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Cytomegalovirus in Pregnancy

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1. Congenital Cytomegalovirus Infection: A Narrative Review of the Issues in Screening and Management From a Panel of European Experts

Author(s): Lazzarotto T.; Blazquez-Gamero D.; Delforge M.-L.; Foulon I.; Luck S.; Modrow S.; Leruez-Ville M.

Source: Frontiers in Pediatrics; Jan 2020; vol. 8

Publication Date: Jan 2020

Publication Type(s): Review

Available at Frontiers in Pediatrics - from Europe PubMed Central - Open Access

Available at Frontiers in Pediatrics - from Unpaywall

Abstract: Maternal primary and non-primary cytomegalovirus (CMV) infection during pregnancy can result in in utero transmission to the developing fetus. Congenital CMV (cCMV) can result in significant morbidity, mortality or long-term sequelae, including sensorineural hearing loss, the most common sequela. As a leading cause of congenital infections worldwide, cCMV infection meets many of the criteria for screening. However, currently there are no universal programs that offer maternal or neonatal screening to identify infected mothers and infants, no vaccines to prevent infection, and no efficacious and safe therapies available for the treatment of maternal or fetal CMV infection. Data has shown that there are several maternal and neonatal screening strategies, and diagnostic methodologies, that allow the identification of those at risk of developing sequelae and adequately detect cCMV. Nevertheless, many questions remain unanswered in this field. Well-designed clinical trials to address several facets of CMV treatment (in pregnant women, CMV-infected fetuses and both symptomatic and asymptomatic neonates and children) are required. Prevention (vaccines), biology and transmission factors associated with non-primary CMV, and the cost-effectiveness of universal screening, all demand further exploration to fully realize the ultimate goal of preventing cCMV. In the meantime, prevention of primary infection during pregnancy should be championed to all by means of hygiene education.

Database: EMBASE

2. Stillbirth Associated With Infection in a Diverse U.S. Cohort

Author(s): Page J.M.; Bardsley T.; Thorsten V.; Allshouse A.A.; Varner M.W.; Debbink M.P.; Dudley D.J.; Saade G.R.; Goldenberg R.L.; Stoll B.; Hogue C.J.; Bukowski R.; Conway D.; Reddy U.M.; Silver R.M.

Source: Obstetrics and gynecology; Dec 2019; vol. 134 (no. 6); p. 1187-1196

Publication Date: Dec 2019

Publication Type(s): Article

PubMedID: 31764728

Abstract:OBJECTIVE: To better characterize infection-related stillbirth in terms of pathogenesis and microbiology. METHOD(S): We conducted a secondary analysis of 512 stillbirths in a prospective, multisite, geographically, racially and ethnically diverse, population-based study of stillbirth in the United States. Cases underwent evaluation that included maternal interview, chart abstraction, biospecimen collection, fetal autopsy, and placental pathology. Recommended evaluations included syphilis and parvovirus serology. Each case was assigned probable and possible causes of death using the INCODE Stillbirth Classification System. Cases where infection was assigned as a probable or possible cause of death were reviewed. For these cases, clinical scenario, autopsy, maternal serology, culture results, and placental pathology were evaluated. RESULT(S): For 66 (12.9%) cases of stillbirth, infection was identified as a probable or possible cause of death. Of these, 36% (95% CI 35-38%) were categorized as a probable and 64% (95% CI 62-65%) as a possible cause of death. Infection-related stillbirth occurred earlier than non-infection-related stillbirth (median gestational age 22 vs 28 weeks, P=.001). Fetal bacterial culture results were available in 47 cases (71%), of which 35 (53%) grew identifiable organisms. The predominant species were Escherichia coli (19, 29%), group B streptococcus (GBS) (8, 12%), and enterococcus species (8, 12%). Placental pathology revealed chorioamnionitis in 50 (76%), funisitis in 27 (41%), villitis in 11 (17%), deciduitis in 35 (53%), necrosis in 27 (41%), and viral staining in seven (11%) cases. Placental pathology found inflammation or evidence of infection in 65 (99%) cases and fetal autopsy in 26 (39%) cases. In infection-related stillbirth cases, the likely causative nonbacterial organisms identified were parvovirus in two (3%) cases, syphilis in one (2%) case, cytomegalovirus (CMV) in five (8%) cases, and herpes in one (2%) case. CONCLUSION(S): Of infection-related stillbirth cases in a large U.S. cohort, E coli, GBS, and enterococcus species were the most common bacterial pathogens and CMV the most common viral pathogen.

Database: EMBASE

3. Sequelae of Congenital Cytomegalovirus Following Maternal Primary Infections Are Limited to Those Acquired in the First Trimester of Pregnancy.

Author(s): Faure-Bardon, Valentine; Magny, Jean-François; Parodi, Marine; Couderc, Sophie; Garcia, Patricia; Maillotte, Anne-Marie; Benard, Melinda; Pinquier, Didier; Astruc, Dominique; Patural, Hugues; Pladys, Patrick; Parat, Sophie; Guillois, Bernard; Garenne, Armelle; Bussières, Laurence; Guilleminot, Tiffany; Stirnemann, Julien; Ghout, Idir; Ville, Yves; Leruez-Ville, Marianne

Source: Clinical Infectious Diseases; Nov 2019; vol. 69 (no. 9); p. 1526-1532

Publication Date: Nov 2019

Publication Type(s): Academic Journal

Available at Clinical infectious diseases : an official publication of the Infectious Diseases Society of America - from Oxford Journals - Medicine

Abstract: Background The known relationship between the gestational age at maternal primary infection an the outcome of congenital CMV is based on small, retrospective studies conducted between 1980 and 2011. They reported that 32% and 15% of cases had sequelae following a maternal primary infection in the first and second or the third trimester, respectively. We aimed to revisit this relationship prospectively between 2011 and 2017, using accurate virological tools. Methods We collected data on women with a primary infection and an infected child aged at least 1 year at the time of analysis. An accurate determination of the timing of the primary infection was based upon serial measurements of immunoglobulin (Ig) M and IgG and on IgG avidity in sera collected at each trimester. The case outcome was assessed according to a structured follow-up between birth and 48 months. Results We included 255 women and their 260 fetuses/neonates. The dating of the maternal infection was prospective in 86% of cases and retrospective in 14%. At a median follow-up of 24 months, the proportion of sensorineural hearing loss and/or neurologic sequelae were 32.4% (95% confidence interval [CI] 23.72–42.09) after a maternal primary infection in the first trimester, 0 (95% CI 0–6.49) after an infection in the second trimester, and 0 (95% CI 0–11.95) after an infection in the third trimester (P <.0001). Conclusions These results suggest that a cytomegalovirus infection can be severe only when the virus hits the fetus in the embryonic or early fetal period. Recent guidelines recommend auditory follow-ups for at least 5 years for all infected children. This raises parental anxiety and generates significant costs. We suggest that auditory and specialized neurologic follow-ups may be recommended only in cases of a maternal infection in the first trimester.

Database: CINAHL

4. Prospective Cohort Study of Congenital Cytomegalovirus Infection during Pregnancy with Fetal Growth Restriction: Serologic Analysis and Placental Pathology.

Author(s): Tsuge, Mitsuru; Hida, Akira I.; Minematsu, Toshio; Honda, Naotoshi; Oshiro, Yumi; Yokoyama, Mikifumi; Kondo, Yoichi

Source: Journal of Pediatrics; Mar 2019; vol. 206 ; p. 42-42

Publication Date: Mar 2019

Publication Type(s): Academic Journal

PubMedID: NLM30413316

Abstract: Objective: To investigate prospectively the prevalence of congenital cytomegalovirus (CMV) infection and the pathologic features of the placenta in cases of fetal growth restriction (FGR).Study Design: Forty-eight pregnant women who were diagnosed with FGR during pregnancy were enrolled for 15 months. Maternal CMV serologic tests, pathologic examinations of the placenta, and newborn urinary CMV-DNA polymerase chain reaction tests were performed in all the cases. The clinical characteristics and laboratory findings of the pregnant women and their newborns were collected. Biomarkers for inflammation, angiogenesis, and placental hormones were measured in the maternal serum at FGR diagnosis or in the neonatal urine at birth.Results: One of the 48 cases with FGR was a congenital CMV infection. CMV antigen was detected in the placenta of 7 cases with FGR. The change rate of the estimated fetal body weight was significantly lower in FGR cases with placental CMV detection. Placental villitis was observed more frequently in FGR cases with placental CMV detection. Human placental lactogen was significantly decreased in FGR cases with placental CMV detection. Increased C-reactive protein and serum amyloid A levels in the maternal serum were observed more frequently in FGR cases with placental CMV detection. Newborn urine β-2 microglobulin levels were significantly higher in FGR cases with placental CMV detection.Conclusions: Serologic tests for maternal CMV, the change rate of the estimated fetal body weight, analysis of several biomarkers, and placental pathologic examinations might be helpful in comprehensively predicting the possibility of congenital CMV infection.

Database: CINAHL

5. Maternal and fetal cytomegalovirus infection: diagnosis, management, and prevention.

Author(s): Pass, Robert F; Arav-Boger, Ravit

Source: F1000Research; 2018; vol. 7 ; p. 255

Publication Date: 2018

Publication Type(s): Journal Article Review

PubMedID: 29560263

Available at F1000Research - from Europe PubMed Central - Open Access

Available at F1000Research - from Unpaywall

Abstract: Congenital cytomegalovirus infection is a major cause of central nervous system and sensory impairments that affect cognition, motor function, hearing, language development, vestibular function, and vision. Although the importance of congenital cytomegalovirus infection is readily evident, the vast majority of maternal and fetal infections are not identified, even in developed countries. Multiple studies of prenatal cytomegalovirus infections have produced a body of knowledge that can inform the clinical approach to suspected or proven maternal and fetal infection. Reliable diagnosis of cytomegalovirus infection during pregnancy and accurate diagnosis of fetal infection are a reality. Approaches to preventing the transmission of cytomegalovirus from mother to fetus and to the treatment of fetal infection are being studied. There is evidence that public health approaches based on hygiene can dramatically reduce the rate of primary maternal cytomegalovirus infections during pregnancy. This review will consider the epidemiology of congenital cytomegalovirus infection, the diagnosis and management of primary infection during pregnancy, and approaches to preventing maternal infection.

Database: Medline

6. Antenatal treatment options for primary cytomegalovirus infections

Author(s): Kagan K.O.; Sonek J.; Hamprecht K.

