Review Article

Congenital cytomegalovirus infection in pregnancy: a review of prevalence, clinical features, diagnosis and prevention

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Human cytomegalovirus (CMV) is under-recognised, despite being the leading infectious cause of congenital malformation, affecting ~0.3% of Australian live births. Approximately 11% of infants born with congenital CMV infection are symptomatic, resulting in clinical manifestations, including jaundice, hepatosplenomegaly, petechiae, microcephaly, intrauterine growth restriction and death. Congenital CMV infection may cause severe long-term sequelae, including progressive sensorineural hearing loss and developmental delay in 40–58% of symptomatic neonates, and ~14% of initially asymptomatic infected neonates. Up to 50% of maternal CMV infections have nonspecific clinical manifestations, and most remain undetected unless specific serological testing is undertaken. The combination of serology tests for CMV-specific IgM, IgG and IgG avidity provide improved distinction between primary and secondary maternal infections. In pregnancies with confirmed primary maternal CMV infection, amniocentesis with CMV-PCR performed on amniotic fluid, undertaken after 21–22 weeks gestation, may determine whether maternofetal virus transmission has occurred. Ultrasound and, to a lesser extent, magnetic resonance imaging are valuable tools to assess fetal structural and growth abnormalities, although the absence of fetal abnormalities does not exclude fetal damage. Diagnosis of congenital CMV infection at birth or in the first 3 weeks of an infant's life is crucial, as this should prompt interventions for prevention of delayed-onset hearing loss and neurodevelopmental delay in affected infants. Prevention strategies should also target mothers because increased awareness and hygiene measures may reduce maternal infection. Recognition of the importance of CMV in pregnancy and in neonates is increasingly needed, particularly as therapeutic and preventive interventions expand for this serious problem.

Key words: congenital infection, cytomegalovirus, fetal diseases, hygiene, pregnancy, sensorineural hearing loss.

Introduction

Human cytomegalovirus (CMV) has become the most common infectious cause of congenital malformation, following the successful global introduction of immunisation programs in young women for Rubella, and more recently for Varicella.[1–3] Congenital CMV is one of the most common causes of serious congenital malformation in Australia and most developed countries, being associated with developmental delay, sensorineural hearing loss (SNHL) and fetal death.[1–3] Congenital CMV infection is the leading infectious cause of hearing impairment in children, with 40–50% of infants born with symptomatic CMV infection and 7–15% of asymptomatic CMV-infected newborns developing SNHL.[4] Australian data show up to 10% of neonates failing universal hearing screening have congenital CMV, and in the absence of diagnosed genetic cause for SNHL, CMV is the likely cause.[5] Importantly, these infants with SNHL may have other undiagnosed complications of CMV that may also benefit from early intervention.[6]

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Cytomegalovirus is a highly prevalent infectious agent in the general population; seropositivity rates in adult women range between 40 and 90%, with the highest rates occurring in individuals from lower socio-economic background.[7–10] Primary CMV infection occurs following close personal contact and is transmitted via body fluids or fomites between individuals, or vertically across the placenta resulting in congenital infection in the fetus.[11,12] Currently, there is poor awareness of the risks of congenital CMV,[13] in particular the potential for simple hygiene interventions to reduce the incidence of CMV infection in pregnant women,[14] and many cases of congenital CMV are undiagnosed.[2] Increased education of parents and healthcare providers, and increased testing during pregnancy and/or in the neonatal period are options to reduce the risks and burden of congenital CMV infection.[15]

Global estimates of congenital CMV infection – the relevance of primary and secondary maternal infections

