Am J Neurodegener Dis 2026;15(3):25-39
www.AJND.us /ISSN:2165-591X/AJND0173812

Review Article

Imaging features of fetal cytomegalovirus infection: a systematic review of prenatal ultrasound and MRI

Mostafa Hashemianfar[1], Shokouh Sadeghizade[1], Pooya Kiani[1], Mehrangiz Dadkhah[1], Fahimeh Khademi[1], Mahnaz Fosouli[1], Shahin Fesharaki[1], Mobina Mohammadrezaee[2], Abdolbaset Zeitoonli[3], Samira Rafiee[4], Mobina Kordeforushani[4], Farshad Riahi[1]

[1]Department of Radiology, Isfahan University of Medical Sciences, Isfahan, Iran; [2]School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran; [3]School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran; [4]Department of Obstetrics and Gynaecology, Tehran University of Medical Sciences, Tehran, Iran

Received May 6, 2026; Accepted October 20, 2026; Epub October 25, 2026; Published October 30, 2026

Abstract: Background: Congenital cytomegalovirus (CMV) infection is the most common congenital viral infection, affecting about 0.7% of live births and causing substantial neurodevelopmental impairment. Prenatal ultrasound and magnetic resonance imaging (MRI) are key diagnostic tools, but their complementary roles are not fully defined. This study systematically reviews current evidence on their diagnostic performance and prognostic value. Methods: PubMed/MEDLINE and Web of Science were searched for studies published between January 2020 and October 2025. Inclusion criteria were confirmed fetal CMV infection by amniotic fluid polymerase chain reaction, use of prenatal ultrasound and/or MRI, and reported imaging findings and/or postnatal outcomes. Results: Nine cohorts (22-190 fetuses) showed ultrasound frequently detects cerebral and extracerebral abnormalities, with abnormal findings associated with termination, intrauterine death, or severe sequelae. MRI added clinically relevant information in about 10-20%, refining detection of cortical malformations, white-matter injury, and temporal cysts and often reclassifying prognostic severity. Combined targeted ultrasound and MRI achieved high sensitivity and negative predictive value for severe long-term outcomes, but normal imaging did not exclude later sensorineural hearing loss or mild deficits. Conclusion: Integrated use of detailed ultrasound and fetal MRI offers complementary strengths for diagnosing and risk stratifying fetal CMV infection, yet normal structural imaging cannot reliably exclude later sequelae, so all affected infants require structured long-term follow-up.

Keywords: Cytomegalovirus, magnetic resonance imaging, ultrasound, fetus

Introduction

Congenital infection with cytomegalovirus (CMV) is the most prevalent congenital viral infection, with around 0.7% of births affected and is the largest non-genetic cause of sensorineural hearing loss (SNHL) and an important infectious cause of neurodevelopmental impairment [1]. Maternal infection is usually asymptomatic or has non-specific flu-like symptoms. Fetal infection might be due to primary infection or non-primary infection due to reactivation or reinfection [2, 3]. While the likelihood of maternal-fetal transmission increases with gestational age, severe fetal brain injury, congenital abnormalities, and long-term neurodevelopmental sequelae are most significantly associated with periconceptional and first-trimester infection [3-5]. Therefore, prenatal counseling is difficult because the risk of transmission, fetal damage, and postnatal prognosis are not only dependent on maternal serology [2, 6].

The diagnostic approach to CMV in pregnancy involves maternal serology, fetal virology, and postnatal confirmation [7]. Diagnosis of primary maternal infection is generally supported by CMV IgG seroconversion or positive CMV IgM with positive IgG and low IgG avidity. Diagnosis of fetal infection is made by detection of CMV DNA in amniotic fluid by polymerase chain reaction following an appropriately timed amniocentesis, usually after 21 weeks of gestation and at least 6 weeks after presumed maternal infection [3, 8]. CMV testing of urine, saliva, or blood

within the first three weeks of life confirms neonatal congenital CMV infection [9]. Common laboratory and clinical abnormalities in neonates include thrombocytopenia, an increase in liver enzymes, jaundice, petechiae, hepatosplenomegaly, low birth weight, microcephaly, seizures, retinitis or chorioretinitis, and SNHL [2, 10].

Prenatal imaging is central after suspected or confirmed fetal CMV infection because it provides the main non-invasive method for detecting fetal organ involvement and refining prognosis [6, 11, 12]. Ultrasound, particularly dedicated fetal neurosonography, is the first-line modality for evaluating both cerebral and extracerebral manifestations, including ventriculomegaly, intracranial calcifications, periventricular echogenicity or cysts, intraventricular adhesions, germinal-matrix abnormalities, abnormalities of the corpus callosum, cortical malformations, cerebellar hypoplasia, microcephaly, echogenic bowel, hepatosplenomegaly, placentomegaly, fetal growth restriction, ascites, and hydrops [5, 11, 13]. Fetal magnetic resonance imaging (MRI) is a complementary modality that may better characterize white-matter injury, cortical development, migrational abnormalities, destructive lesions, and posterior fossa involvement, particularly when performed in later gestation or when ultrasound findings are subtle or equivocal [6]. However, normal prenatal ultrasound and MRI do not fully exclude later sequelae, especially SNHL, and therefore imaging results must be interpreted alongside gestational age at infection, amniotic-fluid viral load, and postnatal follow-up findings [2, 6, 11].

Recent studies indicate that the prognostic value of imaging depends strongly on the clinical context and expertise of the examination [4, 5]. Routine fetal ultrasound without knowledge of maternal CMV status has limited ability to identify infected fetuses who will develop long-term sequelae, whereas targeted imaging in known fetal infection shows substantially higher performance for predicting symptomatic disease and severe outcomes [4]. Severe imaging features such as microcephaly, cortical malformation, cerebellar hypoplasia, severe fetal growth restriction, and hydrops are associated with poor prognosis, whereas isolated mild findings may still be clinically relevant because they can precede sensorineural deficits despite the absence of severe cognitive impairment [5]. In fetuses with initially normal ultrasound, follow-up imaging and fetal MRI may reveal additional abnormalities, and prior meta-analytic data suggest that MRI can detect anomalies missed by ultrasound in a clinically meaningful minority of cases. These findings support longitudinal, multimodal assessment rather than reliance on a single normal examination [2, 6].

Management options are still limited and depend on whether prevention of fetal transmission, fetal risk stratification, or treatment of newborn sickness are the targets [6-10]. High-dose maternal valacyclovir has shown evidence of lowering vertical transmission after an early primary maternal infection, but CMV hyperimmune globulin was not demonstrated to diminish congenital infection or fetal/neonatal death in a large randomized experiment [14, 15]. Symptomatic infants with involvement of the central nervous system may be treated with ganciclovir or oral valganciclovir after birth, and 6 months of valganciclovir has been associated with modestly better longer-term hearing and neurodevelopmental outcomes than shorter treatment, although hematologic toxicity needs to be monitored [16]. The outcome varies from normal development to progressive hearing loss, visual impairment, epilepsy, motor delay, and cognitive dysfunction and depends on the date of infection, viral load, imaging abnormalities, and clinical status of the neonate [2, 11].