Source: Current Opinion in Obstetrics and Gynecology; 2018; vol. 30 (no. 6); p. 355-360

Publication Date: 2018

Publication Type(s): Review

PubMedID: 30169462

Available at Current opinion in obstetrics & gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Purpose of review Cytomegalovirus (CMV) infection is by far the most common fetal viral infection. It carries a risk of longterm sequelae for the neonate; though the severity depends on the gestational age at the time of infection. Improvement in primary prevention of a CMV infection during pregnancy can be achieved by providing information regarding hygiene to the mother. Once a maternal infection occurs, treatment options include prevention of maternal-fetal transmission and, once transmission occurs, attempts to reduce the severity of its effect on the fetus. Recent findings Several recent studies have shown that providing detailed information regarding the effects of CMV on the fetus and providing common sense hygiene advice reduced new primary infections by more than 75%. In cases with a documented maternal primary CMV infection, treatment with intravenous immunoglobulins have been tried to reduce maternal fetal transmission with a variable degree of success. In the randomized controlled study of Revello et al., immunoglobulins did not reduce the transmission rate. In a recent study, immunoglobulins were given only to women with very recent first trimester infections. In this study, the transmission rate was 2.5%, which is significantly less than expected. Leruez-Ville et al. treated mothers with known transmission of CMV to the fetus with 8 g of valaciclovir daily. They observed a significant reduction in the number of neonatal symptoms in

the treated cases. Summary Protocols are available to prevent primary CMV infections during pregnancy and, in cases where an infection does occur, steps can be taken to reduce its effect on the fetus thereby reducing the chance of long-term sequelae.

Database: EMBASE

7. Maternal Immunity and the Natural History of Congenital Human Cytomegalovirus Infection.

Author(s): Britt, William J

Source: Viruses; Aug 2018; vol. 10 (no. 8)

Publication Date: Aug 2018

Publication Type(s): Research Support, N.i.h., Extramural Journal Article Review

PubMedID: 30081449

Abstract: Congenital human cytomegalovirus (HCMV) is the most common viral infection of the developing fetus, and a significant cause of neurodevelopmental abnormalities in infants and children. Congenital HCMV infections account for an estimated 25% of all cases of hearing loss in the US. It has long been argued that maternal adaptive immune responses to HCMV can modify both the likelihood of intrauterine transmission of HCMV, and the severity of fetal infection and risk of long term sequelae in infected infants. Over the last two decades, multiple studies have challenged this paradigm, including findings that have demonstrated that the vast majority of infants with congenital HCMV infections in most populations are born to women with established immunity prior to conception. Furthermore, the incidence of clinically apparent congenital HCMV infection in infants born to immune and non-immune pregnant women appears to be similar. These findings from natural history studies have important implications for the design, development, and testing of prophylactic vaccines and biologics for this perinatal infection. This brief overview will provide a discussion of existing data from human natural history studies and animal models of congenital HCMV infections that have described the role of maternal immunity in the natural history of this perinatal infection.

Database: Medline

8. The risk of herpes simplex virus and human cytomegalovirus infection during pregnancy upon adverse pregnancy outcomes: A meta-analysis.

Author(s): Shi, Ting-Li; Huang, Li-Ju; Xiong, Yi-Quan; Zhong, Yan-Yun; Yang, Jin-Jun; Fu, Ting; Lei, Xie-Fen; Chen, Qing

Source: Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology; Jul 2018; vol. 104 ; p. 48-55

Publication Date: Jul 2018

Publication Type(s): Meta-analysis Journal Article Review

PubMedID: 29729547

Abstract:BACKGROUND AND OBJECTIVESHerpes simplex virus (HSV) and human cytomegalovirus (HCMV) are widespread infections in humans, yet their impact on adverse pregnancy outcomes is controversial. The objective of this study was to evaluate the impact of HSV and HCMV infections during pregnancy on adverse pregnancy outcomes.METHODSA systematic literature search was performed using Web of Science, Scopus, Medline, Embase, PubMed, and the Cochrane Library database for relevant publications up to 2nd August 2017. The odds ratio (OR) and relative risk (RR), and their corresponding 95% confidence intervals (CIs) were selected as the effect size. Statistical analysis was conducted using STATA 12.0.RESULTSIn total, 20 eligible studies were identified and included in the meta-analysis. Of these, 13 and 12 studies were related to the impact of HSV and HCMV upon adverse pregnancy outcomes, respectively. Collectively, the results indicated that HSV infection during pregnancy increased the risk of spontaneous abortion, premature birth and stillbirth with an OR of 3.81 (95% CI: 1.96-7.41), 3.83 (95% CI: 1.17-12.54), and 1.78 (95% CI: 1.08-2.95), respectively. HCMV infection during pregnancy also represented a risk factor for spontaneous abortion, premature birth and stillbirth with an OR of 1.61 (95% CI: 1.14-2.27), 1.86 (95% CI: 1.26-2.76) and 5.74 (95% CI: 2.04-16.12), respectively.CONCLUSIONSMaternal HSV and HCMV infection during pregnancy increase the risk of spontaneous abortion, premature birth, and stillbirth.

Database: Medline

9. Congenital cytomegalovirus: Impact on child health.

Author(s): SCHLEISS, MARK R.

Source: Contemporary Pediatrics; Jul 2018; vol. 35 (no. 7); p. 16-22

Publication Date: Jul 2018

Publication Type(s): Periodical

Available at Contemporary pediatrics - from ProQuest (Health Research Premium) - NHS Version

Available at Contemporary pediatrics - from PubMed

Abstract: The article examines the impact of congenital cytomegalovirus (cCMV) on pediatric practice and discusses evolving concepts in counseling and education, diagnosis in the newborn and medical management of the disease. Topics discussed include global prevalence of cCMV infection, and virology as gold standard for diagnosing cCMV. Also mentioned is the importance of newborn cCMV screening and prospects for the development of CMV vaccines.

Database: CINAHL

10. Congenital cytomegalovirus infection.

Author(s): Joseph, Amelia; Mahida, Nikunj; Clark, Gemma; Irving, William; Soo, Shiu

Source: Paediatrics & Child Health; Jun 2018; vol. 28 (no. 6); p. 277-281

Publication Date: Jun 2018

Publication Type(s): Academic Journal

Abstract: Congenital cytomegalovirus is the most common intrauterine infection and the leading non-genetic cause of sensorineural hearing loss. Worldwide, the birth prevalence is estimated at 7 per 1000 with the highest rates seen in developing countries. The highest intrauterine transmission rates and risk of neurodevelopmental sequelae are associated with primary maternal infections. Transmission occurs less frequently after non primary maternal infections due to reactivation or reinfection. 10–15% of infected infants are symptomatic at birth, with neurological symptoms present in two-thirds. Infants who are asymptomatic at birth may go on to develop late neurodevelopmental sequelae, with sensorineural hearing loss being the commonest late consequence. Prenatal, neonatal and retrospective diagnosis can be challenging. Early treatment of symptomatic neonates with the antiviral drug valganciclovir can reduce the long-term neurodevelopmental sequelae. Universal or targeted screening for congenital CMV is not currently advocated. The development of an effective vaccine appears to be some years away. This review highlights the important considerations for clinicians regarding the diagnosis, investigation and management of children with possible or confirmed congenital CMV infection.

Database: CINAHL

11. Congenital cytomegalovirus infection.

Author(s): Fowler, Karen B; Boppana, Suresh B

Source: Seminars in perinatology; Apr 2018; vol. 42 (no. 3); p. 149-154

Publication Date: Apr 2018

Publication Type(s): Journal Article Review

PubMedID: 29503048

Available at Seminars in perinatology - from Unpaywall

Abstract: Each year, thousands of children are born with or develop permanent disabilities such as hearing loss, vision loss, motor and cognitive deficits from congenital CMV infection (cCMV). However, awareness of cCMV and its associated sequelae is very low in pregnant women and healthcare providers. Both targeted and universal approaches to screen newborns for CMV infection are now achievable due to recent scientific advances including the development of a rapid, high-throughput method for detecting CMV in saliva, the efficacy of antiviral treatment in symptomatic infants, and the demonstration of cost effectiveness of CMV screening. Future studies are needed to address gaps in our understanding on the role of non-primary maternal CMV infections, the evaluation of antiviral treatment in asymptomatic infants, and the implementation of prevention strategies for cCMV.

Database: Medline

12. Outcome of Preterm Infants With Postnatal Cytomegalovirus Infection.

Author(s): Gunkel, Julia; de Vries, Linda S.; Jongmans, Marian; Koopman-Esseboom, Corine; van Haastert, Ingrid C.; Eijsermans, Maria C. J.; van Stam, Carolien; van Zanten, Bert G. A.; Wolfs, Tom F. W.; Nijman, Joppe

Source: Pediatrics; Feb 2018; vol. 141 (no. 2); p. 1-10

Publication Date: Feb 2018

Publication Type(s): Academic Journal

Abstract:OBJECTIVES: To assess whether preterm infants with postnatal cytomegalovirus infection develop neurologic sequelae in early childhood. METHODS: Infants <32 weeks' gestation were prospectively screened for cytomegalovirus (CMV) at term-equivalent age. Neurodevelopment was compared between CMV-positive and CMV-negative infants by using the Griffiths Mental Development Scales (GMDS) at 16 months' corrected age (CA); the Bayley Scales of Infant and Toddler Development, Third Edition or the GMDS at 24 to 30 months' CA; and the Wechsler Preschool and Primary Scale of Intelligence, Third Edition and Movement Assessment Battery for Children, Second Edition at 6 years of age. At 6 years old, hearing was assessed in CMV-positive children. RESULTS: Neurodevelopment was assessed in 356 infants at 16 months' CA, of whom 49 (14%) were infected and 307 (86%) were noninfected. Infected infants performed significantly better on the GMDS locomotor scale. There were no differences at 24 to 30 months' CA on the Bayley Scales of Infant and Toddler Development, Third Edition or GMDS. At 6 years of age, infected children scored lower on the Wechsler Preschool and Primary Scale of Intelligence, Third Edition, but mean scores were within normal range, reaching significance only in verbal IQ (96 [SD 17] vs 103 [SD 15] points; P = .046). Multiple regression indicated no impact of CMV status but significant influence of maternal education and ethnicity on verbal IQ. No significant differences in motor development were found and none of the infected children developed sensorineural hearing loss. CONCLUSIONS: In this cohort study, postnatal cytomegalovirus infection in preterm children did not have an adverse effect on neurodevelopment within the first 6 years of life.

Database: CINAHL

13. Cytomegalovirus in pregnancy and the neonate

Author(s): Emery V.C.; Lazzarotto T.

Source: F1000Research; 2017; vol. 6

Publication Date: 2017

Publication Type(s): Review

Available at F1000Research - from Europe PubMed Central - Open Access

Available at F1000Research - from Unpaywall

Abstract: Congenital cytomegalovirus (CMV) remains a leading cause of disability in children. Understanding the pathogenesis of infection from the mother via the placenta to the neonate is crucial if we are to produce new interventions and provide supportive mechanisms to improve the outcome of congenitally infected children. In recent years, some major goals have been achieved, including the diagnosis of primary maternal CMV infection in pregnant women by using the anti-CMV IgG avidity test and the diagnosis and prognosis of foetal CMV infection by using polymerase chain reaction real-time tests to detect and quantify the virus in amniotic fluid. This review summarises recent advances in our understanding and highlights where challenges remain, especially in vaccine development and anti-viral therapy of the pregnant woman and the neonate. Currently, no therapeutic options during pregnancy are available except those undergoing clinical trials, whereas valganciclovir treatment is recommended for congenitally infected neonates with moderately to severely symptomatic disease.