The current global estimate for congenital CMV infection is 0.3–0.7% of all live births.[16,17] The risk of congenital CMV transmission is highest in a pregnant woman with no immunity who acquires primary CMV infection during pregnancy.[18,19] Approximately, one-third (30–39%) of primary maternal CMV infections result in transmission of virus to the fetus,[12,16,20,21] and up to 13% of these infections will result in symptomatic congenital disease in the newborn;[16,17] however, transmission to the fetus and effects on the fetus vary with gestational age at infection. CMV-infected newborns who are asymptomatic at birth also have a 14% future risk of neurodevelopmental sequelae such as SNHL and learning difficulties.[17] Secondary CMV infections in pregnant women with preconceptual immunity (either through reactivation of latent virus or re-infection with a new strain of CMV) can also lead to congenital CMV transmission and fetal infection,[22,23] with a lower transmission rate of ~1.4%.[16] This suggests populations with higher seroprevalence rates may have a lower risk of primary maternal CMV infection and therefore lower rates of symptomatic congenital CMV. However, data from populations with low socio-economic status and near universal preconception immunity usually have higher overall rates of congenital CMV infection (1–2%)[24–26] compared with the global average (0.3–0.7% of live births).[16] More importantly, the prevalence of clinical symptoms at birth and CMV-induced SNHL in populations with lower socio-economic status are often similar to those in developed countries.[18,26] This suggests maternal secondary infections in less developed countries may play a significant role in congenital CMV transmission and may contribute comparably to the burden of disease as primary infections in countries of higher socio-economic status.[16] Furthermore, socio-economic factors such as poor nutrition, inadequate health care and different hygiene may contribute to increased maternofetal transmission in developing countries.

Epidemiology of congenital CMV infection in Australia and New Zealand

Approximately 40% of Australian and New Zealand women of childbearing age are at risk of having a primary CMV infection during pregnancy. The CMV seroprevalence rate for pregnant women attending an antenatal clinic of a major teaching hospital in Sydney, Australia, between 2002 and 2005 was 57%,[20] which is comparable with an average seroprevalence of 58% for adults in the 14–44 age group (i.e female childbearing age) examined in a nationwide survey.[8] In New Zealand, the average seroprevalence rate in adult blood donors is 61%, with higher rates in females than males in all age groups examined.[9] These adult seroprevalence rates in Australia and New Zealand are similar to those in the United States.[8–10] CMV infections are common and usually asymptomatic in otherwise healthy children, with the seroprevalence in an Australian survey of children aged 1–2 years being 38%.[8] This suggests that parents of young children are particularly at risk of being exposed to CMV infection, possibly from their infected children. This is consistent with the observed dramatic increase in overall seropositivity found in Australian women in the 35–39 age group (79%) compared to women in the 30–34 age group (56%), which was not consistent with the expected normal steady increase in seropositivity that occurs with age.[8] A significant number (~23%) of women are therefore seroconverting to CMV at a time of life associated with childbearing and childrearing, of relevance given that caring for young children is associated with increased risk of CMV infection.[27,28] If 30% of these women transmit virus during pregnancy, similar to current global estimates,[16] and 11% of these transmissions result in a CMV-affected child at birth, with an additional 13.5% of transmissions resulting in a child that develops later sequelae, it is clear that the burden of congenital CMV disease in Australia has been significantly underestimated.[2]

A single-centre study of 600 pregnant women in Sydney undertaken by our group found a primary CMV infection rate during pregnancy of approximately 1.2% and a rate of congenital CMV infection of approximately 0.3% of live births,[20] consistent with incidence in other populations of high socio-economic status.[16] The rate of symptomatic disease resulting from congenital CMV infection has been estimated at 3.7 per 100 000 live births (0.004%) by the Australian Paediatric Surveillance Unit (APSU).[1] These infections are responsible for at least 9.4 per 100 000 hospital admissions of children between 0 and 4 years old in the Australian population.[29] However, these figures rely on voluntary reporting by a range of clinicians or detection of clinical sequelae requiring hospitalisation[29] and because neonatal and maternal CMV

screening is currently not routinely undertaken,[6] and accurate diagnosis of CMV usually requires directed blood testing,[20] these are likely to be a significant underestimates.[2] It is estimated that 437 children in Australia and 94 children in New Zealand will be born with or develop CMV-related disease every year, based on the average global figures from a large and detailed meta-analysis for rates of congenital CMV infection, symptomatic disease and later sequelae.[16] These figures take into account congenital infections resulting from both primary and secondary maternal infections, in all socio-economic groups within those populations. This is a significant health burden that may be alleviated to some degree by early diagnosis and currently available intervention strategies.