Ultrasound and fetal MRI have been shown to have varying degrees of diagnostic accuracy and prognostic utility in cases of congenital CMV infection, despite the growing popularity of these technologies. Prenatal counseling remains ambiguous due to variations in imaging techniques, examination timing, operator skill, and result evaluation. Even though the number of systematic reviews on prenatal imaging in congenital CMV infection is increasing, most of the syntheses that have already been published have concentrated on particular imaging modalities or specific elements of diagnostic evaluation. Specifically, previous reviews have usually focused on the use of fetal MRI in the assessment of the central nervous system or the role of ultrasonography as a screening and monitoring tool, frequently without a direct comparison between these methods or integra-

tion within a single diagnostic framework [2, 17].

The significance and innovation of the current systematic review are located in the provision of an integrated, feature-based synthesis of prenatal ultrasound and fetal MRI findings, the clarification of their complementary diagnostic yield, and the identification of imaging patterns that are most pertinent for prognosis and counseling in fetal CMV infection, despite the growing but heterogeneous literature.

Materials and methods

Search strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed across multiple electronic databases, including PubMed/MEDLINE and Web of Science, to identify relevant studies published between January 2020 and October 2025.

The search strategy combined Medical Subject Headings (MeSH) with free-text keywords. The core search terms included: ("congenital cytomegalovirus" OR "fetal CMV infection" OR "cCMV") AND ("prenatal ultrasound" OR "neurosonography" OR "sonography") AND ("fetal MRI" OR "fetal magnetic resonance imaging" OR "prenatal MRI"). The search was supplemented by manually screening the reference lists of the included articles and relevant review papers to identify additional studies missed by the initial database search. No language restrictions were initially applied, although only the articles available in English were included in the final analysis.

Inclusion and exclusion criteria

Original articles that examined the role of prenatal ultrasound and MRI in diagnosing fetal CMV were eligible for inclusion in this systematic review. The main interest was pregnant women with fetuses diagnosed with congenital CMV, confirmed by polymerase chain reaction (PCR) tests, demonstrating the presence of the virus in the amniotic fluid. Each study was required to use prenatal imaging techniques, including detailed fetal ultrasounds, especially those focusing on the brain, or prenatal MRIs. These studies could compare different imaging modalities, correlate imaging findings with postnatal developmental outcomes, or provide in-depth analysis of a single imaging technique. A critical inclusion criterion was the reporting of at least one definitive result, such as the frequency of specific imaging features (e.g., ventriculomegaly, calcifications, or cortical malformations), diagnostic accuracy of the imaging modalities, or correlation between prenatal imaging findings and subsequent developmental challenges in infants, such as motor disorders, cognitive delays, or conditions akin to cerebral palsy.

Exclusion criteria were case reports and brief communications without data on the diagnostic performance. Editorial opinions, conference abstracts unavailable in full text or failing to meet the inclusion criteria, and animal studies were excluded. We excluded reviews that merely summarized existing literature without new findings, including meta-analyses or systematic reviews. We excluded studies that did not confirm congenital CMV by amniocentesis, did not have detailed prenatal imaging data, or did not show an association between imaging findings and clinical outcomes. All identified citations were imported into a reference management software and duplicates were removed.

Study selection and data extraction

Two reviewers independently evaluated the titles and abstracts of all the identified articles based on the established eligibility criteria. Complete texts of potentially pertinent articles were obtained and evaluated for final inclusion by the same two reviewers. Disagreements about whether a study was eligible were settled through discussion and agreement, or, if necessary, by asking a third reviewer. A PRISMA flowchart was created to show the success of the study selection process.

Imaging indicators

We identified standardized criteria for prenatal imaging features in all studies employing either US or fetal MRI investigations. These were classified according to the location of abnormal findings: either cerebral or extracerebral. Cerebral ultrasound biomarkers included ventriculomegaly, brain calcification within or

around ventricles, periventricular echogenicity or cysts, germinal matrix alterations, ventricular adhesions, corpus callosum anomalies, cortical lesions, cerebellar hypoplasia, microcephaly, temporal horn cysts, and lenticulostriate vasculopathy. Extracerebral imaging criteria were echogenic bowel, hepatosplenomegaly, placentomegaly, fetal growth restriction, ascites, and hydrops.

For the evaluation of fetal MRI, we identified data on white-matter abnormalities, cortical developmental and migration disorders, destructive processes, posterior fossa lesions, temporal lobe cysts, other supratentorial or infratentorial lesions, and, whenever present, diffusion-weighted imaging characteristics (apparent diffusion coefficient values in major white-matter areas). Furthermore, we recorded study-level data related to the diagnostic and prognostic value of these markers in terms of sensitivity, specificity, predictive values, and reclassification of imaging severity after additional MRI assessment following neurosonography using the definition of the study authors for severe vs mild imaging findings.

Data synthesis and analysis

A quantitative meta-analysis was not conducted due to anticipated heterogeneity in study design, imaging protocols, and outcome definitions among included studies. Instead, a narrative synthesis of the evidence was performed. The findings are given in a structured and logical way. Main subjects discussed were (1) patient demographics and study populations, (2) diagnostic performance and characteristic prenatal ultrasound findings and (3) diagnostic performance and characteristic prenatal MRI findings with its additional benefits over ultrasound. The text and tables give a good overview of the current evidence, by summarising the findings. The main goal of this synthesis was to integrate the findings from both test categories to develop a comprehensive prenatal imaging pathway for fetal CMV infections.

Quality assessment

M.H. and S.S. assessed the quality of the published interventions. The third author (M.K.) ensured that any disagreements were resolved. To determine the possibility of bias in each of the included studies, the QUADAS-2 instrument was used to evaluate the population, technique, analysis, and reporting requirements of each study. The tool comprises of four main categories: flow and timing, reference standards, index tests, and patient selection. For each specific study, every category was evaluated as either “low”, “high”, or “unclear” unclear. The ratings for every domain were then shown along with a subjective judgment of the overall quality of the included studies.

Results

Study selection

A comprehensive search of electronic databases identified 272 records, with no additional records identified from other sources. After removal of 99 duplicate records, 173 records remained for title and abstract screening. Of these, 152 records were excluded because they were non-original articles (n = 75), animal studies (n = 21), or were not related to the research question (n = 56). The full texts of the remaining 21 reports were sought for retrieval, and all were successfully retrieved and assessed for eligibility. Subsequently, 12 reports were excluded because fetal cytomegalovirus (CMV) infection was not confirmed by amniotic fluid polymerase chain reaction (PCR) (n = 7), or because detailed prenatal imaging data and/or correlations between imaging findings and clinical outcomes were not reported (n = 5). Ultimately, 9 studies met the inclusion criteria and were included in the review. The study selection process is shown in **Figure 1**, and the characteristics of the included studies are summarized in **Table 1**.

Quality assessment

Figure 2 shows the risk of bias across the various domains in the included studies. Only one study (Aertsen et al. [18]) was flagged with a high risk of bias, primarily because of issues with the index test. Several other studies (Di Mascio et al. [6], Lipitz et al. [19], Leruez-Ville et al. [4], Birnbaum et al. [20], and Minsart et al. [21]) have focused on different domains. Lipitz et al. [19], Leruez-Ville et al. [4], Birnbaum et al. [20], and Minsart et al. [21] were concerned with the index test, whereas Di Mascio et al. [6] were concerned with the reference standard. The remaining studies (Massoud et al. [5], Elkan Miller et al. [22], and Van de Eede et al.