Database: EMBASE

14. Cytomegalovirus infection in pregnant women and its association with bad obstetric outcomes in Northern India.

Author(s): Fatima, Tanzeem; Siddiqui, Haris; Ghildiyal, Sneha; Baluni, Manjari; Singh, Dharam Veer; Zia, Amreen; Dhole, T N

Source: Microbial pathogenesis; Dec 2017; vol. 113 ; p. 282-285

Publication Date: Dec 2017

Publication Type(s): Journal Article

PubMedID: 29051058

Abstract:BACKGROUNDCytomegalovirus (CMV) infection during pregnancy is far more complex than other infections, due to ability of the virus to be frequently reactivated during the child bearing age and may vertically transmitted to the developing fetus in spite of maternal immunity. Therefore, in the current study we determined the prevalence of CMV infection in pregnant women and tried to identify the role of maternal CMV infection in adverse pregnancy outcomes in Northern India. In this case-control study, 517 pregnant women, out of them 200 in case group and 317 in the control group. The overall 31.72% (164/517) cases were found with active CMV infection. CMV positivity (p=0.026) was significantly associated with bad obstetric history (75/200, 37.50%) compared to normal pregnancy (89/317, 28.07%). CMV infection was predominantly observed in age group 21-25 years. CMV positivity have been found to be significantly higher in women from rural area as compare to those from urban area (p=0.028). However, no significant difference has been observed in case of occupation, income, and haemoglobin level.

Database: Medline

15. Intrauterine therapy of cytomegalovirus infection with valganciclovir: review of the literature

Author(s): Seidel V.; Siedentopf J.-P.; Henrich W.; Weizsacker K.; Feiterna-Sperling C.; Buhrer C.; Hofmann J.

Source: Medical Microbiology and Immunology; Oct 2017; vol. 206 (no. 5); p. 347-354

Publication Date: Oct 2017

Publication Type(s): Review

PubMedID: 28733760

Abstract: Congenital cytomegalovirus (CMV) infection is the leading cause for sensorineural hearing loss and mental retardation in children without genetic diseases worldwide. There is little evidence guiding therapeutic strategies during pregnancy when intrauterine fetal CMV infection is confirmed. We provide a systematic review of the use of ganciclovir (GCV) or VGCV during pregnancy discussing safety of its use for mother and fetus and describe two cases of intrauterine therapy of fetal CMV infection with valganciclovir (VGCV). A PubMed database search was done up to November 16, 2016 without any restrictions of publication date or journal, using the following keywords: "valganciclovir" or "ganciclovir" and "pregnan*". Furthermore, citations were searched and expert references were obtained. Reported cases were considered if therapy was in humans and initiation of treatment of the CMV infection was during pregnancy. In total, seven case reports were retrieved which described GCV or VGCV use during pregnancy for fetal or maternal CMV infection. In the four cases of treatment for maternal CMV infection, no negative effects on the fetus were reported. Three cases of GCV administration to pregnant woman with the intention of fetal treatment after proven fetal infection were found. We additionally present two cases of VGCV treatment in pregnancy from our center of tertiary care. VGCV seems to be a safe treatment for congenital CMV infection for the mother and the fetus. Therapeutic concentrations can be achieved in the fetus by oral intake of the mother and CMV replication can be suppressed. Larger studies are needed to evaluate this therapeutic intervention and the long-term effects.Copyright © 2017, Springer-Verlag GmbH Germany.

Database: EMBASE

16. Cytomegalovirus infection in pregnancy.

Author(s): Kagan, Karl; Hamprecht, Klaus; Kagan, Karl Oliver

Source: Archives of Gynecology & Obstetrics; Jul 2017; vol. 296 (no. 1); p. 15-26

Publication Date: Jul 2017

Publication Type(s): Academic Journal

PubMedID: NLM28508343

Available at Archives of Gynecology and Obstetrics - from SpringerLink - Medicine

Abstract: Purpose: Due to the severe risk of long-term sequelae, prenatal cytomegalovirus infection is of particular importance amongst intrauterine viral infections. This review summarizes the current knowledge about CMV infection in pregnancy.Methods: A search of the Medline and Embase database was done for articles about CMV infection in pregnany. We performed a detailed review of the literature in view of diagnosis, epidemiology and management of CMV infection in pregnancy.Results: The maternal course of the infection is predominantly asymptomatic; the infection often remains unrecognized until the actual fetal manifestation. Typical ultrasound signs that should arouse suspicion of intrauterine CMV infection can be distinguished into CNS signs such as ventriculomegaly or microcephaly and extracerebral infection signs such as hepatosplenomegaly or hyperechogenic bowel. Current treatment strategies focus on hygienic measures to prevent a maternal CMV infection during pregnancy, on maternal application of hyperimmunoglobulines to avoid materno-fetal transmission in case of a maternal seroconversion, and on an antiviral therapy in case the materno-fetal transmission have occurred.Conclusion: CMV infection in pregnancy may result in a severe developmental disorder of the newborn. This should be taken into account in the treatment of affected and non-affected pregnant women.

Database: CINAHL

17. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy.

Author(s): Rawlinson, William D; Boppana, Suresh B; Fowler, Karen B; Kimberlin, David W; Lazzarotto, Tiziana; Alain, Sophie; Daly, Kate; Doutré, Sara; Gibson, Laura; Giles, Michelle L; Greenlee, Janelle; Hamilton, Stuart T; Harrison, Gail J; Hui, Lisa; Jones, Cheryl A; Palasanthiran, Pamela; Schleiss, Mark R; Shand, Antonia W; van Zuylen, Wendy J

Source: The Lancet. Infectious diseases; Jun 2017; vol. 17 (no. 6); p. e177

Publication Date: Jun 2017

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 28291720

Available at The Lancet. Infectious diseases - from ProQuest (Health Research Premium) - NHS Version

Abstract: Congenital cytomegalovirus is the most frequent, yet under-recognised, infectious cause of newborn malformation in developed countries. Despite its clinical and public health importance, questions remain regarding the best diagnostic methods for identifying maternal and neonatal infection, and regarding optimal prevention and therapeutic strategies for infected mothers and neonates. The absence of guidelines impairs global efforts to decrease the effect of congenital cytomegalovirus. Data in the literature suggest that congenital cytomegalovirus infection remains a research priority, but data are yet to be translated into clinical practice. An informal International Congenital Cytomegalovirus Recommendations Group was convened in 2015 to address these questions and to provide recommendations for prevention, diagnosis, and treatment. On the basis of consensus discussions and a review of the literature, we do not support universal screening of

mothers and the routine use of cytomegalovirus immunoglobulin for prophylaxis or treatment of infected mothers. However, treatment guidelines for infected neonates were recommended. Consideration must be given to universal neonatal screening for cytomegalovirus to facilitate early detection and intervention for sensorineural hearing loss and developmental delay, where appropriate. The group agreed that education and prevention strategies for mothers were beneficial, and that recommendations will need continual updating as further data become available.

Database: Medline

18. Congenital cytomegalovirus - who, when, what-with and why to treat?

Author(s): Lim, Yinru; Lyall, Hermione

Source: The Journal of infection; Jun 2017; vol. 74

Publication Date: Jun 2017

Publication Type(s): Journal Article Review

PubMedID: 28646968

Abstract: Congenital cytomegalovirus (CMV) is the commonest cause of congenital infection worldwide and the leading non-genetic cause of sensorineural hearing loss in children. Appropriate investigations and timely decision on treatment is required as studies have shown that treatment with antiviral therapy leads to improved hearing and neurodevelopmental outcomes in the long term when started in the first month of life. This paper outlines the epidemiology, investigations in the diagnosis of congenital CMV infection and current evidence surrounding treatment.

Database: Medline

19. Diagnosis and management of infants with congenital cytomegalovirus infection

Author(s): Gantt S.; Bitnun A.; Renaud C.; Kakkar F.; Vaudry W.

Source: Paediatrics and Child Health (Canada); May 2017; vol. 22 (no. 2); p. 72-74

Publication Date: May 2017

Publication Type(s): Review

Available at Paediatrics & child health - from Europe PubMed Central - Open Access

Available at Paediatrics & child health - from ProQuest (Health Research Premium) - NHS Version

Abstract: Congenital cytomegalovirus infection (cCMV) is the most common congenital infection, occurring in approximately 0.5% of live births. Most infected newborns are asymptomatic, but up to 20% develop sensorineural hearing loss or other permanent neurologic sequelae. The presentation of newborns with symptomatic cCMV is highly variable, and the infection is usually not diagnosed in the absence of a screening program. Newborn cCMV screening programs are estimated to be beneficial and cost-effective, and are increasingly being implemented. Diagnosis requires direct detection of virus in a sample obtained before 3 weeks of life, and is best performed by polymerase chain reaction (PCR) of saliva or urine, either of which is more sensitive than dried blood spot. Antiviral treatment of selected newborns with cCMV-related disease appears to improve hearing and neurocognitive outcomes. All infected infants should be evaluated promptly to determine appropriate therapy, and receive close audiologic and developmental follow-up.

Database: EMBASE

20. Congenital Cytomegalovirus infection: advances and challenges in diagnosis, prevention and treatment.

Author(s): Marsico, Concetta; Kimberlin, David W

Source: Italian journal of pediatrics; Apr 2017; vol. 43 (no. 1); p. 38

Publication Date: Apr 2017

Publication Type(s): Journal Article Review

PubMedID: 28416012

Abstract: Cytomegalovirus (CMV) is the most frequent cause of congenital infection worldwide, with an estimated incidence in developing countries of 0.6-0.7% of all live births. The burden of disease related to congenital CMV in substantial, as it is the leading non-genetic cause of sensorineural hearing loss and an important cause of neurodevelopmental disabilities in children. Despite its clinical significance, congenital CMV infection often goes undetected because the majority of infected infants are asymptomatic at birth and screening programs have not been substantially implemented. Other than behavioral measures, effective interventions aimed at the prevention of maternal infection and of mother-to-child transmission are lacking. Due to a convergence of recent advances in both diagnostic and therapeutic strategies in infants with congenital CMV, though, the field likely will be changing rapidly over just the next few years. Specifically, a highly-sensitive screening test with high throughput potential has been developed, and treatment of infants symptomatically infected with congenital CMV has proven to be well-tolerated and effective in improving long-term hearing and neurodevelopmental outcomes.This review highlights the clinical importance of congenital CMV infection, the developments in laboratory diagnostics, and the benefits of antiviral therapy. It also identifies the global efforts still required in the prevention of maternal infection and in the optimization of antiviral therapy to further reduce the burden of congenital CMV disease.