Clinical features of congenital CMV infection

Clinical manifestations in the mother

Cytomegalovirus infections in pregnant women are often asymptomatic. Previous studies have demonstrated <5% of pregnant women with primary CMV infection experienced a mononucleosis-like syndrome of fever, pharyngitis, cervical adenopathy, fatigue, malaise, myalgia, headache, hepatosplenomegaly and rash.[12,30,31] A more recent study by Nigro *et al.*[32] reported a much higher rate of symptoms associated with CMV infection, with 31% (32 of 102) of pregnant women who acquired primary infection experiencing persistent fever, asthenia, myalgia and flu-like symptoms. Moreover, the prevalence of relevant symptoms in women with primary CMV infection was significantly higher than in women with recurrent or nonactive infection ($P < 0.001$).[32] A review of congenital CMV cases reported to the APSU between 1999 and 2003 reported that 55% of mothers had evidence of, or could recall experiencing, a febrile illness during their pregnancy.[33] However, these clinical characteristics represent nonspecific indicators of maternal CMV infection. This suggests nonspecific illness during pregnancy could be indicative of primary CMV infection for at least one-half of congenital CMV cases, similarly observed in overseas studies,[32] and suggests a significant portion of pregnant women for whom diagnostic testing by serology and/or further testing may be appropriate.

In addition to clinical symptoms, laboratory abnormalities such as lymphocytosis and increased serum levels of liver enzymes (alanine transaminase and aspartate transaminase) may also indicate the onset of CMV infection. A prospective study conducted on 102 pregnant women with primary CMV infection detected increased levels of lymphocytes in ≥40% and elevated alanine and/or aspartate transaminase levels in 39% and 35% of patients, respectively.[32] In another study of 244 pregnant women with primary CMV infection, lymphocytosis and elevated liver enzymes were evident in 12% and 36% of affected women, respectively.[34] Although raising the suspicion of CMV infection, these laboratory investigation results are nonspecific for CMV and thus are not considered in the diagnostic algorithm for CMV infection. Determining the timing of primary CMV infection is important to be able to determine fetal risk of infection; hence, careful examination of the history and laboratory investigation results may enable appropriate further investigation.

Clinical manifestations in the fetus and newborn

Fetal abnormalities associated with intrauterine CMV infection may be detected using ultrasound. Prenatal ultrasound findings in fetuses with CMV infection include cerebral abnormalities such as cerebral ventriculomegaly, brain calcifications, microcephaly and occipital horn anomalies, and noncerebral abnormalities such as echogenic bowel, intrauterine growth restriction (IUGR), hepatomegaly, ascites and cardiomegaly.[35–40] However, other features of congenital CMV disease such as chorioretinitis, petechiae and neurodevelopmental defects are not detectable by antenatal imaging; therefore, the absence of fetal abnormalities does not exclude fetal damage. CMV is also associated with fetal death where ultrasound features of infection may be less obvious.[41,42] A significant thickening of placentae in pregnant women with primary CMV infection whose fetuses or newborns have CMV disease, compared to those women whose fetuses were free from CMV disease ($P < 0.0001$), has also been reported.[43] The latter group, in turn, had significantly thicker placentae than those of seropositive control pregnancies ($P < 0.0001$),[43] suggesting CMV infection of the placenta causes extensive placental inflammation.

Physical signs of neonatal infection such as jaundice, petechiae, hepatosplenomegaly and neurological abnormalities such as microcephaly and intracranial calcification are common and are observed in most (~75%) symptomatic infants with congenital CMV infection, with other signs such as cataracts, microphthalmia, cardiac abnormalities and myocarditis being less frequent.[2,33,44–49] Hepatobiliary abnormalities, as indicated by elevated levels of aspartate transaminase and conjugated hyperbilirubinemia, varied among different study populations and were evident in 23–80% of symptomatic newborns,[44,45,47,49] but are likely to return to normal within a few weeks. In contrast, CNS involvement can cause permanent neurological damage in affected infants, with the majority of those affected developing one or more sequelae, including SNHL, mental retardation, motor deficits, chorioretinitis and seizures.[33,50] CNS involvement was evident in 54% of 175 symptomatic babies reported to the APSU between 1999 and 2009.[2] Other prospective studies have also shown that 40–65% of children born with symptomatic infection developed SNHL, mental retardation and microcephaly.[4,44,51]

Although less common, symptomatic infants may have other clinical features, including prematurity, IUGR, hypotonia, poor feeding and lethargy.[2,33,44,49]