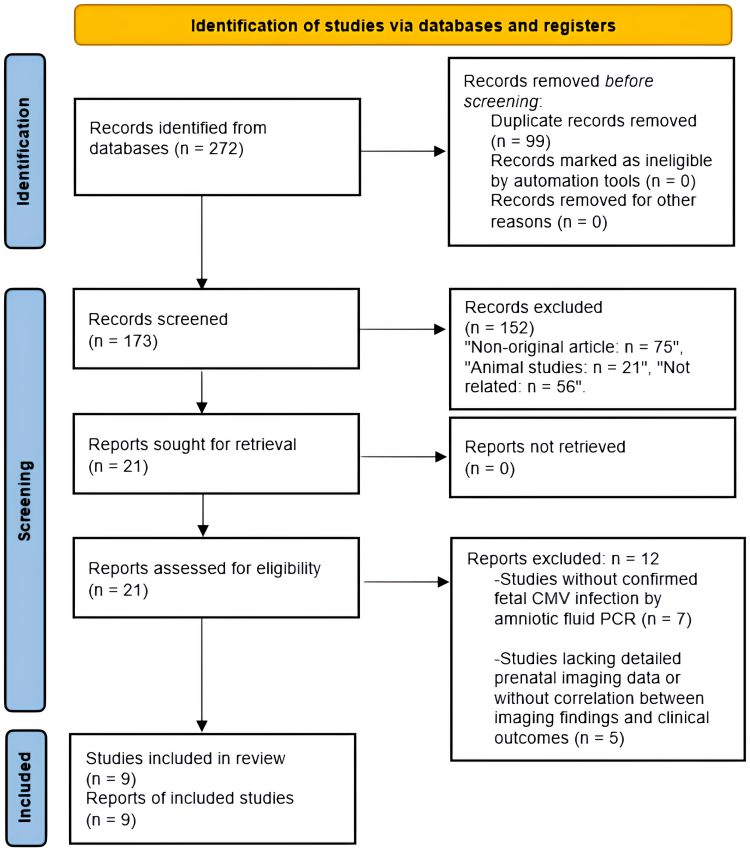


Figure 1. PRISMA flow diagram for enrollment of studies.

[23]) were judged to have a low risk of bias across all domains.

Patient demographics and study populations

Across the nine included studies, all cohorts comprised pregnancies with confirmed fetal CMV infection, most commonly diagnosed by CMV DNA detection in amniotic fluid following amniocentesis. Maternal age, where reported, fell within the typical reproductive range (approximately the late twenties to late thirties). Sample sizes ranged from 22 fetuses to 190 pregnancies, with most cohorts including between roughly 40 and 130 cases. Table 1 summarises the main demographic characteristics and the diagnostic and prognostic contributions of prenatal ultrasound and MRI in each study.

Diagnostic performance of prenatal ultrasound and magnetic resonance imaging for cytomegalovirus infection

Leruez-Ville et al. [4] examined 71 fetuses diagnosed with CMV infections during pregnancy. Targeted prenatal imaging, which included serial ultrasounds together with fetal brain MRI, showed that any sequelae were predicted with a sensitivity of 91%, while for severe cases, sensitivity was 100%, with negative predictive values of 96% and 100%, respectively, while the presence of at least one severe cerebral abnormality had a positive predictive value of 80% for severe sequelae.

Van den Eede et al. [23] reported ultrasound abnormalities associated with CMV infection in 63% of 190 pregnancies with positive amniocentesis for CMV, whereas the other 37% had normal neurosonography throughout the entire study period. The combination of neurosonography and MRI was able to differentiate normal from adverse pregnancy outcomes with 84% accuracy. Normal neurosonography and MRI were associated with normal postnatal outcome in 88% of the children.

Massoud et al. [5] retrospectively evaluated 49 fetuses with confirmed congenital CMV infection after maternal infection in the first or second trimester and defined prenatal imaging as normal, mildly abnormal, or severely abnormal. Of the fetuses with normal imaging (n = 16), 15 (94%) had a normal postnatal outcome and 1 (6%) had mild sensorineural or vestibular sequelae. No severe sequelae, intrauterine deaths, or terminations were observed. In contrast, all fetuses with severe imaging features (n = 17) experienced adverse outcomes, including termination of pregnancy in 12 (71%), intrauterine death in 4 (24%), and survival with severe sequelae in 1 (6%). Fetuses with mild imaging features (n = 16) had intermediate outcomes: 5 (31%) with normal development, 5 (31%) with mild sequelae, and 6 (38%) undergoing termination, without severe sequelae or intrauterine death. Fetal MRI was performed in 26 of 49 fetuses (53.1%) and yielded additional clinically relevant information in 5 (19.2%), pri-

Table 1. Summary of study results on prenatal imaging and outcomes in congenital cytomegalovirus Infection

First Author	Year	Study Design	Study Population	Imaging Approach	Main Findings	Predictive Value/ Outcome	Conclusion
Leruez-Ville et al. [4]	2021	Retrospective cohort	237 CMV+ fetuses	US only/US + targeted MRI	Routine US detected 26% sequelae; targeted US 91%, MRI improved to 95%.	Routine US sensitivity 26%, targeted 91%, MRI adds 4-5%	Targeted US with MRI best for detecting severe fetal outcomes
Massoud et al. [5]	2023	Retrospective multicenter	49 CMV+ fetuses	US then MRI	Severe prenatal features (e.g., microcephaly, cortical disorder) linked with major cerebral lesions. Mild features linked with higher risk of mild sequelae, mostly hearing loss; normal imaging = low risk.	Severe: cognitive delay, mild: SNHL	Severe US findings predict poor outcome, but normal imaging rarely has sequelae
Di Mascio et al. [6]	2023	Multicenter retrospective	95 CMV+ fetuses	MRI only	MRI detected additional brain anomalies in ~10% of fetuses. CMV viral load was independently associated with anomalies found on MRI.	MRI findings linked to high viral load	MRI after normal US detects additional anomalies, especially with high viral load
Aertsen et al. [18]	2022	Retrospective imaging cohort	40 fetuses, 1st trimester CMV+	MRI only	MRI diffusion detected microstructural changes (often US normal).	NSG abnormal: 54%, MRI abnormal: 47%	MRI reveals subtle abnormalities not seen on US in high-risk CMV cases
Lipitz et al. [19]	2020	Prospective cohort	123 1st trimester CMV+ fetuses	Serial US + MRI	30% abnormal US, 30% abnormal MRI; MRI finding more predictive of neurodevelopmental delay, but normal imaging does not exclude hearing loss.	~28% rate of childhood sequelae; prenatal imaging not always predictive	Imaging normal does not exclude risk of sequelae; MRI adds prognostic value
Birnbaum et al. [20]	2020	Retrospective cohort	22 CMV+ fetuses	US only	All isolated US detected HCGM cases with normal outcomes.	100% favorable if isolated; non-isolated severe = TOP	Isolated, late germinal matrix findings have favorable outcome; non-isolated = poor
Minsart et al. [21]	2020	Retrospective cohort	84 CMV+ fetuses	US only	41.9% abnormal US led to severe outcomes, mostly late trimester.	41.9% severe outcome with any anomaly	Severe outcome risk is high when US is abnormal, especially in third trimester
Elkan Miller et al. [22]	2021	Prospective cohort	135 2nd/3rd trimester CMV+ fetuses	Serial US + MRI	7% developed mild adverse outcomes; 3% partial unilateral SNHL; 5% minor neurodevelopmental delay; abnormal imaging findings did not predict outcomes.	~28% sensitivity and low PPV for both US and MRI	Imaging in later pregnancy less predictive for adverse outcomes
Van den Eede et al. [23]	2025	Retrospective cohort	190 CMV+ fetuses	US only/serial US + MRI	26% abnormal US at amniocentesis, 63% developed later on serial scans, MRI added detection in 14%. Most common initial findings: echogenic bowel, periventricular echogenicity.	Serial US + MRI 95% sensitivity (US alone lower)	Serial US and MRI maximize prenatal detection of CMV-associated anomalies

US, ultrasound; MRI, magnetic resonance imaging; CMV, cytomegalovirus; PPV, positive predictive value; SNHL, sensorineural hearing loss; TOP, termination of pregnancy; NSG, neurosonography.

