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Evaluation of Cytomegalovirus Infection Diagnosis and Management during Pregnancy

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Abstract

Background: Cytomegalovirus (CMV) is a virus that belongs to the herpes viruses' family. It is a deoxyribonucleic acid (DNA) virus. Once the virus gets to access the fetus's body, it starts attacking the nervous system. This has been connected with early-pregnancy abortions or congenital defects while almost one-third demise. **Objectives:** Clinical practitioners fail to convey this knowledge to the public to improve their awareness. Therefore, in this paper, we will review the available literature discussing the classification, clinical features, and management of CMV infection to print a concise picture of this important disease that will provide practitioners with a clear picture of this issue. **Methodology:** We conducted the literature search within the PubMed database using the keywords: "Cytomegalovirus", "Prenatal infection", "Fetal infection", "Congenital infection", "Fetal diagnosis", "CMV prevention", and "CMV hyperimmune globulin" from 1990 to 2020. **Review:** The incidence of noncongenital CMV infection in the developed world reaches almost 3 in every 10 completed pregnancies. Almost one-fifth of a newborn with a congenital CMV infection are symptomatic at birth. The gold standard diagnostic test for congenital CMV is viral isolation in the bodily fluid (e.g. urine and/or saliva) within the first three weeks of life. There are no effective therapies for CMV infections. **Conclusion:** Clinicians need to be aware of the importance of educating pregnant women on the dangers of CMV infections and be actively vigilant for identifying CMV infection in fetuses and infants.

Keywords: Cytomegalovirus, Prenatal infection, Fetal infection.

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Introduction

Cytomegalovirus (CMV) is a virus that belongs to the herpes viruses' family. It is a deoxyribonucleic acid (DNA) virus. Recent literature suggests that CMV infection exists in 25% of women of reproductive age (Kenneson and Cannon, 2007). Once an individual gets infected with CMV, the viruses remain in the body indefinitely. The CMV remains in a dormant state and does not cause any injury to the infected body (Gaytant, 2003). However, once the immune status decreases in the infected for any reason, the virus exits the dormant state and becomes active (Boppana et al., 2001).

The virus needs to become active for it to be transmitted to the fetus or the newborn infant. While pregnant, the virus transmits vertically from the mother's body to the fetus (Selem et al., 2018; Ghaffari et al., 2019; Abbas et al., 2019). Once the virus gets to access to the fetus's body, it starts attacking the nervous system. This has been connected with early-pregnancy abortions or congenital defects while almost one-third demise (Raynor, 1993).

The primary concern in CMV infections in pregnant women is the devastating and serious effects it has on the fetus rather than the effects on the mother. The effects could become even more harmful if the mother gets a recent infection but does not develop any CMV-specific antibodies. Currently, there are two distinctive clinical pictures for maternal-fetal CMV infections: (1) perinatal

congenital cytomegalic infection and (2) postnatal congenital cytomegalic infection (Nelson and Demmler, 1997).

Population awareness regarding CMV infections is considered poor. For example, cross-sectional surveys have found that only a small number of women in the reproductive age heard of congenital CMV infections or their associated poor outcome on fetuses (Cannon et al., 2012; Wizman et al., 2016). Studies in the US have found that less than 50% of obstetric clinicians discussed CMV-infection prevention with their patients. Studies from multiple European countries reported similar findings (Korver et al., 2009; Cordier et al., 2012).

There is a large body of evidence that explains the dangers of maternal CMV infection and its ability to cause disability to newborns. However, clinical practitioners fail to convey this knowledge to the public to improve their awareness. Therefore, in this paper, we will review the available literature discussing the classification, clinical features, and management of CMV infection to print a concise picture of this important disease that will provide practitioners with a clear picture of this issue.

Methodology:

We conducted the literature search within the PubMed database using the keywords: “Cytomegalovirus”, “Prenatal infection”, “Fetal infection”, “Congenital infection”, “Fetal diagnosis”, “CMV prevention”, and “CMV hyperimmune globulin” from 1990 to 2020. We also used the Google Scholar database for additional literature search. After reading the abstracts, we manually selected the relevant papers for this review. In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics; Cytomegalovirus, Prenatal infection, and CMV prevention. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

Discussion

Incidence and Risk of Transmission

The incidence of con Congenital CMV infection in the developed world reaches almost 3 in every 10 completed pregnancies (Alford et al., 1990). Vertical transmission (i.e. from a mother to her child) is the direct result of primary maternal CMV infection. Three in every 4 pregnant women with a primary infection transmit the disease (Fowler et al., 1992).