Database: Medline

21. Cytomegalovirus infection in pregnancy.

Author(s): Davis, Nicole L; King, Caroline C; Kourtis, Athena P

Source: Birth defects research; Mar 2017; vol. 109 (no. 5); p. 336-346

Publication Date: Mar 2017

Publication Type(s): Journal Article Review

PubMedID: 28398680

Abstract: Cytomegalovirus (CMV) is a DNA herpesvirus that is common worldwide. The two known main sources of primary CMV infection during pregnancy are through sexual activity and contact with young children. Primary infection occurs in approximately 1 to 4% of pregnancies, and is mostly asymptomatic in immunocompetent adults. However, primary infection may manifest as a mild mononucleosis or flu-like syndrome with persistent fever and fatigue. CMV can be transmitted from mother-to-child in utero, intrapartum, or during breastfeeding. Intrauterine transmission can lead to congenital CMV infection, a leading cause of permanent hearing and vision loss and neurological disability among children. Congenital CMV transmission rates are as high as 50% in women who acquire primary CMV infection during pregnancy, and less than 2% in women with nonprimary infection. There is no licensed CMV vaccine. Good hygiene practices and avoiding intimate contact with young children (e.g., kissing on the mouth and sharing utensils) have been suggested as an approach to prevent maternal primary CMV infection during pregnancy, but remains an unproven method of reducing the risk of congenital CMV infection. Approximately 1 in 10 infants who acquire CMV in utero will have clinical signs at birth, and an additional 10 to 15% will go on to develop late-onset sequelae. Antiviral treatment prenatally and postnatally has not proven effective at preventing congenital or postnatal CMV infection, and is not recommended for routine clinical care. However, antiviral treatment when initiated in the first month of life for symptomatic congenital CMV infection is recommended for improved neurodevelopmental and audiologic outcomes. Birth Defects Research 109:336-346, 2017. © 2017 Wiley Periodicals, Inc.

Database: Medline

22. Fetal cytomegalovirus infection.

Author(s): Leruez-Ville, Marianne; Ville, Yves

Source: Best practice & research. Clinical obstetrics & gynaecology; Jan 2017; vol. 38 ; p. 97-107

Publication Date: Jan 2017

Publication Type(s): Journal Article Review

PubMedID: 27923540

Abstract: Cytomegalovirus (CMV) congenital infection affects 0.7% of live births worldwide and is the leading cause of congenital neurological handicap of infectious origin. However, systematic screening for this infection has not been implemented in pregnancy or at birth in any country. This apparent paradox had been justified by persisting gaps in the knowledge of this congenital infection: uncertain epidemiological data, difficulty in the diagnosis of maternal infection, absence of validated prenatal prognostic markers, unavailability of an efficient vaccine and scarcity of data available on the treatment. However, in the last decade, new data have emerged towards better management of this congenital infection, including solid epidemiological data, good evidence for the accuracy of diagnosis of maternal CMV infection and good evidence for the feasibility of predicting the outcome of fetal infection by a combination of fetal imaging and fetal laboratory parameters. There is also some evidence that valaciclovir treatment of mothers carrying an infected fetus is feasible, safe and might be effective. This review provides an update on the evidence for diagnosis, prognosis and treatment of congenital infection in the antenatal period. These suggest a benefit to a proactive approach for prenatal congenital infections.

Database: Medline

23. Primary Human Cytomegalovirus (HCMV) Infection in Pregnancy.

Author(s): Buxmann, Horst; Hamprecht, Klaus; Meyer-Wittkopf, Matthias; Friese, Klaus

Source: Deutsches Arzteblatt international; Jan 2017; vol. 114 (no. 4); p. 45-52

Publication Date: Jan 2017

Publication Type(s): Journal Article Review

PubMedID: 28211317

Available at Deutsches Arzteblatt international - from Europe PubMed Central - Open Access

Available at Deutsches Arzteblatt international - from Unpaywall

Abstract:BACKGROUNDIn 0.5-4% of pregnancies, the prospective mother sustains a primary infection with human cytomegalovirus (HCMV). An HCMV infection of the fetus in the first or second trimester can cause complex post-encephalitic impairment of the infant brain, leading to motor and mental retardation, cerebral palsy, epilepsy, retinal defects, and progressive hearing loss.METHODSThis review is based on pertinent publications from January 2000 to October 2016 that were retrieved by a selective search in PubMed employing the terms "cytomegalovirus and pregnancy" and "congenital cytomegalovirus."RESULTS85-90% of all neonates with HCMV infection are asymptomatic at birth. The main long-term sequela is hearing impairment, which develops in 8-15% of these affected children. Hygienic measures can lower the risk of primary HCMV infection in pregnancy by 50-85%. The first randomized and controlled trial (RCT) of passive immunization with an HCMV-specific hyper - immune globulin (HIG) preparation revealed a trend toward a lower risk of congenital transmission of the virus (30% versus 44% with placebo, p = 0.13). The effect of HIG was more marked in the initial non-randomized trial (15% versus 40%, p = 0.02). The RCT also showed HIG to be associated with a higher frequency of fetal growth retardation and premature birth (13% versus 2%, p = 0.06). Valaciclovir is a further, non-approved treatment option.CONCLUSIONIn the absence of an active vaccine against HCMV, counseling about hygienic measures may currently be

the single most effective way to prevent congenital HCMV infection. Moreover, HCMV serologic testing is recommended in the guideline of the Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, AWMF). Further randomized trials of treatment with HIG and with valaciclovir are urgently needed so that the options for the prevention and treatment of congenital HCMV infection can be assessed.

Database: Medline

24. Optimum treatment of congenital cytomegalovirus infection.

Author(s): Leruez-Ville, Marianne; Ville, Yves

Source: Expert review of anti-infective therapy; 2016; vol. 14 (no. 5); p. 479-488

Publication Date: 2016

Publication Type(s): Journal Article Review

PubMedID: 27043943

Abstract: Congenital cytomegalovirus infection affects 0.7% of live births and is the leading cause of congenital neurological handicaps of infectious origin. However, systematic screening of this infection has not been implemented in pregnancy or at birth in any country. This apparent paradox has been justified by the unavailability of an efficient vaccine and by the scarcity of data available on the treatment of congenital CMV. However, in the last decade interesting new data on the management of this congenital infection has emerged including new results on both neonatal and postnatal treatments. This review provides an update on the potential benefits of antiviral treatment and on passive immunisation both in the neonatal and the antenatal periods. These suggest a benefit to a proactive approach for neonatal and prenatal congenital infections.

Database: Medline

25. An update on congenital cytomegalovirus infection

Author(s): Momberg Z.; Geerts L.

Source: Obstetrics and Gynaecology Forum; 2016; vol. 26 (no. 1); p. 20-24

Publication Date: 2016

Publication Type(s): Review

Abstract: Counselling regarding congenital CMV infection is challenging as it may have a protracted clinical course from the time of suspected maternal infection until evidence of fetal damage. Gestational age at infection is the strongest predictor of adverse outcome but is often impossible to determine. Fetal infection, confirmed by amniotic fluid PCR, cannot be reliably diagnosed before 20 weeks gestation but this is usually not an issue outside of routine screening programmes. Although a positive PCR confirms fetal infection, it does not have prognostic value in the individual patient and it must be remembered that a negative PCR result is not fully reassuring as the sensitivity is not 100%. Fetal blood parameters, obtained by cordocentesis, are most useful for prognosticating in addition to ultrasound features, but manifestations of fetal damage (particularly central nervous system involvement) may only become apparent late in the third trimester. If imaging features of central nervous system involvement are present, late termination of pregnancy can be considered due to the high likelihood of severe brain damage, in line with the South Africa Termination of Pregnancy Act. A vaccine against CMV would be the best solution to this difficult and unpredictable clinical problem, but a phase III trial is still needed to prove efficacy. Hygiene education is beneficial in primary prevention but has not been implemented widely in South Africa. For secondary prevention or treatment, CMV hyper-immune globulin has not demonstrated efficacy so far.

Valaciclovir is currently the most promising drug and careful case selection of infected fetuses without CNS involvement would be prudent.

Database: EMBASE

26. Update on treatment of cytomegalovirus infection in pregnancy and of the newborn with congenital cytomegalovirus.

Author(s): Rawlinson, William D; Hamilton, Stuart T; van Zuylen, Wendy J

Source: Current opinion in infectious diseases; Dec 2016; vol. 29 (no. 6); p. 615-624

Publication Date: Dec 2016

Publication Type(s): Journal Article Review

PubMedID: 27607910

Available at Current opinion in infectious diseases - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract:PURPOSE OF REVIEWThe purpose of this review is to assess the recent studies of therapy of pregnant women and neonates, aimed at preventing the consequences of congenital cytomegalovirus (CMV) infection.RECENT FINDINGSA recent randomized controlled trial of treatment of CMV during pregnancy with hyperimmune globulin did not show significant efficacy in prevention of foetal infection and morbidity, although there was a trend towards improvement with treatment. Trials of antiviral therapy of the mother during pregnancy have involved small numbers only, confounded by ethical and practical difficulties, and further studies are needed to demonstrate whether or not antivirals are useful and well tolerated in this setting.Antiviral treatment of neonatal CMV acquired congenitally has been studied in well controlled trials and the antiviral valganciclovir has shown efficacy in reducing the more severe outcomes. Trials are ongoing of the use of antivirals in less severe disease, although results are likely to take several years.SUMMARYCongenital CMV infection is the most frequent cause of congenital malformation in developed countries, with a symptomatic prevalence of 0.64% of all live births. Infection may result in neurodevelopmental delay, foetal or neonatal death, and most frequently, sensorineural hearing loss. Successful control of viral infections during pregnancy and in the newborn period is essential in reducing early and late morbidity and mortality. Control of congenital CMV infection may be via primary prevention methods such as reducing contact with the pathogen, improved hygiene - both for the pregnant mother and for the neonate, or secondary prevention via reduction of vertical transmission from mother to foetus and reduction in consequences of infection by treatment of infected pregnant women and infected neonates.

Database: Medline

27. Comprehensive review and update of cytomegalovirus infection in pregnancy.

Author(s): Navti, Osric; Hughes, Brenna L; Tang, Julian W; Konje, Justin

Source: Obstetrician & Gynaecologist; Oct 2016; vol. 18 (no. 4); p. 301-307

Publication Date: Oct 2016

Publication Type(s): Academic Journal

Available at The Obstetrician & Gynaecologist - from Wiley Online Library

Available at The Obstetrician & Gynaecologist - from Free Medical Journals . com

Abstract: Key Content: Cytomegalovirus (CMV) is the most common cause of congenital viral infections; 75–90% of infections are asymptomatic at birth but 10–25% of infants will develop neurological sequelae.Diagnosis of primary maternal CMV in pregnancy should be based on seroconversion in pregnancy (de novo appearance of virus-specific immunoglobulin G [IgG] in the serum of pregnant women who were previously seronegative) or on detection of specific immunoglobulin M (IgM) and IgG antibodies in association with low IgG avidity.Primary maternal infection is associated with a 30–40% risk of intrauterine transmission and fetal infection, with 20–25% of those infected developing sequelae postnatally.Prenatal diagnosis of fetal CMV is imperfect and based on amniocentesis performed at least 7 weeks after presumed maternal infection and after 21 weeks of gestation.The presence of radiologic findings by ultrasound in combination with CMV DNA viral load in amniotic fluid may have prognostic significance for risk of neurologic sequelae. Learning objectives: To understand the prevalence, diagnosis and implications of CMV infection in pregnancy.To explore the management options in a pregnancy affected by congenital CMV. Ethical issues: Should routine screening for CMV be recommended in pregnancy?How should termination counselling be conducted following prenatal confirmation of fetal infection with amniocentesis?