Whilst infants with asymptomatic CMV infection at birth generally have a better prognosis than symptomatic infants, asymptomatic infants remain at risk, particularly for hearing loss, with 7–15% of asymptomatic children developing SNHL.[52–54] A prospective study of asymptomatic children with CMV infection showed ~50% of children who developed hearing loss had bilateral deficit, which varied from mild to profound impairment.[54] Among those children with hearing loss, approximately 50% had further deterioration of hearing, with a median age at first progression of hearing loss of 18 months.[52,53] Delayed onset of hearing loss was evident in 18% of asymptomatic children, with the median age of detection at 27 months.[53] Other neurological complications such as microcephaly, neuromuscular defects and chorioretinitis may also develop in children with asymptomatic congenital CMV infection at birth, but at a much lower rate compared to symptomatic infection.

Screening and diagnosis of maternal and congenital CMV infection

Screening for maternal CMV infection

Routine screening for CMV is not recommended by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) or the Australian antenatal care clinical practice guidelines.[55,56] The universal screening of pregnant women for seroconversion is the most reliable approach to identify primary CMV infection, but remains a controversial issue.[57] Some countries, including Austria, Belgium, France, Germany, Israel, Italy, Portugal, Spain and the Netherlands, have introduced serologic screening for CMV in some groups of pregnant women, although universal, centrally funded screening is uncommon.[58,59] In Australia, there is a national policy for antenatal serology testing for rubella, syphilis, HIV, hepatitis B and hepatitis C,[56] and a requirement for diagnostic laboratories to store the sera for 12 months from collection. Thus, antenatal serum is often available for retrospective screening of CMV IgM, IgG and IgG avidity if required. Accurate detection of primary maternal CMV infection and determining whether there has been congenital transmission to the fetus and whether there may be consequent fetal effects of the infection are important parameters that can inform the clinician and couples about expected outcomes of the pregnancy and aid decisions regarding prognosis and possible interventions.

Current antenatal interventions include termination of pregnancy and CMV hyperimmune globulin (CMV HIG). Treatment with CMV HIG in women who seroconverted during pregnancy shows some promise in preventing fetal infection and fetal neonatal morbidity,[60–64] although a recent study demonstrated a reduction in congenital CMV transmission that did not reach statistical significance.[65] In these studies, pregnant women with primary CMV infection were given 200 PEI units/kg intravenous dose of HIG monthly (an Australian equivalent dosing of 50 000–70 000 CSL units/kg)[66] from diagnosis until delivery. CMV HIG treatment is not routinely recommended, and further trials are ongoing to provide more robust data on the efficacy of HIG treatment. In addition, antiviral agents do not have proven benefit or safety antenatally; however, some limited evidence exists for the safety and efficacy of antivirals to treat neonatal consequences of CMV, with toxicity remaining as a significant problem.[14,67]

Education of women about CMV, virus transmission and hygiene strategies to prevent CMV infection (Table 1)[68] remains the most important strategy to reduce the risk of congenital CMV infection.[69] Workers who have contact with young children, in particular workers in early childhood education and care services, and healthcare workers caring for children may be at risk of occupational CMV exposure. Women planning a pregnancy and/or currently working in childcare facilities ideally should discuss CMV with their doctor and inform their employer so that their individual risk can be assessed and managed.[70]

Diagnosis of maternal infection

Primary maternal infection is more than 20 times more likely to result in placental transmission than CMV reactivation or re-infection (30% vs 1.4%). It remains important to distinguish between primary and secondary maternal infections,[71] whilst remembering the lower percentage of transmission with reactivation or re-infection still causes more infections overall,[72] and potentially results in significant numbers of infants with clinical abnormalities and long-term disabilities.[22] Distinction between these alternatives is possible with currently available serological assays, although caution is warranted in their interpretation (Fig. 1). When detected, the presence of anti-CMV IgM antibody in the absence of

Table 1 Hygiene practices recommended by the CDC to reduce risk of CMV infection for women who are pregnant or planning to become pregnant[68]

Thoroughly wash hands with soap and warm water after activities such as
Nappy changes
Feeding or bathing young child
Wiping child's runny nose or drool
Handling child's toys
Do not share food, drinks, eating utensils used by young children
Do not put a child's dummy in your mouth
Do not share a toothbrush with a young child
Avoid contact with saliva when kissing a young child
Clean toys, countertops and other surfaces that come in contact with urine or saliva

