - It is controversial whether all pregnant women should be offered routine antenatal

screening for group B streptococcus (GBS) because evidence of its clinical effectiveness and cost effectiveness remains uncertain. Clinical risk factors for intrapartum antibiotic prophylaxis include previous baby affected with GBS, GBS bacteriuria during current pregnancy, preterm labour (< 37 or < 35 weeks), prolonged rupture of membranes > 18 hours, intrapartum fever and those in which GBS was detected incidentally in the pregnancy. However, antenatal treatment of maternal GBS colonisation is not recommended. There is also no good evidence to support the administration of antibiotic prophylaxis if GBS was detected in a previous pregnancy, or in those undergoing elective caesarean section without labour. Penicillin is the drug of choice and clindamycin should be given if the woman is allergic to penicillin¹⁷.

Asymptomatic Bacterial Vaginosis

The presence of bacterial vaginosis during pregnancy varies according to ethnicity and how often a population is screened. Local data are again lacking, but in general Asian populations have a lower incidence compared to North American populations¹⁸. Bacterial vaginosis may be diagnosed by either the Amsel's criteria (thin white-grey homogenous discharge, pH greater than 4.5, release of 'fishy odour' on adding alkali, clue cells present on direct microscopy) or Nugent's criteria (Gram-stained vaginal smear to identify proportions of bacterial morphotypes using a scoring system), while culture of *G. vaginalis* is not recommended as a diagnostic tool because it is not specific. Cervical Papanicolaou tests have limited clinical utility for the diagnosis of bacterial vaginosis because of low sensitivity. Women with bacterial vaginosis infection were found to be 1.85 times more likely to deliver preterm than women without bacterial vaginosis¹⁹. The higher risk of preterm birth remains in women diagnosed with bacterial vaginosis early in pregnancy even if the bacterial vaginosis spontaneously recovers later in pregnancy²⁰.

A systematic review of ten RCTs (n = 4249) found oral or vaginal antibiotics to be highly effective in the eradication of bacterial vaginosis in pregnancy when compared with placebo or no treatment (Peto OR 0.21)²¹. Antibiotics used in the interventions included oral metronidazole, oral metronidazole plus erythromycin, amoxicillin, vaginal metronidazole cream and intravaginal clindamycin cream. No significant differences in the rates of preterm birth or perinatal death were observed between the treated or untreated groups. However, a reduction in risk of preterm premature rupture of membranes was associated with antibiotics (Peto OR 0.32)²².

Recommendation - Pregnant women should not be offered routine screening for bacterial vaginosis because the evidence suggests that the identification and treatment of asymptomatic bacterial vaginosis do not lower the risk for preterm birth and other adverse reproductive outcomes.



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