Database: CINAHL

28. Diagnosis and antenatal management of congenital cytomegalovirus infection.

Author(s): Society for Maternal-Fetal Medicine (SMFM); Hughes, Brenna L; Gyamfi-Bannerman, Cynthia

Source: American journal of obstetrics and gynecology; Jun 2016; vol. 214 (no. 6); p. B5

Publication Date: Jun 2016

Publication Type(s): Journal Article Review

PubMedID: 26902990

Available at American journal of obstetrics and gynecology - from Unpaywall

Abstract: Congenital cytomegalovirus (CMV) is the most common viral infection, affecting nearly 40,000 infants each year in the United States. Of seronegative women, 1-4% will acquire a primary infection during pregnancy, and the majority of these women will be asymptomatic. Prior maternal exposure to CMV does not preclude neonatal infection. The purpose of this document is to review diagnosis of primary maternal CMV infection, diagnosis of fetal CMV infection, and whether antenatal therapy is warranted. We recommend the following: (1) that women with a diagnosis of primary CMV infection in pregnancy be advised that the risk of congenital infection is 30-50%, on average, and that the severity of infection varies widely (Best Practice); (2) for women suspected of having primary CMV infection in pregnancy, we recommend that diagnosis should be either by IgG seroconversion or with positive CMV IgM, positive IgG, and low IgG avidity (grade 1B); (3) amniocentesis is the best option as a prenatal diagnostic tool to detect fetal congenital CMV infection, performed >21 weeks of gestation and >6 weeks from maternal infection (grade 1C); (4) we do not recommend routine screening of all pregnant women for evidence of primary CMV

infection at this time (grade 1B); and (5) we do not recommend antenatal treatment with ganciclovir or valacyclovir; and we recommend that any antenatal therapy, either with antivirals or CMV hyperimmune globulin, should only be offered as part of a research protocol (Best Practice).

Database: Medline

29. Congenital Cytomegalovirus.

Author(s): Mestas, Erin

Source: Advances in neonatal care : official journal of the National Association of Neonatal Nurses; Feb 2016; vol. 16 (no. 1); p. 60-65

Publication Date: Feb 2016

Publication Type(s): Journal Article Review

PubMedID: 26752783

Abstract:BACKGROUNDCongenital cytomegalovirus (CMV) is the leading viral intrauterine infection in the United States. It causes more developmental delays and long-term sequelae than Down syndrome (trisomy 21), neural tube defects, or fetal alcohol syndrome combined. Yet, this virus, a member of the herpes virus family, is not well known to the public and its prevention is typically not discussed in obstetric offices. Although many infants with congenital CMV are asymptomatic at birth, a significant proportion still may develop sequelae. Symptomatic infants face potentially devastating consequences. Pharmacologic treatment is reserved for those with severe organ or central nervous system involvement. Treatment of infants with congenital CMV can be complex and requires extensive outpatient follow-up.PURPOSETo educate nurses and nurse practitioners regarding the risks, signs, treatment, and care related to congenital CMV.METHODS/SEARCH STRATEGIESPubMed was searched to obtain English language publications from 2005 to 2015 for studies examining the current knowledge base of congenital cytomegalovirus, sequelae, and subsequent treatment using key terms "cytomegalovirus" combined with "congenital." A total of 18 articles were retained for analysis.FINDINGS/RESULTSOverall, the greatest risk reduction strategy for CMV transmission is education of pregnant women. In the neonate at risk for congenital CMV, early identification, antiviral treatment, and care coordination are pivotal to maximizing outcomes.IMPLICATIONS FOR PRACTICEIncreasing understanding of congenital CMV, modes of transmission, signs of infection, and intervention strategies as well as its impact on development are essential to maximizing outcomes.IMPLICATIONS FOR RESEARCHThe need for research exists in the area of valganciclovir's impact on sensorineural hearing loss as well as potential vaccines to protect against CMV transmission. Research is also being conducted in the area of passive immunity via administration of CMV-specific hyperimmune globulin therapy to pregnant women diagnosed with a primary CMV infection.

Database: Medline

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

Author(s): Naing, Zin W; Scott, Gillian M; Shand, Antonia; Hamilton, Stuart T; van Zuylen, Wendy J; Basha, James; Hall, Beverly; Craig, Maria E; Rawlinson, William D

Source: The Australian & New Zealand journal of obstetrics & gynaecology; Feb 2016; vol. 56 (no. 1); p. 9-18

Publication Date: Feb 2016

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 26391432

Abstract: 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.

Database: Medline

31. Stillbirths: Rates, risk factors, and acceleration towards 2030

Author(s): Lawn J.E.; Blencowe H.; Shiekh S.; Jassir F.B.; Cousens S.; Waiswa P.; Amouzou A.; You D.; Mathers C.; Hogan D.; Mathai M.; Flenady V.; Froen J.F.; Qureshi Z.U.; Calderwood C.; McClure E.M.; Kinney M.V.; De Bernis L.; Heazell A.; Leisher S.H.; Azad K.; Rahman A.; El-Arifeen S.; Day L.T.; Saha S.L.; Alam S.; Wangdi S.; Ilboudo T.F.; Zhu J.; Liang J.; Mu Y.; Li X.; Zhong N.; Kyprianou T.; Allvee K.; Gissler M.; Zeitlin J.; Bah A.; Jawara L.; Lack N.; De Maria Herandez F.; More N.S.; Nair N.; Tripathy P.; Kumar R.; Newtonraj A.; Kaur M.; Gupta M.; Varghese B.; Isakova J.; Phiri T.; Hall J.A.; Curteanu A.; Manandhar D.; Hukkelhoven C.; Dijs-Elsinga J.; Klungsoyr K.; Poppe O.; Barros H.; Correia S.; Tsiklauri S.; Cap J.; Podmanicka Z.; Szamotulska K.; Pattison R.; Hassan A.A.; Musafili A.; Bergstrom A.; Kujala S.; Langhoff-Roos J.; Lundqvist E.; Kadobera D.; Costello A.; Colbourn T.; Fottrell E.; Prost A.; Osrin D.; King C.; Neuman M.; Hirst J.; Rubayet S.; Smith L.; Manktelow B.N.; Draper E.S.

Source: The Lancet; Feb 2016; vol. 387 (no. 10018); p. 587-603

Publication Date: Feb 2016

Publication Type(s): Review

PubMedID: 26794078

Abstract: An estimated 2.6 million third trimester stillbirths occurred in 2015 (uncertainty range 2.4-3.0 million). The number of stillbirths has reduced more slowly than has maternal mortality or mortality in children younger than 5 years, which were explicitly targeted in the Millennium Development Goals. The Every Newborn Action Plan has the target of 12 or fewer stillbirths per 1000 births in every country by 2030. 94 mainly high-income countries and upper middle-income countries have already met this target, although with noticeable disparities. At least 56 countries, particularly in Africa and in areas aff ected by confl ict, will have to more than double present progress to reach this target. Most (98%) stillbirths are in low-income and middle-income countries. Improved care at birth is essential to prevent 1.3 million (uncertainty range 1.2-1.6 million) intrapartum stillbirths, end preventable maternal and neonatal deaths, and improve child development. Estimates for stillbirth causation are impeded by various classifi cation systems, but for 18 countries with reliable data, congenital abnormalities account for a median of only 7.4% of stillbirths. Many disorders associated with stillbirths are potentially modifi able and often coexist, such as maternal infections (population attributable fraction: malaria 8.0% and syphilis 7.7%), non-communicable diseases, nutrition and lifestyle factors (each about 10%), and maternal age older than 35 years (6.7%). Prolonged pregnancies contribute to 14.0% of stillbirths. Causal pathways for stillbirth frequently involve impaired placental function, either with fetal growth restriction or preterm labour, or both. Two-thirds of newborns have their births registered. However, less than 5% of neonatal deaths and even fewer stillbirths have death registration. Records and registrations of all births, stillbirths, neonatal, and maternal deaths in a health facility would substantially increase data availability. Improved data alone will not save lives but provide a way to target interventions to reach more than 7000 women every day worldwide who experience the reality of stillbirth.

Database: EMBASE

32. Advances in the prevention and treatment of congenital cytomegalovirus infection.

Author(s): James, Scott H.; Kimberlin, David W.

Source: Current Opinion in Pediatrics; Feb 2016; vol. 28 (no. 1); p. 81-85

Publication Date: Feb 2016

Publication Type(s): Academic Journal

PubMedID: NLM26709686

Available at Current Opinion in Pediatrics - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Current Opinion in Pediatrics - from Unpaywall

Abstract: Purpose Of Review: Cytomegalovirus (CMV) is the most common cause of congenital infection in the world. Symptomatic infants are at increased risk of developing permanent sequelae, including sensorineural hearing loss and neurodevelopmental delay. Advances in the treatment and prevention of congenital CMV infection are a high priority nationally and globally.Recent Findings: In symptomatic infants, antiviral therapy with 6 months of oral valganciclovir improves hearing and neurodevelopmental outcomes. Strategies to prevent congenital or maternal CMV infections, including the use of CMV hyperimmune globulin and development of a maternal vaccine, have yet to yield positive results.Summary: The clinical significance of congenital CMV infection, developments in antiviral therapy, and efforts to prevent congenital disease are herein reviewed.

Database: CINAHL

33. A Multifactorial Analysis of the Pregnancy Outcomes in Cytomegalovirus-Infected Women

Author(s): Ding Z.-Y.; Xu F.; Chen D.-Z.; Meng X.-N.; Xu T.-S.; Lu M.-D.; Zhuge H.-X.

Source: Gynecologic and Obstetric Investigation; Aug 2015; vol. 80 (no. 2); p. 106-112

Publication Date: Aug 2015

Publication Type(s): Article

PubMedID: 25792174

Available at Gynecologic and obstetric investigation - from ProQuest (Health Research Premium) - NHS Version

Abstract: Aims: To investigate the impacts of cytomegalovirus (CMV) viral load, TORCH (toxoplasmosis, others, rubella, CMV and herpes) coinfections, CMV glycoprotein B (gB) genotypes and maternal genetic polymorphisms on pregnancy outcomes among CMV-infected women. Method(s): A total of 731 CMV-infected pregnant women (634 and 97 with normal and adverse pregnancy outcomes, respectively) were recruited. CMV load quantification and screening of TORCH coinfections were performed by using real-time polymerase chain reaction (PCR) and immunodetection techniques, respectively. Genotyping of CMV gB and maternal NFKB1-94 ins/del, NFKBIA -826C/T and -881A/G polymorphisms was performed by using PCR-restriction fragment length polymorphism. Result(s): We found that the mean CMV viral load in women with adverse pregnancy outcomes was significantly higher than that in women with normal outcomes at all pregnancy stages ($p < 0.01$). We also found that TORCH coinfections resulted in a 1.65-fold (95% CI = 1.00-2.73) increase in the risk of adverse pregnancy outcomes ($p = 0.05$). Additionally, we noticed no significant difference in the distribution of CMV gB genotypes between women with normal and adverse pregnancy outcomes ($p = 0.42$). We also observed that the ins/ins variant genotype of the NFKB1 polymorphism could reduce the risk of adverse pregnancy outcomes (OR = 0.38, 95% CI = 0.15-0.98; $p = 0.04$). Conclusion(s): CMV viral load, TORCH coinfections and maternal NFKB1 polymorphism could influence pregnancy outcomes among CMV-infected women.