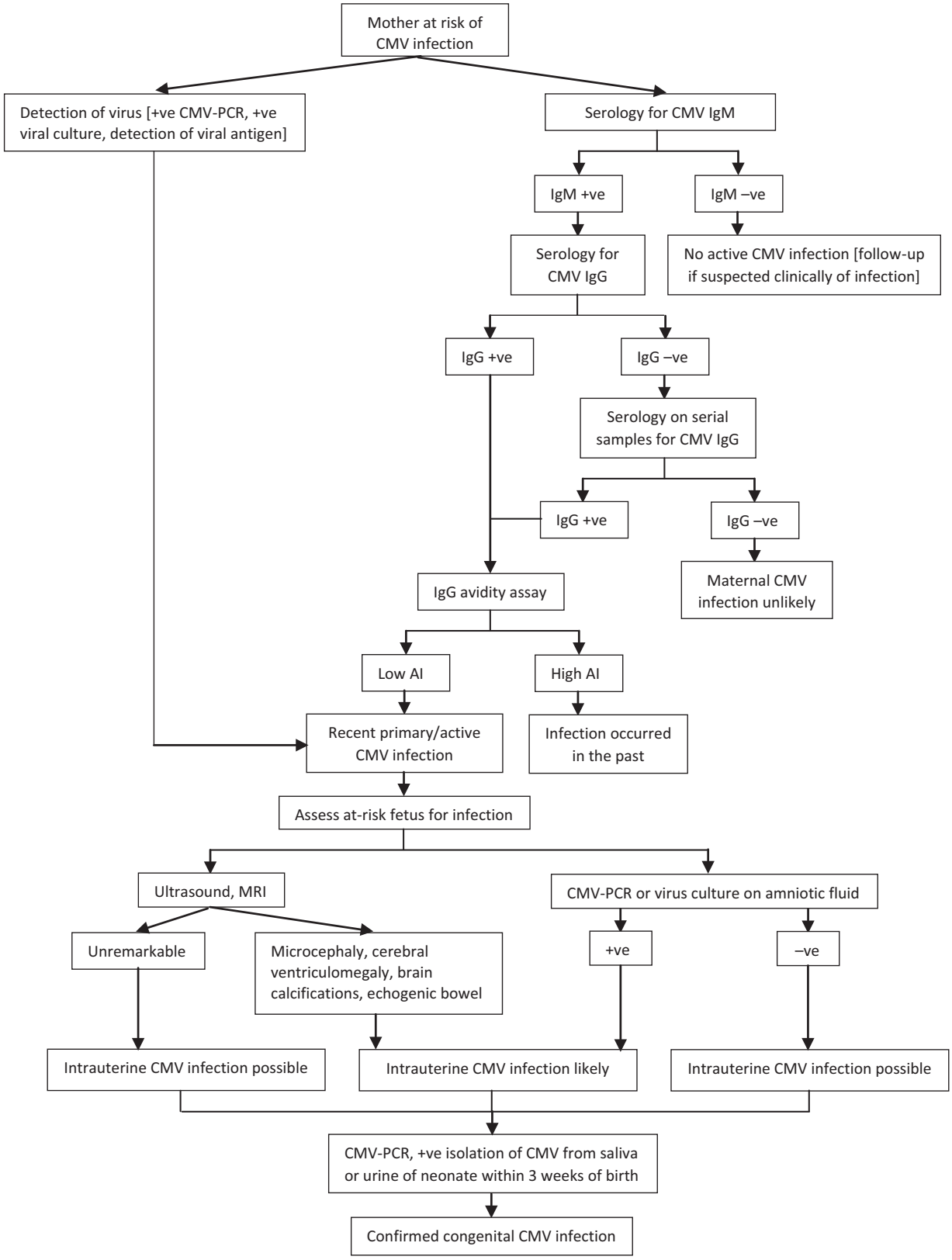

Figure 1 Schematic of the diagnosis of primary maternal CMV infection, and infection in fetus and newborn infant, including serologic, virologic, ultrasonic and magnetic resonance imaging approaches. AI, avidity index; MRI, magnetic resonance imaging; +ve, positive; −ve, negative.