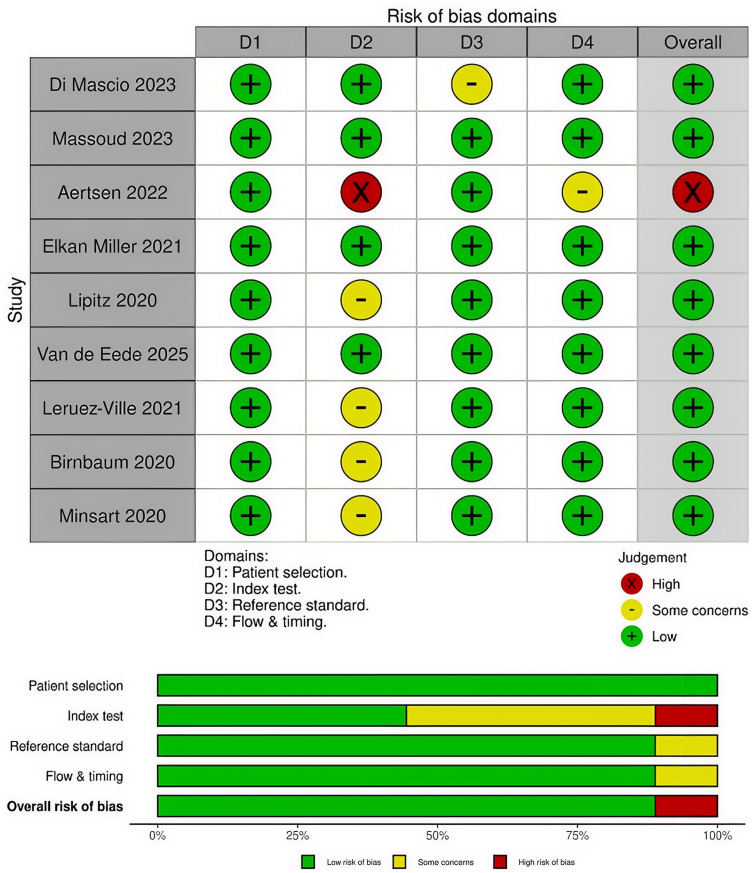


Figure 2. Quality assessment and bias risk assessment in the investigations included in this review.

marily by more precisely delineating polymicrogyria (3 cases) and confirming sonographically suspected clastic lesions (2 cases), thereby refining prognostic counseling.

Birnbaum et al. [20] analyzed 22 fetuses with hyperechogenic caudate germinal matrix and found that 18 fetuses with isolated HCGM (with or without lenticulostriatal vasculopathy) all had normal neurodevelopment at a mean follow-up of 33 months, whereas in the 4 fetuses in whom HCGM was associated with additional major brain abnormalities (including ventriculomegaly, temporal horn cysts, calcifications, and white matter signal changes), all pregnancies were electively terminated for presumed severe cerebral involvement.

Minsart et al. [21] reported that among pregnancies in which maternal CMV infection was diagnosed before 20 weeks' gestation, 43.8% of children with prenatal ultrasound anomalies developed severe outcomes, whereas no severe outcomes were observed after maternal infection at or beyond 20 weeks, underscoring the prognostic importance of infection timing.

Multiple studies demonstrated that fetal MRI provides crucial additional diagnostic information beyond ultrasound findings.

Di Mascio et al. [6] evaluated 95 fetuses with congenital CMV infection and normal neurosonography and found that fetal brain MRI detected additional CNS anomalies in 10.5% of cases; a high amniotic fluid viral load (> 100,000 copies/mL) was the only independent predictor of MRI-detected anomalies (OR 12.0, 95% CI 1.2-124.7).

In 2020, Lipitz et al. [19] evaluated 123 fetuses with first-trimester CMV infection and reported that fetal MRI detected abnormalities in 30.1% of cases overall and in 14.1% of fetuses with normal ultrasound. Abnormal MRI findings were significantly associated with neurodevelopmental abnormalities and with a composite outcome including termination of pregnancy, and severe anatomical MRI lesions (e.g., cortical malformations) were confined to fetuses with poor prognosis. Importantly, even among fetuses with normal prenatal imaging on both ultrasound and MRI (n = 73), 13.7% developed sensorineural hearing loss and 6.8% had mild neurodevelopmental abnormalities, indicating that normal imaging does not completely exclude long-term risks and underscoring the need for structured postnatal follow-up.

Elkan-Miller et al. [22] demonstrated that in fetuses with congenital CMV infection, after maternal infection in the second trimester, the sensitivity (28.6%) and positive predictive value (12%) of prenatal brain MRI for subsequent childhood sequelae were low, while the negative predictive value (94%) was high. Overall,

prenatal imaging was not predictive of adverse childhood outcomes.

Aertsen et al. [18] demonstrated a strong correlation between MRI and neurosonography-based grading of brain abnormalities in first-trimester CMV-infected fetuses (rs = 0.788, P < 0.0001), and complementary strengths of each modality were also demonstrated: MRI identified more temporal cysts (32 vs 24 on neurosonography) and identified two gyration abnormalities missed by neurosonography, while neurosonography was more sensitive for periventricular calcifications (10 vs 2 on MRI) and lenticulostriate vasculopathy (11 vs 0). On diffusion-weighted imaging, CMV-infected fetuses showed significantly increased ADC values in frontal, temporal, and occipital white matter and decreased values in the pons compared with controls, and temporal (bilateral) and left frontal ADC values were significantly higher in fetuses with severe (grade 4-5) MRI abnormalities than in those with milder (grade 1-3) lesions, indicating a quantitative relationship between microstructural white matter changes and anatomical severity.

Discussion

This systematic review presents the current evidence on the use of prenatal ultrasoundand MRI in the diagnosis, risk stratification and prognostication of fetal CMV infections. Our main findings suggest that ultrasound and MRI are both important tools, but have complementary roles in the evaluation of the fetus. Fetal MRI has a higher diagnostic yield for certain cerebral abnormalities and is especially useful when neurosonography is normal or inconclusive. In general, abnormal findings in either modality are associated with a higher risk of adverse outcomes and MRI often refines prognostic stratification, particularly after first-trimester infection, although studies of second- and third-trimester infections indicate that prenatal imaging may have limited ability to predict later sequelae in these later-onset cases. Importantly, a normal prenatal imaging profile, even if confirmed with both modalities, does not rule out the possibility of future adverse outcomes, especially SNHL.