Database: EMBASE

34. Pathology of the Stillborn Infant for the General Pathologist: Part 2

Author(s): Faye-Petersen O.M.; Heller D.S.

Source: Advances in Anatomic Pathology; Mar 2015; vol. 22 (no. 2); p. 71-93

Publication Date: Mar 2015

Publication Type(s): Review

PubMedID: 25664943

Available at Advances in anatomic pathology - from Ovid (Journals @ Ovid) - Remote Access

Available at Advances in anatomic pathology - from Ovid (Journals @ Ovid) - London Health Libraries

Available at Advances in anatomic pathology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: As the information obtained from previable fetal and stillbirth autopsies is used not only to explain the loss to the parents, but for future pregnancy planning, general pathologists need to be comfortable in dealing with these autopsies. The importance of an adequate fetal examination has been emphasized in a recent policy on the subject by the American Board of Pathology http://www.abpath.org/FetalAutopsyPolicy.pdf. This second review paper covers the approach to hydrops fetalis. The approach to the nonanomalous and anomalous fetus was covered in the first part of this series.

Database: EMBASE

35. Perinatal outcome after maternal primary cytomegalovirus infection in the first trimester: A practical update and counseling aid

Author(s): Hui L.; Wood G.

Source: Prenatal Diagnosis; Jan 2015; vol. 35 (no. 1); p. 1-7

Publication Date: Jan 2015

Publication Type(s): Review

Available at Prenatal diagnosis - from Wiley Online Library

Abstract: Cytomegalovirus (CMV) is the most common cause of congenital infection with approximately 0.5% of pregnant women in developed countries seroconverting during pregnancy. In utero transmission occurs in about one third of women who develop primary infection in the first trimester, and these fetuses are at risk for adverse perinatal outcomes and long-term neurological complications. The great promise of a prenatal therapy to reduce fetal infection after maternal primary CMV infection has not been realized to date. The prediction of CMV sequelae is particularly challenging for clinicians because of the heterogeneity of the published literature, the wide spectrum of perinatal outcomes, the adjustment of fetal risk at each stage of assessment, and the variable quality of published data. Given the continued lack of a proven fetal therapy, it is timely to review the natural history of congenital CMV in the modern management era. We have analyzed the recent literature, integrated findings from multiple studies, and calculated stage-specific risks for adverse perinatal outcome to assist in counseling women with first trimester primary CMV infection.

Database: EMBASE

36. Congenital cytomegalovirus infection: Clinical presentation, epidemiology, diagnosis and prevention

Author(s): van Zuylen W.J.; Hamilton S.T.; Naing Z.; Hall B.; Rawlinson W.D.; Shand A.

Source: Obstetric Medicine; Dec 2014; vol. 7 (no. 4); p. 140-146

Publication Date: Dec 2014

Publication Type(s): Review

Available at Obstetric Medicine - from Europe PubMed Central - Open Access

Available at Obstetric Medicine - from Unpaywall

Abstract: Cytomegalovirus is the most common congenital infection causing serious disease in infants. It is the leading infectious cause of sensorineural hearing loss and neurodevelopmental disability in developed countries. Despite the clinical importance of congenital cytomegalovirus, surveys show there is limited awareness and knowledge in the medical and general community about congenital cytomegalovirus infection. This article reviews the clinical features, global epidemiology, transmission and risk factors for cytomegalovirus infections. It also highlights several major advances made in recent years in the diagnosis and prevention of cytomegalovirus infection during pregnancy. Although research is ongoing, no therapy is currently proven to prevent or treat maternal, fetal or neonatal cytomegalovirus infection. Education of women regarding hygiene measures can help prevent cytomegalovirus infection and are currently the best strategy to prevent congenital cytomegalovirus disease.Copyright © The Author(s) 2014.

Database: EMBASE

37. Prevention of congenital cytomegalovirus complications by maternal and neonatal treatments: a systematic review.

Author(s): Hamilton, Stuart T; van Zuylen, Wendy; Shand, Antonia; Scott, Gillian M; Naing, Zin; Hall, Beverley; Craig, Maria E; Rawlinson, William D

Source: Reviews in medical virology; Nov 2014; vol. 24 (no. 6); p. 420-433

Publication Date: Nov 2014

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review Systematic Review

PubMedID: 25316174

Available at Reviews in medical virology - from Wiley Online Library

Abstract: Human cytomegalovirus is the leading non-genetic cause of congenital malformation in developed countries. Congenital CMV may result in fetal and neonatal death or development of serious clinical sequelae. In this review, we identified evidence-based interventions for prevention of congenital CMV at the primary level (prevention of maternal infection), secondary level (risk reduction of fetal infection and disease) and tertiary level (risk reduction of infected neonates being affected by CMV). A systematic review of existing literature revealed 24 eligible studies that met the inclusion criteria. Prevention of maternal infection using hygiene and behavioural interventions reduced maternal seroconversion rates during pregnancy. However, evidence suggested maternal adherence to education on preventative behaviours was a limiting factor. Treatment of maternal CMV infection with hyperimmune globulin (HIG) showed some evidence for efficacy in prevention of fetal infection and fetal/neonatal morbidity with a reasonable safety profile. However, more robust clinical evidence is required before HIG therapy can be routinely recommended. Limited evidence also existed for the safety and efficacy of established CMV antivirals (valaciclovir, ganciclovir and valganciclovir) to treat neonatal consequences of CMV infection, but toxicity and lack of randomised clinical trial data remain major issues. In the absence of a licensed CMV vaccine or robust clinical evidence for anti-CMV therapeutics, patient education and behavioural interventions that

emphasise adherence remain the best preventative strategies for congenital CMV. There is a strong need for further data on the use of HIG and other antivirals in pregnancy, as well as the development of less toxic, novel, antiviral agents.

Database: Medline

38. Systematic review of the birth prevalence of congenital cytomegalovirus infection in developing countries.

Author(s): Lanzieri, Tatiana M; Dollard, Sheila C; Bialek, Stephanie R; Grosse, Scott D

Source: International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases; May 2014; vol. 22 ; p. 44-48

Publication Date: May 2014

Publication Type(s): Journal Article Review Systematic Review

PubMedID: 24631522

Available at International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases - from Free Medical Journals . com

Available at International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases - from Unpaywall

Abstract:BACKGROUNDCongenital cytomegalovirus (CMV) infection is the leading infectious cause of congenital hearing loss and neurodevelopmental disability in developed countries. Information on congenital CMV infection in developing countries appears to be lacking.METHODSWe conducted a systematic literature review to identify studies from developing countries with population-based samples of at least 300 infants that used laboratory methods established as reliable for the diagnosis of congenital CMV infection.RESULTSMost studies were excluded due to biased samples or inadequate diagnostic methods; consequently the search identified just 11 studies that were from Africa, Asia, and Latin America. The number of newborns tested ranged from 317 to 12 195. Maternal CMV seroprevalence ranged from 84% to 100%. CMV birth prevalence varied from 0.6% to 6.1%. CMV-associated impairments were not documented in most studies.CONCLUSIONSBirth prevalence ranges were higher than for Europe and North America, as expected based on the higher maternal CMV seroprevalence. With very limited data available on sequelae, the disease burden of congenital CMV in developing countries remains largely unknown at this time.

Database: Medline

39. Management of pregnancies with confirmed cytomegalovirus fetal infection

Author(s): Benoist G.; Salomon L.J.; Ville Y.; Leruez-Ville M.; Magny J.F.; Jacquemard F.

Source: Fetal Diagnosis and Therapy; 2013; vol. 33 (no. 4); p. 203-214

Publication Date: 2013

Publication Type(s): Review

PubMedID: 23571413

Available at Fetal diagnosis and therapy - from ProQuest (Health Research Premium) - NHS Version

Abstract: Systematic screening for cytomegalovirus (CMV) maternal infection is not recommended in most countries. Nevertheless, primary CMV infection will occur in around 1% of women. The vertical transmission rate is estimated to be around 30-50%. Newborns with congenital CMV infection remain asymptomatic in the majority of cases and around 10% will present with a wide range of abnormalities. Fetal infection can be diagnosed by amniocentesis with amplification of the viral genome in the amniotic fluid by polymerase chain reaction. This prenatal diagnosis is mainly performed when ultrasound abnormalities are observed. The purpose of this mini-review is to describe the management options when a fetus is known to be infected.

Database: EMBASE

40. Congenital cytomegalovirus infection: an obstetrician's point of view

Author(s): Soper D.E.

Source: Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Dec 2013

Publication Date: Dec 2013

Publication Type(s): Review

PubMedID: 24257420

Available at Clinical infectious diseases : an official publication of the Infectious Diseases Society of America - from Oxford Journals - Medicine

Available at Clinical infectious diseases : an official publication of the Infectious Diseases Society of America - from Unpaywall

Abstract: Maternal cytomegalovirus (CMV) is the cause of the most frequent congenital infection in America; however, pregnant women are not routinely screened. Primary CMV infection is associated with a high maternal-to-child transmission rate (40%); up to 15% of these infected neonates will be symptomatic at birth and develop permanent sequelae that usually involve the central nervous system. New interventions are now available to decrease the rate of primary maternal infection as well as to treat pregnant women with primary infection, thus decreasing the fetal and neonatal morbidity associated with this disease. Based on these data, strategies for maternal screening need to be reconsidered.

Database: EMBASE

41. Viral infections: Contributions to late fetal death, stillbirth, and infant death

Author(s): Williams E.J.; Embleton N.D.; Ward Platt M.P.; Berrington J.E.; Clark J.E.; Bythell M.