CMV-specific IgG (IgM+/IgG−) is a transient marker of recent primary infection, although this situation clinically is rare, due to the rapid rise in IgG, and that serological testing is usually undertaken more than a week into primary CMV infection. More often, the diagnosis is suspected on the basis of IgG seroconversion and/or low IgG avidity, in the presence of CMV-specific IgM. Maternal CMV IgM is often not produced or is delayed in more than 50% of confirmed congenital CMV cases,[33,73] and IgG seroconversion during pregnancy is difficult to document in the absence of universal antenatal CMV screening. Anti-CMV IgM may be produced in both primary and secondary CMV infections,[74,75] and one should not rely on detection of CMV IgM antibodies, alone, to confirm or exclude primary maternal CMV infection. The IgG antibodies produced in response to primary CMV infection are initially low avidity, maturing over time to bind more strongly to CMV antigens.[76] Measurement of IgG avidity can therefore be used to distinguish recent primary infection from past or secondary infections[74,75,77,78] (Table 2), as long as sufficient IgG titres have been produced.[79] The kinetics of IgG avidity varies with the diagnostic kit used[80] and is likely to vary between individuals as delayed IgG maturation has been observed in some CMV-infected pregnant women.[81–83]

Diagnosis of fetal infection

The primary non-invasive fetal assessment tool following identification of confirmed or suspected primary maternal CMV infection is fetal ultrasound. The ultrasound features of congenital CMV infection are outlined above and may not be visible early in the infection, or at all, and may not be predictive of fetal severity of effects of the infection.[39] Fetal MRI may also be utilised, especially for the detection of neurological abnormalities, particularly where a fetal ultrasound has detected no abnormality.[84] Amniocentesis may be used to determine congenital CMV infection in the fetus. CMV-PCR on amniotic fluid obtained during amniocentesis is a highly sensitive (92–98%) and specific (90–98%) test for CMV,[34,35,85] but the efficacy is dependent on the timing of obtaining the specimen. Amniotic fluid taken before 21–22 weeks

Table 2 Summary of diagnostic tests for identification of CMV infection in mother, fetus and newborn infant

Diagnostic test	Indicator of infection	Advantages	Disadvantages
Prenatal			
Maternal CMV IgM/IgG serology	IgM positivity IgG seroconversion Low IgG avidity	Indication of primary maternal infection with up to 40% possibility of transmission to fetus, depending on gestation	Not indicative of fetal infection
Qualitative CMV-PCR (amniotic fluid)	CMV DNA positive	Indicative of congenital infection	Not indicative of fetal effects of infection
Real-time PCR (amniotic fluid)	CMV DNA positive, with high viral load (>10^4 copies/mL)	Indicative of symptomatic fetal infection† and potential for late-onset sequelae	Definitive viral load cut-off values for symptomatic fetal infection not established
Ultrasound	Fetal abnormalities: cerebral ventriculomegaly, echogenic bowel, intrauterine growth restriction	Non-invasive, suggestive of symptomatic fetal infection if fetal CMV infection confirmed	Not specific for CMV Not sensitive screening test for detecting fetal CMV infection
At birth			
Maternal CMV IgM/IgG serology	IgM detection IgG seroconversion Low IgG avidity	Suggestive of infection during pregnancy	Seroconversion during first trimester of pregnancy often not detectable at birth; No indication of symptomatic fetal infection
Qualitative CMV-PCR (cord blood, infant urine, placenta/infant saliva)	CMV DNA positive	Suggestive of infection during pregnancy and potential for late-onset sequelae	No indication of symptomatic fetal infection
Real-time PCR (cord blood, infant urine, placenta/infant saliva)	CMV DNA positive, with high viral load (>10^4 copies/mL)	Indicative of symptomatic fetal infection† and potential for late-onset sequelae	Definitive viral load cut-off values for symptomatic fetal infection not established

Symptomatic infection = evidence of infant infection at birth, such as hypotrophy, microcephaly, jaundice, hepatosplenomegaly, thrombocytopenia and related petechiae, seizures. Asymptomatic infection = no evidence of infection at birth. May develop sensorineural hearing loss. Other neurological complications such as microcephaly, neuromuscular defects and chorioretinitis can also develop in children asymptomatic at birth from congenital CMV infection, but at a much lower rate compared to symptomatic infection. †Refer to discussion under 'Diagnosis of fetal infection' for a range of opinions regarding the correlation between CMV load and fetal outcomes.