Although congenital CMV infection is commonly framed as a cause of neurodevelopmental impairment, the imaging and outcome data synthesized in this review also support its interpretation as a condition with important neurodegenerative implications. Many of the sequelae described across studies - including progressive SNHL, epilepsy, motor dysfunction, and later cognitive deficits - are not fully explained by a single, static prenatal insult and instead suggest that CMV-related injury may evolve within the developing central nervous system. From this perspective, the structural abnormalities detected on prenatal ultrasound and MRI could be regarded not only as markers of congenital malformation but also as early indicators of disrupted neuronal development, white matter injury, and potential ongoing tissue damage that may continue after birth. This framing is especially important for readers who are interested in neurodegeneration because it links prenatal imaging patterns to progressive CNS vulnerability instead of just showing them as separate structural findings.

The concept that congenital CMV infection may behave as a neurodegenerative condition is supported by converging virological, neuropathological, and neuroimmunological evidence, which provides plausible mechanistic explanations for the progressive sequelae observed in affected children. First, human CMV is directly neurotropic; it infects neural progenitor cells, neurons, astrocytes, and microglia, and infection of the germinal matrix and ependyma produces necrotizing ventriculitis that underlies the characteristic periventricular calcifications [24-26]. Because neural progenitor cells and their neuronal and glial derivatives are fully permissive to CMV, infection can deplete or functionally impair the progenitor pool, thereby disrupting neurogenesis, neuronal migration, and gliogenesis; this mechanistic sequence is reflected in the cortical malformations, polymicrogyria, cerebellar hypoplasia, and gyral abnormalities detected on prenatal imaging [25-27].

Second, CMV establishes a persistent infection in the CNS and elicits a chronic neuroinflammatory response in which activated microglia and astrocytes are central players. Infected and bystander glial cells release proinflammatory cytokines and chemokines (e.g., TNF-α, IL-1β, IL-6, CCL2, CXCL10) and upregulate inducible nitric oxide synthase, driving microglial

activation, astrogliosis, and microglial nodules that are hallmark neuropathological findings of fetal and infant CMV encephalitis [24, 28-31]. Critically, this inflammatory cascade can injure uninfected neurons through bystander mechanisms; thus, tissue damage may continue to progress even after active viral replication is controlled [24, 31]. Third, CMV infection induces oxidative stress. Viral replication, together with the associated inflammatory response, generates reactive oxygen and nitrogen species that damage lipids, proteins, and DNA, impair mitochondrial function, and are toxic to oligodendrocytes, thereby contributing to white-matter injury and disturbed myelination frequently observed on fetal MRI [24, 32]. Fourth, CMV can establish latency, particularly within cells of the monocyte-microglial lineage, and periodic reactivation or low-grade antigen persistence may perpetuate neuroinflammation and sustain tissue injury over years - a pattern that parallels the chronic microglial activation implicated in other neurodegenerative diseases [24, 33]. Within the auditory system, CMV infects the stria vascularis, spiral ganglion neurons, and hair cells, and the resulting progressive labyrinthitis and cochlear neuronal loss explain why SNHL in congenital CMV infection is frequently delayed in onset and progressive rather than present and stable at birth [34].

This mechanistic framework helps interpret the imaging-outcome relationships synthesized in our review. Periventricular and parenchymal calcifications represent foci of necrotizing infection and dystrophic gliosis; white-matter hyperintensities may reflect gliosis, demyelination, and edema in the setting of active neuroinflammation; ventriculomegaly may indicate parenchymal loss rather than simple obstruction; and cortical malformations and cerebellar hypoplasia point to disruption of progenitor-cell biology early in gestation [24, 26, 28]. Viewed in this way, prenatal imaging abnormalities are not merely static anatomical findings but may represent early structural signatures of an ongoing neuroinflammatory and neurodegenerative process. This interpretation also explains why some children with normal prenatal imaging later develop SNHL or cognitive deficits, as molecular and inflammatory injury can evolve below the resolution of current structural imaging techniques [24, 34]. Clinically, this supports the concept that congenital CMV infection should be managed as a chronic CNS condition requiring longitudinal neurodevelopmental and audiological surveillance, and it highlights the potential of advanced quantitative techniques (e.g., diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI), and magnetic resonance spectroscopy (MRS)) and emerging biomarkers of neuroinflammation to capture the progressive component of the disease.

Our findings support and align with those of prior systematic reviews assessing the utility of prenatal imaging using either fetal MRI, ultrasound, or their combination for the diagnosis of congenital CMV infection. In line with Vande Walle et al. [17], we found that fetal MRI detects additional brain abnormalities in a clinically relevant minority of fetuses with normal or inconclusive ultrasound, particularly white-matter lesions, subependymal or temporal lobe cysts, and cortical malformations, and that abnormal MRI is strongly associated with adverse neurodevelopmental outcomes. Similarly, consistent with ultrasound-focused syntheses that conducted by Rybak-Krzyszkowska et al. [35], ventriculomegaly, periventricular echogenicity or cysts, intracranial calcifications, and hyperechogenic bowel emerged as the most frequent prenatal ultrasound indicators of CMV-related brain and systemic involvement in our review, and their presence - especially when severe or progressive-was associated with poor prognosis. However, while Buca et al.'s meta-analysis [2] quantified the low risk of symptomatic infection and neurodevelopmental impairment when prenatal imaging was normal, our feature-based synthesis highlights how particular very severe patterns of imaging, such as ventriculomegaly ≥ 15 mm, polymicrogyria, cerebellar hypoplasia, and extensive white matter injury, may provide a continuum of risk stratification beyond simply normal versus abnormal images, therefore providing improved risk stratification for counseling purposes than could be done based solely on a normal versus abnormal classification.

Compared with the comprehensive review by Stefanska et al. [11], which evaluated ultrasound and fetal MRI in parallel but primarily at the level of modality-level performance, our work integrates imaging indicators across modalities into a single, feature-oriented framework and explicitly links them to both long-term

neurodevelopmental outcome and emergency obstetric implications. Moreover, while prior reviews have emphasized that normal prenatal imaging does not exclude later sensorineural hearing loss, our synthesis reinforces this message by showing that a substantial minority of children develop hearing loss despite normal or only mildly abnormal prenatal imaging, underscoring the need for systematic postnatal audiological follow-up in all infants with congenital CMV.

Ultrasound in pregnancy remains the primary method of screening for the assessment of fetuses with congenital CMV infections. Readily available, inexpensive, and very sensitive for detecting many abnormalities. As demonstrated by Leruez-Ville et al. [4], targeted prenatal imaging in fetuses with known CMV infection-combining serial ultrasound and fetal MRI-identified all fetuses who later developed severe long-term sequelae, with 100% sensitivity and 100% negative predictive value for severe outcomes, whereas routine screening ultrasound alone had substantially lower sensitivity. Furthermore, Birnbaum et al. [20] and Minsart et al. [21] confirmed that the presence and nature of sonographic findings are powerful predictors of outcomes. Birnbaum et al. [20] showed that HCGM, when isolated on detailed neurosonography (with or without lenticulostriate vasculopathy), is associated with excellent prognosis, with all liveborn children demonstrating normal neurodevelopment at follow-up. In contrast, when HCGM was accompanied by additional major abnormalities such as ventriculomegaly, temporal horn cysts, calcifications or white-matter signal changes, all pregnancies were electively terminated for presumed severe cerebral involvement, underscoring how prognosis depends on the full neurosonographic context rather than on a single finding in isolation.