Source: Journal of Pediatrics; Aug 2013; vol. 163 (no. 2); p. 424-428

Publication Date: Aug 2013

Publication Type(s): Article

PubMedID: 23507026

Abstract: Objective: To determine the role of viral infections in causing fetal and infant death. Study design: We assessed a well-validated population database of fetal (>=20 weeks gestation) and infant death for infective deaths and deaths from viruses over a 21-year period (1988-2008). We analyzed by specific viral cause, timing (late fetal loss [20-23 weeks], stillbirth [>=24 weeks], neonatal death [0-27 days], and post-neonatal infant death [28-364 days]) and across time. Result(s): Of the 989 total infective deaths, 108 were attributable to viral causes (6.5% of late fetal losses, 14.5% of stillbirths, 6.5% of neonatal deaths, and 19.4% of postneonatal infant deaths). Global loss (combined fetal and infant losses per 100 000 registerable births) was 139.6 (95% CI, 130.9-148.3) for any infective cause and 15.2 (95% CI, 12.3-18.1) for viral infections. More than one-third (37%) of viral-attributed deaths were before live birth, from parvovirus (63%) or cytomegalovirus (33%). Parvovirus accounted for 26% (28 of 108) of all viral deaths. Cytomegalovirus was associated with a global loss rate of 3.1 (95% CI, 1.8-4.4) and an infant mortality rate of 1.3 (95% CI, 0.4-2.1) per 100 000 live births; 91% of cases were congenital infections. Herpes simplex virus caused death only after live births (infant mortality rate, 1.4; 95% CI, 0.5-2.3). No changes in rates were seen over time. Conclusion(s): We have identified a substantial contribution of viral infections to global fetal and infant losses. More than one-third of these losses occurred before live births. Considering our methodology, our estimates represent the minimum contribution of viral illness. Strategies to reduce this burden are needed.

Database: EMBASE

42. Human cytomegalovirus-induces cytokine changes in the placenta with implications for adverse pregnancy outcomes.

Author(s): Hamilton, Stuart T; Scott, Gillian; Naing, Zin; Iwasenko, Jenna; Hall, Beverley; Graf, Nicole; Arbuckle, Susan; Craig, Maria E; Rawlinson, William D

Source: PloS one; 2012; vol. 7 (no. 12); p. e52899

Publication Date: 2012

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 23300810

Abstract: Human cytomegalovirus (CMV) infection of the developing fetus can result in adverse pregnancy outcomes including death in utero. Fetal injury results from direct viral cytopathic damage to the CMV-infected fetus, although evidence suggests CMV placental infection may indirectly cause injury to the fetus, possibly via immune dysregulation with placental dysfunction. This study investigated the effects of CMV infection on expression of the chemokine MCP-1 (CCL2) and cytokine TNF-α in placentae from naturally infected stillborn babies, and compared these changes with those found in placental villous explant histocultures acutely infected with CMV ex vivo. Tissue cytokine protein levels were assessed using quantitative immunohistochemistry. CMV-infected placentae from stillborn babies had significantly elevated MCP-1 and TNF-α levels compared with uninfected placentae ($p = 0.001$ and $p = 0.007$), which was not observed in placentae infected with other microorganisms ($p = 0.62$ and $p = 0.71$) ($n = 7$ per group). Modelling acute clinical infection using ex vivo placental explant histocultures showed infection with CMV laboratory strain AD169 (0.2 pfu/ml) caused significantly elevated expression of MCP-1 and TNF-α compared with uninfected explants ($p = 0.0003$ and $p<0.0001$) ($n = 25$ per group). Explant infection with wild-type Merlin at a tenfold lower multiplicity of infection (0.02 pfu/ml), caused a significant positive correlation between increased explant infection and upregulation of MCP-1 and TNF-α expression ($p = 0.0001$ and $p = 0.017$). Cytokine dysregulation has been associated with adverse outcomes of pregnancy, and can negatively affect placental development and function. These novel findings demonstrate CMV infection modulates the placental immune environment in vivo and in a multicellular ex vivo model, suggesting CMV-induced cytokine modulation as a potential initiator and/or exacerbator of placental and fetal injury.

Database: Medline

43. Update on the prevention, diagnosis and management of cytomegalovirus infection during pregnancy.

Author(s): Lazzarotto, T; Guerra, B; Gabrielli, L; Lanari, M; Landini, M P

Source: Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases; Sep 2011; vol. 17 (no. 9); p. 1285-1293

Publication Date: Sep 2011

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 21631642

Abstract: Human cytomegalovirus (CMV) is the leading cause of congenital infection, with morbidity and mortality at birth and sequelae. Each year approximately 1-7% (Rev Med Virol 2010; 20: 311) of pregnant women acquire a primary CMV infection. Of these, about 30-40% transmit infection to their fetuses. The risk of serious fetal injury is greatest when maternal infection develops in the first trimester or early in the second trimester. Between 10 and 15% of congenitally infected infants are acutely symptomatic at birth and most of the survivors have serious long-term complications. Until a few years ago, laboratory testing was not possible to precisely define the maternal immune status, the recent development of advanced serological tests (IgG avidity test, IgM immunoblot and neutralizing antibody testing) allow us to identify, among pregnant women with suspected CMV, those with primary infection who are therefore at high risk of transmitting CMV to the fetus. This is done with the use of a screening test. As most maternal infections are asymptomatic, the only way to disclose primary infection is to implement specific serological testing as early in pregnancy as possible (before week 12-16 of gestation). Given the high risk of mother-fetus transmission and fetal damage, prenatal diagnosis is recommended to women with primary CMV infection contracted in the first half of pregnancy and in case of fetal abnormalities suggestive of infection. The correct interpretation of serological and virological tests followed by appropriate counselling by an expert physician is an effective tool to reduce the number of unnecessary pregnancy terminations by over 70%.

Database: Medline

44. Human cytomegalovirus infection is detected frequently in stillbirths and is associated with fetal thrombotic vasculopathy.

Author(s): Iwasenko, Jenna M; Howard, Jonathan; Arbuckle, Susan; Graf, Nicole; Hall, Beverley; Craig, Maria E; Rawlinson, William D

Source: The Journal of infectious diseases; Jun 2011; vol. 203 (no. 11); p. 1526-1533

Publication Date: Jun 2011

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 21592980

Available at The Journal of infectious diseases - from Oxford Journals - Medicine

Available at The Journal of infectious diseases - from Unpaywall

Abstract:BACKGROUNDHuman cytomegalovirus (CMV) is the most common congenital infection in developed countries and is a known cause of intrauterine fetal death. We examined CMV infection in stillbirths and the relationship with histopathological findings at autopsy.METHODSWe collected liver, kidney, and placenta specimens from 130 stillbirths. CMV DNA and protein were detected using polymerase chain reaction and immunohistochemistry, along with routine autopsy of stillborn infants.RESULTSOverall, CMV DNA was detected in 15% of singleton, >20-week stillborn infants. CMV DNA was detected in kidney (9%), liver (11%), and placenta (5%) specimens, with 75% of infections confirmed by immunohistochemistry. Fetal thrombotic vasculopathy was the only histopathological abnormality associated with CMV infection (in 60% CMV-infected vs 28% uninfected stillbirths P = .010).CONCLUSIONSStillbirth has multiple etiologies. However, the detection of CMV DNA in 15% of fetal tissues or placentae suggests a strong association between CMV infection in pregnancy and stillbirth. Molecular testing during postmortem investigation has an important role to determine the contribution of CMV infection.

Database: Medline

45. Cytomegalovirus infections during pregnancy.

Author(s): Nigro, Giovanni; Adler, Stuart P

Source: Current opinion in obstetrics & gynecology; Apr 2011; vol. 23 (no. 2); p. 123-128

Publication Date: Apr 2011

Publication Type(s): Journal Article Review

PubMedID: 21157339

Available at Current opinion in obstetrics & gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract:PURPOSE OF REVIEWTo review current prenatal diagnosis and management of congenital cytomegalovirus (CMV) infections with emphasis on maternal screening and available interventions.RECENT FINDINGSRecent findings include an enhanced understanding of the epidemiology, pathogenesis, and treatment of CMV infections; a knowledge of high-risk women particularly those with chronic exposure to a young child in the home; the availability of accurate methods for the serologic diagnosis of a primary CMV infection using either single or serial blood samples; accurate methods for the diagnosis of fetal infection via amniotic fluid; sensitive fetal and placental indicators for neonatal outcomes, and the availability of potentially effective interventions such as hygienic intervention and CMV hyperimmune globulin.SUMMARYThese findings suggest that serologic testing for CMV during pregnancy may be appropriate either using one-time testing or serial serologic testing throughout the first two trimesters of pregnancy and that education of

pregnant women about CMV is necessary so that they can asses their risk and make informed choices about serologic screening.

Database: Medline

46. Imaging of fetal cytomegalovirus infection

Author(s): Malinger G.; Lev D.; Lerman-Sagie T.

Source: Fetal Diagnosis and Therapy; Mar 2011; vol. 29 (no. 2); p. 117-126

Publication Date: Mar 2011

Publication Type(s): Review

PubMedID: 21088375

Available at Fetal diagnosis and therapy - from ProQuest (Health Research Premium) - NHS Version

Abstract: Fetuses with congenital cytomegalovirus infection may remain asymptomatic or present with a wide range of brain pathologies. These findings are not always obvious but may on some occasions be demonstrated by ultrasound and MRI, they include ventriculomegaly, microcephaly, increased periventricular echogenicity, calcifications, periventricular pseudocysts, intraventricular synechia, malformations of cortical development, cerebellar lesions and T2 abnormal temporal signals. The purpose of this mini-review is to describe US and MRI findings characteristic of congenital cytomegalovirus infection, with particular emphasis on their time of appearance, frequency and specificity. Copyright © 2010 S. Karger AG, Basel.

Database: EMBASE

47. Screening, diagnosis, and management of cytomegalovirus infection in pregnancy.

Author(s): Yinon, Yoav; Farine, Dan; Yudin, Mark H

Source: Obstetrical & gynecological survey; Nov 2010; vol. 65 (no. 11); p. 736-743

Publication Date: Nov 2010

Publication Type(s): Journal Article Review

PubMedID: 21375790

Available at Obstetrical & gynecological survey - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrical & gynecological survey - from Unpaywall

Abstract:UNLABELLEDCongenital cytomegalovirus (CMV) is the most common intrauterine infection and the leading infectious cause of sensorineural hearing loss and mental retardation. This article reviews the issues that relate to the diagnosis and management of this disease, detailing the points that led to the recent published guidelines by the Society of Obstetricians and Gynaecologists of Canada. A MEDLINE/Cochrane search of CMV infection, pregnancy, and prenatal diagnosis found 195 studies between 1980 and 2010. Of these, we examined 59 relevant studies. The probability of intrauterine transmission following primary infection is 30% to 40%, but only 1% after secondary infection. About 10% to 15% of congenitally infected infants will have symptoms at birth, and 20% to 30% of them will die, whereas 5% to 15% of the asymptomatic infected neonates will develop sequelae later. Children with congenital CMV infection following first trimester infection are more likely to have central nervous system sequelae, whereas infection acquired in the third trimester has a high rate of intrauterine transmission but a favorable outcome. The prenatal diagnosis of fetal CMV infection should be based on amniocentesis performed 7 weeks after the presumed time of infection and after 21 weeks of gestation. Sonographic findings often imply poor prognosis, but their

absence does not guarantee a normal outcome. The value of quantitative determination of CMV DNA in the amniotic fluid is not yet confirmed. The effectiveness of prenatal therapy for fetal CMV is not yet proven, although CMV-specific hyperimmune globulin may be beneficial. Routine serologic screening of pregnant women or newborns has never been recommended by any public health authority.TARGET AUDIENCEObstetricians & Gynecologists, Family Physicians.LEARNING OBJECTIVESAfter completion of this educational activity, the obstetrician/gynecologist should be better able to evaluate the principles of prenatal diagnosis of congenital CMV infection so doctors will be familiar with the tests and procedures needed, in order to reach a diagnosis of congenital CMV; to assess the natural history and outcome of congenital CMV infection enabling obstetricians to counsel prenatally pregnant women with CMV; and to analyze the prognostic markers for fetal CMV, so managing physicians will be able to predict more accurately the outcomes of fetuses infected by CMV.

