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The Potential Hidden Burden of Primary Cytomegalovirus Infection During Pregnancy: How to Mitigate Burden & The Challenges for Screening and Prevention

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Characteristics of the Virus

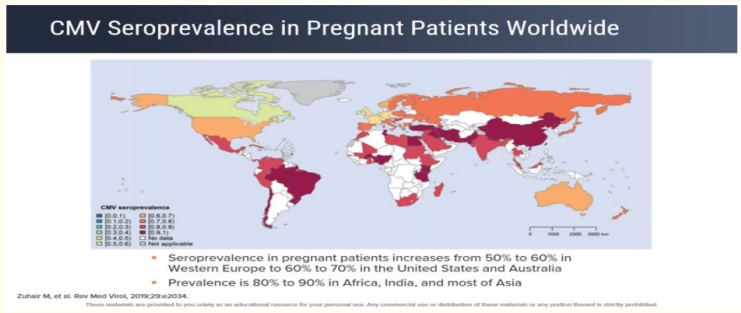
Cytomegalovirus (CMV) is a DNA virus a member of the herpesvirus family, which includes herpes simplex virus types 1 and 2, varicella-zoster virus, and Epstein-Barr virus. These viruses share a characteristic ability to establish lifelong latency. After initial infection, which may cause few symptoms, CMV becomes latent, residing in cells without causing detectable damage or illness. CMV, is a common virus that infects people of all ages. Over half of adults have been infected with CMV by age 40. Most people infected with CMV are asymptomatic (90%).

PERSONS at most risk

Mothers with young children at home or daycare and day care workers or home day care workers.

Disease burden

CMV is one of the most common congenital infections, affecting 0·67% of all livebirths globally. The rate of vertical transmission is 30-40% after maternal primary infection throughout pregnancy. Among symptomatic congenital cytomegalovirus disease at birth 40-60% of infants born will have long-term sequelae. CMV is the most common infectious agent causing birth defects in USA leading to 30% Nongenetic SNHL. With High rate of hospitalization and higher rates of mortalities. Family burden; significant time commitment, financial lost and impact on quality of life. Reactivation or re-infection usually asymptomatic. Fetal loss/death estimated of mortality to be 4-12% of symptomatic neonates.



The long-term health problems

a. Asymptomatic:
   - up to 20% progressive permanent sensorineural loss.
   - 1.6-3.4 need hearing aids or cochlear implants.
   - Abnormal brain imaging.

b. Symptomatic:
   - up to 74% progressive permanent sensorineural loss.
   - other sequels:
     - cognitive impairment.
     - growth disorders.
     - motor impairment/cerebral palsy.
     - neurodevelopmental disorders.
     - seizors/epilepsy.
     - vision problems.
     - death in newborn period or later in childhood.

Mode of transmission

It sheds in mostly bodily fluids: blood, breast milk, nasal mucus, saliva, vaginal fluid, semen, tears, urine and stools. In utero, intrapartum, potentially breast feeding/milk. Transmission risk increase with advancing in pregnancy (third trimester) while sever outcome is more in case infection occurred in first trimester. A pregnant woman can pass CMV to her fetus following primary infection, reinfection with a different CMV strain, or reactivation of a previous infection during pregnancy. Risk of transmission for primary infection is 30 to 40% in the first and second trimesters, and 40 to 70% in the third trimester. The risk of transmission following non-primary infection is much lower (3%). The risk of complications to the fetus is greatest if a primary infection occurs during the first trimester.

Challenges

- Natural immunity does not prevent reinfection or congenital transmission.
- Both primary or nonprimary infection (reinfection/reactivation) may cause congenital infection.
- Congenital infection manifest occurs in spectrum and difficult to diagnose.
- Current barriers to increase access to cytomegalovirus-specific antiviral therapy in pregnancy include the fact that the studied *valaciclovir dose* is high (almost triple the usual dose) and *ganciclovir* is not licensed for use in pregnancy. Lack of proven treatment to prevent congenital infection.
- Because the signs of CMV infection are similar to other medical conditions, laboratory testing is needed to confirm congenital

CMV.

- Since 1970 get vaccine but no licensed one available, still phase III trial underway.
- Limitation of IgM to differentiate primary from secondary infection.
- CMV Rise with increase seroprevalence in a women in a population.

Laboratory diagnosis after birth

Tests on a baby's saliva, urine, or blood done using polymerase chain reaction (*PCR*) to detect CMV DNA, or viral culture to detect live virus within two to three weeks after birth can confirm if the baby has congenital CMV. Congenital CMV infection cannot be diagnosed with antibody testing (IgG, IgM). Limitation of IgM to differentiate primary from secondary infection. Tests of saliva or urine are preferred for newborns.

Mitigation

Education and awareness

Most of women are unaware of CMV congenital anomalies. Why?. CMV has nonspecific symptoms, has no specific preventive actions/ measures, the guidelines related to CMV are universal and after initial, infection it establish latent infection. Education and awareness is the only current available strategy to prevent CMV transmission during pregnancy. It must be discussed with pregnant women and those planning for pregnancy:

- You can pass CMV to your baby.
- Babies with congenital CMV may show signs at birth.
- Avoid transmission/ reduce your risk? You may be able to lessen your risk of getting CMV by reducing contact with saliva and urine from babies and young children. The saliva and urine of children with CMV have high amounts of the virus. You can avoid getting a child's saliva in your mouth by not sharing food or kiss young child from cheek, utensils, or cups with a child, wash your hands after changing diapers, after whipping child drool or running nose Do not shar tooth brush. These cannot eliminate your risk of getting CMV but may lessen the chances of getting it.

Treatment

Early treatment may help Babies who show signs of congenital CMV at birth may be treated with antivirals that may decrease the severity of health problems and hearing loss but should be used with caution due to side effects. For babies with signs of congenital CMV at birth, antiviral medications, primarily valganciclovir, may improve hearing and developmental outcomes. *Valganciclovir* can have serious side effects and has only been studied in babies with signs of congenital CMV. There is limited information on the effectiveness of valganciclovir to treat babies with hearing loss alone.

Monitor children with congenital CMV as the baby diagnosed with congenital CMV infection should have regular hearing and vision screening. Hearing loss can be present at birth or develop later and may progress with age.

Hearing aids for children with hearing loss, as early interventions, can help strengthen communication and language skills. Improvements in these areas can lead to positive social interactions and educational development.

Finally in addition to the above-mentioned measures for mitigation, the evidence point to the need accelerate developing effective vaccines. Since CMV is the most common infectious agent causing birth defects globally added to these few routine antenatal cytomegalovirus screening is offered in only a few countries; there is an urgent public health need to create a unified, more precise and equitable approach to screening and surveillance especially in poor countries adopted by WHO and that global policies on CMV screening and treatment in pregnancy should now be reviewed in the context that antiviral medication can reduce the risk of vertical transmission More researches for safe and effective treatment during pregnancy and in newborn especially as some pregnant women are receiving inconsistent care across countries, following different policies.

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