Ultrasound also excels in detecting certain features such as periventricular calcifications and lenticulostriate vasculopathy, which, as noted by Aertsen et al. [18], are more readily visualized with sonography than with MRI. However, the major limitations of ultrasound are operator dependency and reduced sensitivity to subtle brain parenchymal lesions, especially those involving cortical development and white matter integrity. Fetal MRI provides critical added value. Our review confirms the findings of multiple high-quality studies that MRI serves as a vital adjunct to ultrasound. Di Mascio et al. [6] found that, among 95 fetuses with congenital CMV infection and normal neurosonography, fetal brain MRI detected additional CNS anomalies in 10.5% of cases, with a high amniotic-fluid viral load (> 100,000 copies/mL) as the only independent predictor of MRI-detected lesions. Lipitz et al. [19] similarly reported that 30.1% of fetuses with first-trimester infection had abnormal MRI, including 14.1% of those with normal ultrasound, and that anatomical MRI abnormalities - particularly cortical malformations-were strongly associated with poor prognosis. These include subtle white matter hyperintensities, polymicrogyria and temporal cysts, lesions with significant prognostic implications that can be missed on ultrasound. Massoud et al. [5] demonstrated that MRI altered the severity classification of brain lesions in 14.5% of cases, and this directly affected the predicted prognosis.

The complementary nature of these imaging modalities is best illustrated by Aertsen et al. [18], who demonstrated a strong correlation between MRI and neurosonography grading ($r = 0.788$) while revealing distinct strengths for each modality. MRI was superior in identifying temporal cysts (32 vs 24 on neurosonography) and gyral abnormalities, whereas ultrasound was better for detecting calcifications (10 vs 2 on MRI) and lenticulostriate vasculopathy (11 vs 0). The HCGM case, as described by Birnbaum et al. [20], further illustrates this complementarity. While neurosonography excels in identifying HCGM and assessing associated abnormalities, MRI can provide valuable additional information when ultrasound findings are subtle or inconclusive, particularly when evaluating the temporal areas and white matter integrity. This evidence strongly supports a two-step imaging protocol in which fetal MRI is performed following detailed neurosonography, especially in fetuses considered to be at high risk or when isolated findings, such as HCGM, require comprehensive evaluation to exclude associated abnormalities.

The prognostic value of prenatal imaging extends beyond simple detection to risk stratification and counseling. Massoud et al. [5] showed that imaging severity sharply stratifies

prognosis: all fetuses with severe prenatal imaging features had adverse outcomes (71% termination, 24% intrauterine death, 6% survival with severe sequelae), whereas normal imaging was associated with mostly favourable outcomes (94% normal development, 6% mild sensorineural/vestibular sequelae), and mild abnormalities conferred intermediate risk, with roughly equal proportions of normal outcome, mild sequelae, and termination for uncertain prognosis.

Birnbaum et al. [20] added an important dimension by showing that isolated HCGM is reassuring, with 100% normal outcomes when comprehensive evaluation excludes associated abnormalities, such as ventriculomegaly, lenticulostriate vasculopathy, or temporal horn cysts. However, when HCGM is accompanied by other anomalies, the prognosis is poor. This underscores the fact that the context of findings, not merely their presence, determines prognostic significance and highlights the critical importance of thorough expert neurosonographic evaluation.

Elkan-Miller et al. [22] reported that, following second-trimester maternal infection, prenatal brain MRI had low sensitivity (28.6%) and a low positive predictive value (12%) but a high negative predictive value (94%) for subsequent childhood sequelae, and overall prenatal imaging did not reliably predict adverse outcomes in this group. Lipitz et al. found that MRI-detected cortical malformations had a 100% association with sequelae, supporting MRI's role of MRI in risk stratification.

Minsart et al. [21] reported that among pregnancies in which maternal CMV infection was diagnosed before 20 weeks' gestation, 43.8% of children with prenatal ultrasound anomalies developed severe outcomes, whereas no severe outcomes were observed when maternal infection occurred at or beyond 20 weeks, highlighting the prognostic importance of infection timing. Advanced techniques, such as DWI, as investigated by Aertsen et al. [18], offer promising quantitative parameters that may eventually enhance prognostic assessment.

A critical caveat must be emphasized when interpreting these prognostic data. Despite the clear benefits of advanced imaging, our review highlights an important caveat: normal prenatal imaging does not guarantee favorable outcomes. Lipitz et al. [19] reported that even among fetuses with normal ultrasound and MRI scans, 13.7% developed SNHL and 6.8% had other neurodevelopmental issues. This finding is critical for parental counselling. This underscores that congenital CMV is a systemic disease, and that SNHL, a common and serious sequela, may develop from mechanisms not visible with current structural imaging techniques, such as direct viral damage to the inner ear. Therefore, although imaging provides invaluable prognostic information regarding gross neurological function, its ability to predict hearing loss remains limited. All infants with congenital CMV infection, regardless of prenatal imaging results, require long-term audiological follow-up.

The relevance of prenatal CMV imaging extends into the emergency obstetric setting, where undiagnosed infection in high-risk pregnancies may manifest as intrauterine growth restriction, abnormal Doppler findings, or pathological fetal heart rate patterns, potentially necessitating urgent interventions including emergency caesarean section and carrying serious neonatal adverse outcomes including mortality [36, 37]. The results of this review reinforce the emergency implications of prenatal imaging: targeted imaging in fetuses with known CMV infection identified all fetuses who later developed severe long-term sequelae, with severe cerebral abnormalities such as cerebellar hypoplasia or ventriculomegaly ≥ 15 mm reliably signaling markedly increased risk [4]; severe imaging patterns (e.g., polymicrogyria or schizencephaly) were invariably associated with adverse outcomes, predominantly termination of pregnancy or intrauterine death [5]; and MRI detected additional brain abnormalities in 10% of fetuses with normal ultrasound but a high amniotic fluid viral load (> 100,000 copies/mL), directing prompt escalation toward emergency monitoring or termination decisions [6]. Van den Eede et al. [23] further showed that CMV-related ultrasound abnormalities were present in 63% of pregnancies with CMV-positive amniocentesis, and that combining serial neurosonography with fetal MRI distinguished favorable from adverse outcomes, with normal imaging associated with a normal postnatal outcome in 88% of children.

Prompt ultrasound and MRI can therefore guide acute decision-making and affect the management and prognostication of both the mother and fetus. In high-acuity situations, imaging guides the emergency response, including decision-making for immediate delivery and updating clinicians regarding the extent of fetal compromise, consistent with guidelines that recommend imaging as the first evaluation in pregnant women presenting with acute symptoms while weighing urgency against maternal-fetal safety [38]. Prenatal imaging should be systematically integrated into clinical care protocols at every visit, extending beyond routine screening. It serves as a crucial element in managing and promptly assessing potentially serious fetal conditions. This approach aims to prevent maternal-fetal mortality and facilitate rapid screening and intervention in pregnant women with CMV infection.

Limitations

This systematic review has several limitations. First, the included studies were heterogeneous in terms of the population, timing of maternal infection, imaging protocols, and definitions of neurodevelopmental outcomes. This variability makes it hard to directly compare and meta-analysis. Second, there is a possibility of publication bias, which means that those studies with significant or positive results are more prone to be published. Finally, the fast development of MRI technology makes older studies not indicative of the full diagnostic potential of current techniques, e.g. DWI. Fourth, because this is an imaging-based synthesis, we cannot directly measure the underlying neuroinflammatory, microglial, or oxidative burden in the fetal brain. The mechanistic evidence linking CMV to progressive neurodegeneration derives largely from experimental and neuropathological studies, and longitudinal human data on late neurocognitive outcomes in adolescence and adulthood remain limited [24, 26, 33]. The correlation between prenatal imaging signatures and the severity of ongoing neuroinflammatory injury, as well as their impact on the trajectory of postnatal neurodegeneration, remains to be determined.