Database: Medline

48. Public health and laboratory considerations regarding newborn screening for congenital cytomegalovirus

Author(s): Dollard S.C.; Schleiss M.R.; Grosse S.D.

Source: Journal of inherited metabolic disease; Oct 2010; vol. 33

Publication Date: Oct 2010

Publication Type(s): Review

PubMedID: 20532822

Available at Journal of inherited metabolic disease - from Wiley Online Library Science , Technology and Medicine Collection 2019

Available at Journal of inherited metabolic disease - from SpringerLink - Medicine

Available at Journal of inherited metabolic disease - from ProQuest (Health Research Premium) - NHS Version

Abstract: Congenital cytomegalovirus (CMV) infection is the most common infection in newborns worldwide and causes hearing loss and other neurological disability in 15-20% of infected infants. Only about half of the hearing loss resulting from congenital CMV infection is currently detected by universal newborn hearing screening because of late-onset hearing loss. Thus, much of the hearing loss and the majority of other CMV-associated disabilities remain undetected for years after birth and are never connected to CMV infection. Congenital CMV may be appropriate to include in national newborn screening (NBS) programs because it is more common than other disorders tested for by NBS programs and is a major cause of disability. Significant obstacles to the implementation of screening for congenital CMV include the lack of a standardized, high-throughput screening test and a protocol for follow-up of CMV-infected children. Nonetheless, screening newborns for congenital CMV infection merits further consideration.

Database: EMBASE

49. Congenital cytomegalovirus infection: treatment, sequelae and follow-up

Author(s): Lombardi G.; Garofoli F.; Stronati M.

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; Oct 2010 ; p. 45-48

Publication Date: Oct 2010

Publication Type(s): Review

PubMedID: 20807160

Abstract: Cytomegalovirus (CMV) is the most common cause of congenital infection affecting about 1% of all the live births worldwide. Its prevalence in the developed world seems to be slightly lower, ranging between 0.6 and 0.7%. Symptoms can be detected at birth in 10-15% of the congenitally infected of which 50-90% will develop sequelae, the most frequent being sensorineural hearing loss (SNHL), visual defect, psychomotor impairment, mental retardation, cerebral palsy and seizures. Eighty-five to 90% of the infected newborns are asymptomatic but 10-15% of them are equally at risk for sensorineural sequelae, like 20-30% of all the infected children. Therefore it is important a time prolonged and closer follow-up of infected children that we propose should be until 6 years of age. This should lead to an early intervention, better management and eventually even control the long-term sequelae. Infants born with symptomatic congenital infection have a worse prognosis than those with no evidence of clinical disease, and ganciclovir (GCV) intravenous 6 mg/kg every 12h for 6 weeks is the most used therapy for symptomatic newborns. Valganciclovir (V-GCV) syrup is a pro-drug of GCV and presents high oral bioavailability. To date, it is possible to administer this drug at home, and the tolerability profile may allow for wider indications and longer treatments.

Database: EMBASE

50. Cytomegalovirus seroconversion rates and risk factors: implications for congenital CMV.

Author(s): Hyde, Terri B; Schmid, D Scott; Cannon, Michael J

Source: Reviews in medical virology; Sep 2010; vol. 20 (no. 5); p. 311-326

Publication Date: Sep 2010

Publication Type(s): Journal Article Review

PubMedID: 20645278

Available at Reviews in medical virology - from Wiley Online Library

Abstract: Congenital CMV infection is caused by in utero mother-to-fetus transmission and is a leading cause of birth defects and developmental disabilities. The highest risk of disability is to children born to women who have a primary infection during pregnancy, which can be detected by measuring seroconversion. We reviewed studies that reported rates of CMV seroconversion in different populations. Among pregnant women, annual seroconversion rates typically ranged from 1 to 7% (summary annual rate = 2.3%, 95% CI = 2.1-2.4%). Healthcare workers, including those caring for infants and children, had seroconversion rates similar to pregnant women (summary annual rate = 2.3%, 95% CI = 1.9-2.9%). Among day-care providers, seroconversion rates ranged from 0 to 12.5% (summary annual rate = 8.5%, 95% CI = 6.1-11.6%). Parents whose child was not shedding CMV were much less likely to seroconvert (summary annual rate = 2.1%, 95% CI = 0.3-6.8%) than were parents who had a child shedding CMV (summary annual rate = 24%, 95% CI = 18-30%). Nevertheless, over the course of a year, most parents exposed to a CMV-shedding child do not become infected. Other groups with elevated risk included families with a CMV-shedding member, female minority adolescents and women attending sexually transmitted disease clinics. The relatively low rate of

CMV seroconversion in most populations is encouraging for behavioural interventions and for vaccine strategies attempting to prevent infection during pregnancy.

Database: Medline

51. Detection of parvovirus B19, cytomegalovirus and enterovirus infections in cases of intrauterine fetal death.

Author(s): Petersson, Karin; Norbeck, Oscar; Westgren, Magnus; Broliden, Kristina

Source: Journal of perinatal medicine; 2004; vol. 32 (no. 6); p. 516-521

Publication Date: 2004

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 15576274

Abstract:AIMSMaternal infections with parvovirus B19, cytomegalovirus (CMV) and enterovirus have been associated with intrauterine fetal death (IUFD), but the incidence of these infections is not clear. This prospective study was conducted to estimate this incidence.METHODSA prospective study of 38 months was conducted on cases of IUFD referred to Huddinge University Hospital, Stockholm, Sweden. Placental biopsies, fetal blood and amniotic fluid were collected from cases of IUFD (n=52). Placental biopsies from normal pregnancies at term (n=53) were used as controls. These tissues were examined for parvovirus B19 DNA, CMV DNA and enterovirus RNA using polymerase chain reaction (PCR). Maternal viral serology was measured in 46 cases and virus isolation for enterovirus in maternal stool samples was performed in 31 cases.RESULTSViral nucleic acid was recovered in at least one tissue sample from six cases of fetal death (parvovirus B19 in two cases, CMV in three and enterovirus in one), while all placental biopsies from controls were found negative. Serological signs of primary maternal infection were found in two of the cases, and virus isolation for enterovirus was negative in all samples examined.CONCLUSIONParvovirus B19, CMV and enterovirus may be considered as etiologic agents in cases of fetal death. PCR on placental and/or fetal tissue improves diagnostic accuracy for these infections.

Database: Medline

Strategy 816850

#	Database	Search term	Results
1	Medline	exp CYTOMEGALOVIRUS/	20494
2	Medline	exp "CYTOMEGALOVIRUS INFECTIONS"/	25268
3	Medline	(Cytomegalovirus OR CMV).ti	25339
4	Medline	(1 OR 2 OR 3)	37559
5	Medline	exp PREGNANCY/	882237
6	Medline	exp "PREGNANCY COMPLICATIONS"/	421714
7	Medline	(pregnan*).ti,ab	482661
8	Medline	(fetus OR foetal OR fetal).ti	108521
9	Medline	exp FETUS/	155745
10	Medline	(stillbirth OR stillborn).ti,ab	10468
11	Medline	exp STILLBIRTH/	4663
12	Medline	exp "FETAL DEATH"/	29045
13	Medline	exp "PREGNANCY OUTCOME"/	87702
14	Medline	(5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13)	1096638
15	Medline	(4 AND 14)	3423
16	Medline	exp STILLBIRTH/ep	1827
17	Medline	(4 AND 16)	4
20	Medline	15 [Document type Review] [Languages English]	446

21	Medline	(4 AND 11)	16
22	Medline	(4 AND 12)	98
23	EMBASE	exp "CYTOMEGALOVIRUS INFECTION"/	35241
24	EMBASE	exp CYTOMEGALOVIRUS/	39424
25	EMBASE	(Cytomegalovirus OR CMV).ti	30918
26	EMBASE	(23 OR 24 OR 25)	68595
27	EMBASE	exp PREGNANCY/	651706
28	EMBASE	exp "PREGNANCY COMPLICATIONS"/	119814
29	EMBASE	(pregnan*).ti,ab	618848
30	EMBASE	(fetus OR foetal OR fetal).ti	117801
31	EMBASE	exp FETUS/	188459
32	EMBASE	(stillbirth OR stillborn).ti,ab	14426
33	EMBASE	exp STILLBIRTH/	16846
34	EMBASE	exp "FETAL DEATH"/	36691
35	EMBASE	exp "PREGNANCY OUTCOME"/	57387
36	EMBASE	exp "FETUS DISEASE"/	114169
37	EMBASE	(27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36)	1047892
38	EMBASE	(26 AND 33)	100
39	EMBASE	(26 AND 37)	4904
40	EMBASE	39 [DT FROM 2010] [Publication types Review]	311

		[English language]	
41	EMBASE	exp NEWBORN/	518133
42	EMBASE	exp "NEWBORN MORBIDITY"/ OR exp "NEWBORN MORTALITY"/	19236
43	EMBASE	(41 OR 42)	528874
44	EMBASE	(26 AND 43)	2763
45	EMBASE	44 [DT FROM 2010] [Publication types Review] [English language]	62
46	CINAHL	exp "CYTOMEGALOVIRUS INFECTIONS"/	2777
47	CINAHL	exp CYTOMEGALOVIRUSES/	1235
48	CINAHL	(Cytomegalovirus OR CMV).ti	2419
49	CINAHL	(46 OR 47 OR 48)	3670
50	CINAHL	exp PREGNANCY/	190532
51	CINAHL	exp "PREGNANCY COMPLICATIONS"/	83089
52	CINAHL	(pregnan*).ti,ab	118790
53	CINAHL	(fetus OR foetal OR fetal).ti	19098
54	CINAHL	exp FETUS/	23442
55	CINAHL	(stillbirth OR stillborn).ti,ab	3970
56	CINAHL	exp "PERINATAL DEATH"/	7217
57	CINAHL	exp "INFANT, NEWBORN"/	124972
58	CINAHL	(newborn* OR neonate*).ti	19105
59	CINAHL	exp "PREGNANCY	21749

		OUTCOMES"/	
60	CINAHL	(50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59)	333861
61	CINAHL	(49 AND 60)	937
62	CINAHL	61 [DT FROM 2010] [Languages eng]	556
63	CINAHL	(49 AND 56) [DT FROM 2010] [Languages eng]	8