gestation or <6–9 weeks postmaternal infection does not usually contain detectable CMV,[86,87] most likely due to the time taken for CMV to be excreted by the infected fetus into the amniotic fluid. A standard CMV culture on amniotic fluid is a useful technique and encouraged to perform alongside PCR detection due to <100% sensitivity of CMV-PCR. Differences of opinion exist regarding the CMV load present in amniotic fluid (determined using real-time CMV-PCR), for diagnosis of fetal outcomes associated with congenital CMV infection. It has been suggested that CMV loads of $>10^3$ copies in amniotic fluid correlate with fetal infection, and the higher viral loads indicative of symptomatic disease.[85,88,89] Other groups have not found a correlation between CMV load in amniotic fluid and fetal outcomes,[90] and one study was unable to detect virus in amniotic fluid for three children who were CMV-infected at birth.[91] This group found a correlation between CMV load and gestation at the time of amniocentesis,[91] and it is well established that the timing of amniocentesis, relative to suspected infection, is critical for accurate diagnosis of congenital CMV infection.[92] However, fetal infection can often be asymptomatic, and extreme caution is therefore recommended in using amniotic fluid detection of CMV as a prognostic indicator of fetal outcome.[93]

Diagnosis of the CMV-infected newborn

Routine hearing assessment of newborns is now recommended in Australia and New Zealand. Consequently, congenital CMV infection is often diagnosed post-natally, and often only in cases where symptoms such as SNHL or other signs of congenital infection are evident.[33] Congenital CMV infection is defined as active CMV infection detectable within the first 3 weeks of life.[17] This was previously diagnosed by isolation and detection of virus from the urine or saliva of CMV-infected newborns by standard culture or immunofluorescent techniques and can still be a useful tool in confirming congenital CMV transmission. Anti-CMV IgM antibodies can also be detected in 70% of CMV-infected newborns.[94] However, CMV-PCR provides a more sensitive method for identification of congenital CMV[71] and can be performed on different types of clinical specimen, including blood, dried blood spots, urine and saliva[41,95] (Table 2). False-positive CMV-PCR results have been reported in saliva through contamination with CMV-infected maternal breast milk,[96] and in cases of positive CMV-PCR on saliva, these should ideally be confirmed with PCR testing of urine upon availability. In general, and in our experience, false-positive results from salivary testing are avoided by taking samples more than 1 h after breastfeeding has ceased. The sensitivity of CMV-PCR on dried blood spots may be lower compared with immunofluorescent culture detection on saliva specimens.[97] However, CMV-PCR testing of newborn screening cards is particularly useful in retrospective determination of congenital CMV infection in previously undiagnosed infants presenting with late-onset symptoms and sequelae.[98] CMV-PCR is also useful for diagnosis of CMV infection in pregnancies that have ended in miscarriage or stillbirth, accompanied by histopathologic analysis of placental and fetal tissue. As congenital infection with CMV likely causes serious clinical sequelae, early diagnosis and referral to specialists can reduce the risks of congenital CMV disease. Some evidences exist for the efficacy of ganciclovir/valganciclovir in stabilising or improving SNHL in neonates with symptomatic CMV disease involving CNS,[67,99] suggesting the inclusion of CNS involvement as a criterion for consideration of post-natal antiviral treatment.

Conclusion

Cytomegalovirus remains the major infectious cause of congenital abnormalities in the developing fetus and newborn. The majority of primary maternal CMV infections are clinically silent and are likely to go undetected unless indicated by maternal seroconversion or abnormal fetal ultrasonographic findings during pregnancy. Although the diagnosis of primary maternal CMV infection is a complex process, reliable diagnosis can be made by demonstration of seroconversion, and determination of the avidity index of anti-CMV IgG. In cases of confirmed or suspected primary maternal CMV infection, virological testing on amniotic fluid obtained during amniocentesis, as well as prenatal ultrasound and possibly MRI assessment, is necessary for determination of virus transmission and assessment of fetal abnormalities. Most importantly, a careful interpretation of serological and virological data, as well as appropriate counselling, is crucial for effective management of congenital CMV infection and disease during pregnancy. Whilst awaiting effective vaccines and antiviral drugs, preventative strategies must be based on educating clinicians, and women of childbearing age about the mode of transmission and the critical importance of basic hygiene for effective prevention of congenital CMV infection.

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