Future directions

Several important research directions have emerged from this review. First, standardized imaging protocols and classification systems for prenatal CMV evaluation are required to facilitate cross-study comparisons and enable the development of validated prognostic scoring systems. Second, prospective, multicenter studies with long-term follow-up are needed to accurately quantify the prognostic accuracy of specific imaging findings and their combinations with detailed neurodevelopmental assessments beyond early childhood. Third, studies need to establish the best timing and indications for fetal MRI, whether to do it in all cases or only in selected cases based on ultrasound results, viral load, or other risk factors. These recommendations are based on cost-effectiveness analysis. Fourth, further research using advanced MRI techniques like DWI should be performed to assess if quantitative parameters can improve the precision of prognosis and detect abnormalities at an earlier stage. Finally, research on new biomarkers combining virologic, immunological and imaging data could improve prognostic models and clinical management.

Conclusion

This systematic review shows that detailed prenatal ultrasound and fetal MRI provide complementary information for diagnosing and risk-stratifying fetuses with congenital CMV infection. Ultrasound remains the primary screening tool, while fetal MRI refines prognostic assessment by better characterizing cortical malformations, white-matter injury, and temporal lobe lesions, especially when neurosonography is normal or equivocal. Severe or progressive imaging abnormalities strongly predict adverse outcomes, whereas normal or mildly abnormal imaging usually indicates more favorable prognosis; however, normal imaging does not exclude later SNHL, so long-term postnatal follow-up is required for all affected infants.

Acknowledgements

The authors acknowledge the use of ChatGPT 4.0 to improve language clarity and assist with grammar checking. All content has been reviewed and revised by the authors. The authors take full responsibility for the accuracy and originality of the work.

Disclosure of conflict of interest

None.

Address correspondence to: Farshad Riahi, Department of Radiology, Isfahan University of Medical Sciences, Isfahan, Iran. Tel: 818-519-1953; +98-9122872184; Fax: +98-3137265007; E-mail: farshadriahi@ymail.com

References

[1] Leruez-Ville M, Foulon I, Pass R and Ville Y. Cytomegalovirus infection during pregnancy: state of the science. Am J Obstet Gynecol 2020; 223: 330-349.

[2] Buca D, Di Mascio D, Rizzo G, Giancotti A, D'Amico A, Leombroni M, Makatsarya A, Familiari A, Liberati M, Nappi L, Flacco ME, Manzoli L, Salomon LJ, Scambia G and D'Antonio F. Outcome of fetuses with congenital cytomegalovirus infection and normal ultrasound at diagnosis: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2021; 57: 551-559.

[3] Hughes BL and Gyamfi-Bannerman C; Society for Maternal-Fetal Medicine (SMFM). Diagnosis and antenatal management of congenital cytomegalovirus infection. Am J Obstet Gynecol 2016; 214: B5-B11.

[4] Leruez-Ville M, Ren S, Magny JF, Jacquemard F, Couderc S, Garcia P, Maillotte AM, Benard M, Pinquier D, Minodier P, Astruc D, Patural H, Ugolin M, Parat S, Guillois B, Garenne A, Parodi M, Bussières L, Stirnemann J, Sonigo P, Millischer AE and Ville Y. Accuracy of prenatal ultrasound screening to identify fetuses infected by cytomegalovirus which will develop severe long-term sequelae. Ultrasound Obstet Gynecol 2021; 57: 97-104.

[5] Massoud M, Chollet M, Cabet S, Butin M, Mekki Y, Lina-Granade G, Fichez A, Attia J, Ville D and Guibaud L. Predicting outcome of congenital cytomegalovirus infection by differentiating and revisiting severe versus mild prenatal imaging features. Fetal Diagn Ther 2023; 50: 143-157.

[6] Rafieezadeh D, Khalaji A, Goli A, Gharavinia A and Mohammadi H. A comparative study of artifact reduction techniques in metal-implanted CT scans. Int J Physiol Pathophysiol Pharmacol 2026; 18: 1-7.

[7] Pass RF and Arav-Boger R. Maternal and fetal cytomegalovirus infection: diagnosis, management, and prevention. F1000Res 2018; 7: 255.

[8] Faure-Bardon V, Fourgeaud J, Guilleminot T, Magny JF, Salomon LJ, Bernard JP, Leruez-Ville M and Ville Y. First-trimester diagnosis of congenital cytomegalovirus infection after maternal primary infection in early pregnancy: feasibility study of viral genome amplification by PCR on chorionic villi obtained by CVS. Ultrasound Obstet Gynecol 2021; 57: 568-572.

[9] Garozzo MT, Pecorino B, Poli G, Maiolino L, Sciuto L, Scalia G, Ruggieri M, Polizzi A and Praticò AD. Maternal transmission, neonatal outcomes, and predictors of adverse effects in congenital cytomegalovirus infection. Pediatr Neonatol 2026; 67: 523-531.

[10] Britt WJ. Maternal immunity and the natural history of congenital human cytomegalovirus infection. Viruses 2018; 10: 405.

[11] Stefanska K, Berbeka K, Madej D, Witkowski P, Rybak-Krzyszkowska M, Sawicki S and Illa M. Role of ultrasound and fetal MRI in the prenatal assessment of congenital cytomegalovirus infection: a systematic review. J Clin Med 2026; 15: 3645.

[12] Roozpeykar S, Azizian M, Zamani Z, Farzan MR, Veshnavei HA, Tavoosi N, Toghyani A, Sadeghian A and Afzali M. Contrast-enhanced weighted-T1 and FLAIR sequences in MRI of meningeal lesions. Am J Nucl Med Mol Imaging 2022; 12: 63-70.

[13] Bahrami M, Hekmatnia A, Alikhani F, Movahedi M, Roshan M and Kiani P. Evaluation of relevance of sonographic findings with prognosis and outcomes of pregnancy in preeclampsia patients in comparison with control group. J Isfahan Med Sch 2025; 43: 264-274.

[14] Shahar-Nissan K, Pardo J, Peled O, Krause I, Bilavsky E, Wiznitzer A, Hadar E and Amir J. Valaciclovir to prevent vertical transmission of cytomegalovirus after maternal primary infection during pregnancy: a randomised, double-blind, placebo-controlled trial. Lancet 2020; 396: 779-785.

[15] Hughes BL, Clifton RG, Rouse DJ, Saade GR, Dinsmoor MJ, Reddy UM, Pass R, Allard D, Mallett G, Fette LM, Gyamfi-Bannerman C, Varner MW, Goodnight WH, Tita ATN, Costantine MM, Swamy GK, Gibbs RS, Chien EK, Chauhan SP, El-Sayed YY, Casey BM, Parry S, Simhan HN, Napolitano PG and Macones GA; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. A trial of hyperimmune globulin to prevent congenital cytomegalovirus infection. N Engl J Med 2021; 385: 436-444.