Evidence shows that non-primary maternal infection is likely to be present with more prominent symptomatology and a coarser severity (Gaytant et al., 2003). Recently, re-infection with a new CMV strain has been suggested to result in the worst outcome (Boppana et al., 2001).

Almost one-fifth of a newborn with a congenital CMV infection are symptomatic at birth. Symptoms include (1) hepatic dysfunction, (2) disseminated intravascular coagulation, (3) chorioretinitis, (4) microcephaly, and (5) jaundice. (Korver et al., 2009; Cordier et al., 2012). The overwhelming majority (80%) of a newborn with a congenital CMV infection remain asymptomatic, however, they might suffer from late-onset complications such as (1) developmental delays, (2) declined vision, and (3) hearing loss (Lazzarotto et al., 2000).

Screening

There is growing controversy regarding the value of fetal CMV infection screening (Ville, 1998). CMV screening could aid in the prevention of congenitally-acquired infections. Pregnant women could be informed through educational programs on avoiding contracting an infection (Yow, 1989).

A study showed that an early-pregnancy CMV screening resulted in the detection of a majority of congenital CMV infections (Naessens et al., 2005). Nonetheless, there are no recommendations that support serological CMV screening in pregnant women. Few clinical situations warrant the serological testing for CMV, e.g. detection of typical findings suggestive of CMV on ultrasound (Naessens et al., 2005).

Results

Diagnosis

The majority of pregnant women infected with CMV typically follow an asymptomatic course. While only a minority (less than 5%) develop symptoms or progress to mononucleosis syndrome (Gaytant et al., 2002). Currently, anti-CMV IgG testing offers the most reliable method of detecting primary CMV infection in pregnant women (Macé et al., 2004). IgG avidity testing provides 100% specificity and 94.3% sensitivity.

Among women with positive CMV infection, ultrasonographic screening is warranted to look for findings of fetal CMV infection. Another, more invasive, way of identifying fetal CMV infection is amniocentesis (Lazzarotto et al., 2000). Table 1 shows the most frequently reported sonographic findings of fetal CMV infection (Lipitz et al., 2002; Malinger et al., 2003).

For newborns, the gold standard diagnostic test for congenital CMV is viral isolation in the bodily fluid (e.g. urine and/or saliva) within the first three weeks of life. CMV-specific IgM in serum can also be used to diagnose congenital CMV, however, they are positive in only 70% of infected infants (Revello et al., 1999). After diagnosis, a battery of clinical and laboratory findings can be used to follow-up the patients. Table 2 reports the common symptom and laboratory findings in the infected neonates (Boppana et al., 1992).

Management

Although major advances have been made in the diagnosis of fetal CMV infection, there are no effective therapies. A small body of evidence suggests the usage of CMV immunoglobulin (IG) in pregnant women who are proven to have an infection (Nigro et al., 2005).

The theory behind IG usage is that IG is thought to reduce the inflammatory process of the placental by neutralizing the CMV. Further, cytokine-mediated cellular injury is thought to be decreased by IG (Nigro et al., 2005). CMV immunoglobulin can be used as a possible alternative termination in cases where sonographic evidence supports the diagnosis of CMV infection (Duff, 2007).

In light of the absence of an effective vaccine, the only recommendation for seronegative pregnant women is the practice of good personal hygiene. Pregnant women are advised to limit close contact with bodily fluid (i.e. salivary secretions and urine) from young children and to ensure thorough washing of hands after contact (Adler et al., 1996).

Conclusion:

In conclusion, cytomegalovirus infection is by far the most prevalent congenitally-acquired infection worldwide. It can result in devastating early- and late-onset complications such as delayed development and deafness. Clinicians need to be aware of the importance of educating pregnant women on the dangers of CMV infections and be actively vigilant for identifying CMV infection in fetuses and infants.

Table 1. Most Frequently Reported Sonographic Findings of Fetal CMV Infection

Location	Features
General	Fetal Growth Restriction, Oligohydramnios, Hydrops Fetalis
Carinal	Cerebral Ventriculomegaly, Intracranial Calcifications, and Microcephaly
Abdomen	Ascites, Hyperechogenic Bowel, and Liver Calcifications
Pulmonary	Pleural Effusion

Table 2. Common Symptom and Laboratory Findings in CMV-infected Neonates

Symptoms	Laboratory Findings
Central Nervous System Abnormalities	High Alanine Aminotransferase Levels (>80 U/L)
Prematurity (<38 Weeks' Gestation)	Thrombocytopenia (<100,000 cells/mm3)
Small Size for Gestational Age,	Conjugated Hyperbilirubinemia (>2 mg/dl)
Jaundice	
Hepatosplenomegaly	

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