[16] Kimberlin DW, Jester PM, Sánchez PJ, Ahmed A, Arav-Boger R, Michaels MG, Ashouri N, Englund JA, Estrada B, Jacobs RF, Romero JR, Sood SK, Whitworth MS, Abzug MJ, Caserta MT, Fowler S, Lujan-Zilbermann J, Storch GA, DeBiasi RL, Han JY, Palmer A, Weiner LB, Bocchini JA, Dennehy PH, Finn A, Griffiths PD, Luck S, Gutierrez K, Halasa N, Homans J, Shane AL, Sharland M, Simonsen K, Vanchiere JA, Woods CR, Sabo DL, Aban I, Kuo H, James SH, Prich-

ard MN, Griffin J, Giles D, Acosta EP and Whitley RJ; National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Valganciclovir for symptomatic congenital cytomegalovirus disease. N Engl J Med 2015; 372: 933-943.

[17] Vande Walle C, Maris F, Schiettecatte E and Herregods N. The value of magnetic resonance imaging in congenital cytomegalovirus infection: a systematic review. Pediatr Radiol 2024; 54: 2157-2174.

[18] Rafieezadeh D and Abbaspour M. Exploring the seas for cancer cures: the promise of marine-derived bioactive peptide. Int J Biochem Mol Biol 2024; 15: 100-106.

[19] Lipitz S, Elkan Miller T, Yinon Y, Weissbach T, De-Castro H, Hoffman C, Katorza E and Weisz B. Revisiting short- and long-term outcome after fetal first-trimester primary cytomegalovirus infection in relation to prenatal imaging findings. Ultrasound Obstet Gynecol 2020; 56: 572-578.

[20] Birnbaum R, Winsteen A, Brusilov M, Wolman I, Ben-Sira L, Malinger G and Krajden Haratz K. A unique brain germinal matrix involvement in cytomegalovirus infected fetuses: a retrospective neurosonographic analysis with outcome correlation. Prenat Diagn 2021; 41: 877-883.

[21] Minsart AF, Rypens F, Smiljkovic M, Kakkar F, Renaud C, Lamarre V, Boucher M and Boucoiran I. Prenatal findings, neonatal symptoms and neurodevelopmental outcome of congenital cytomegalovirus infection in a university hospital in Montreal, Quebec. J Perinat Med 2020; 48: 234-241.

[22] Elkan Miller T, Weisz B, Yinon Y, Weissbach T, De Castro H, Avnet H, Hoffman C, Katorza E and Lipitz S. Congenital cytomegalovirus infection following second and third trimester maternal infection is associated with mild childhood adverse outcome not predicted by prenatal imaging. J Pediatric Infect Dis Soc 2021; 10: 562-568.

[23] Van den Eede E, De Keersmaecker B, Lagrou K, Van der Veeken L, Vanwinkel S, Vangoitsenhoven M, Aertsen M and De Catte L. Prevalence and timing of prenatal ultrasound findings in cytomegalovirus-infected pregnancies. Acta Obstet Gynecol Scand 2025; 104: 302-308.

[24] Cheeran MC, Lokensgard JR and Schleiss MR. Neuropathogenesis of congenital cytomegalovirus infection: disease mechanisms and prospects for intervention. Clin Microbiol Rev 2009; 22: 99-126.

[25] Teissier N, Fallet-Bianco C, Delezoide AL, Laquerriere A, Marcorelles P, Khung-Savatovsky S, Nardelli J, Cipriani S, Csaba Z, Picone O, Golden JA, Van Den Abbeele T, Gressens P and Adle-Biassette H. Cytomegalovirus-Induced brain malformations in fetuses. J Neuropathol Exp Neurol 2014; 73: 143-158.

[26] Kawasaki H, Kosugi I, Meguro S and Iwashita T. Pathogenesis of developmental anomalies of the central nervous system induced by congenital cytomegalovirus infection. Pathol Int 2017; 67: 72-82.

[27] Luo MH, Schwartz PH and Fortunato EA. Neonatal neural progenitor cells and their neuronal and glial cell derivatives are fully permissive for human cytomegalovirus infection. J Virol 2008; 82: 9994-10007.

[28] Gabrielli L, Bonasoni MP, Lazzarotto T, Lega S, Santini D, Foschini MP, Guerra B, Baccolini F, Piccirilli G, Chiereghin A, Petrisli E, Gardini G, Lanari M and Landini MP. Histological findings in foetuses congenitally infected by cytomegalovirus. J Clin Virol 2009; 46 Suppl 4: S16-S21.

[29] van den Pol AN, Mocarski E, Saederup N, Vieira J and Meier TJ. Cytomegalovirus cell tropism, replication, and gene transfer in brain. J Neurosci 1999; 19: 10948-10965.

[30] Lokensgard JR, Cheeran MC, Hu S, Gekker G and Peterson PK. Glial cell responses to herpesvirus infections: role in defense and immunopathogenesis. J Infect Dis 2002; 186 Suppl 2: S171-S179.

[31] Cheeran MC, Hu S, Yager SL, Gekker G, Peterson PK and Lokensgard JR. Cytomegalovirus induces cytokine and chemokine production differentially in microglia and astrocytes: antiviral implications. J Neurovirol 2001; 7: 135-147.

[32] Schleiss MR. Congenital cytomegalovirus infection: molecular mechanisms mediating viral pathogenesis. Infect Disord Drug Targets 2011; 11: 449-465.

[33] Heneka MT, Carson MJ, El Khoury J, Landreth GE, Brosseron F, Feinstein DL, Jacobs AH, Wyss-Coray T, Vitorica J, Ransohoff RM, Herrup K, Frautschy SA, Finsen B, Brown GC, Verkhratsky A, Yamanaka K, Koistinaho J, Latz E, Halle A, Petzold GC, Town T, Morgan D, Shinohara ML, Perry VH, Holmes C, Bazan NG, Brooks DJ, Hunot S, Joseph B, Deigendesch N, Garaschuk O, Boddeke E, Dinarello CA, Breitner JC, Cole GM, Golenbock DT and Kummer MP. Neuroinflammation in Alzheimer's disease. Lancet Neurol 2015; 14: 388-405.

[34] Teissier N, Delezoide AL, Mas AE, Khung-Savatovsky S, Bessières B, Nardelli J, Vauloup-Fellous C, Picone O, Houhou N, Oury JF, Van Den Abbeele T, Gressens P and Adle-Biassette H. Inner ear lesions in congenital cytomegalovirus infection of human fetuses. Acta Neuropathol 2011; 122: 763-774.

[35] Rybak-Krzyszkowska M, Górecka J, Huras H, Staśkiewicz M, Kondracka A, Staniczek J, Górczewski W, Borowski D, Grzesiak M, Krzeszowski W, Massalska-Wolska M and Jaczyńska R. Ultrasonographic signs of cytomegalovirus infection in the fetus-a systematic review of the literature. Diagnostics (Basel) 2023; 13: 2397.

[36] Powel JE, Zantow EW, Bialko MF, Farley LG, Lawlor ML, Mullan SJ, Vricella LK and Tomlinson TM. Predictive index for adverse perinatal outcome in pregnancies complicated by fetal growth restriction. Ultrasound Obstet Gynecol 2023; 61: 367-376.

[37] Faraz S, Abu-Nayla U, Mirza F, Aftab N and Malik SA. Cytomegalovirus (CMV) infection in pregnancy resulting in neonatal mortality due to congenital CMV: a case report. Cureus 2025; 17: e84413.

[38] Eibschutz L, Lu MY, Jannatdoust P, Judd AC, Justin CA, Fields BKK, Demirjian NL, Rehani M, Reddy S and Gholamrezanezhad A. Emergency imaging protocols for pregnant patients: a multi-institutional and multi- specialty comparison of physician education. Emerg Radiol 2024; 31: 851-866.