# NON-INVASIVE MANAGEMENT OF MATERNAL CYTOMEGALOVIRUS INFECTION DURING PREGNANCY

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# ABSTRACT

## Problem statement

Primary maternal cytomegalovirus (CMV) infection occurs in 0.8-6% of all pregnancy worldwide. The vertical transmission rate is 32%. 87.3% of CMV-infected newborns are asymptomatic at birth and 10-15% of these will develop CMV-related sequelae, particularly sensorineural hearing loss (SNHL). Up until now, no antenatal treatment of CMV infection has been satisfactorily validated. Amniocentesis, the gold standard to confirm fetal congenital infection, does neither completely discriminate between infected and uninfected newborn, nor does it predict neurological outcome. For these reasons, it is considered an invasive method and the indication in asymptomatic foetuses is still debated. We propose a first-line non-invasive fetal management using systematic ultrasound (US) and cerebral magnetic resonance imaging (MRI) for primary maternal CMV infection. An amniocentesis is performed only if the medical imaging screening highlights abnormal findings.

## Methods

In a retrospective study from January 2011 to February 2015, 40 pregnant women with a history of primary CMV infection were reviewed. These patients were assessed using a non-invasive prenatal management by repeated detailed US every 4 weeks and a fetal MRI at around 32 weeks. Amniocentesis 6 weeks after infection and at least at 20 weeks of gestation was conducted to identify congenital infection only if imaging technic highlighted abnormal findings or at the request of the patient after informed consent. Three patients who underwent an amniocentesis for other causes were included. Detection of CMV in the urine sample of the newborn by polymerase chain reaction (PCR) or viral culture established the postnatal diagnosis of congenital infection. The impact of congenital infection was evaluated postnatally by means of clinical examination, blood test, auditory brainstem responses, ophthalmology assessment and transfontanellar ultrasound. Lumbar puncture with cerebrospinal fluid (CSF) analysis was performed in case of abnormal postnatal imaging. Follow-up with periodic auditory and ophthalmologic assessment were also proposed for CMV-positive newborns. Medical abortions were analysed at necropsy**.**

## Results

CMV seroconversion occurred periconceptionally in 6 cases (15%), in the first trimester in 17 cases (42,5%), in the second trimester in 15 (37,5%) and in the third trimester in 2 (5%). Results are illustrated on Figure 1. Four foetuses had a positive screening based on abnormal findings at US and/or MRI. Among these, one had a negative PCR on amniocentesis and was confirmed as postnatally non-infected. Two medical abortions were performed. One of the foetuses had abnormal MRI and ultrasound while the other had abnormal findings only diagnosed on MRI. At necropsy, both foetuses showed diffuse organic CMV abnormalities. The last foetus had normal MRI but positive amniocentesis. Congenital CMV was confirmed at birth but the baby was asymptomatic. 37 of the 41 foetuses had a negative screening relying on both imaging technics. Among them, 11 children (29,7%) had positive CMV in urine at birth. 4 children had aspecific transfontanellar

ultrasound abnormalities but all had negative PCR in the CSF and were considered asymptomatic. One child was diagnosed with a peripheral facial palsy at the age of three months and was therefore considered symptomatic although this is not a specific sign. At the age of one year, however the facial palsy recovered. None of these children developed SNHL or visual impairment with a mean age of follow-up of 478 days (range 31-916). However, three children had seromucous otitis and their auditory assessment is not reliable. This study also illustrates the large heterogeneity in the follow-up and the poor observance for assessment.

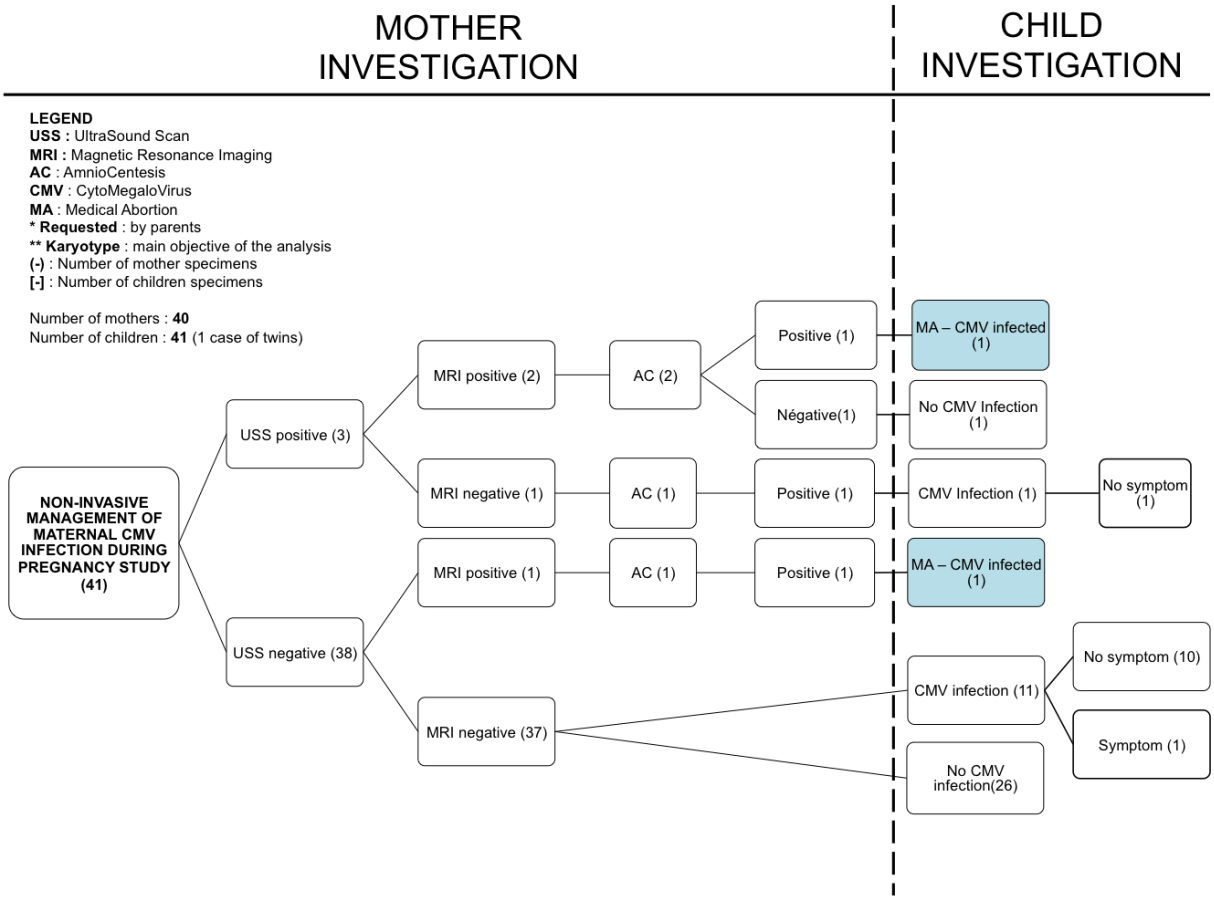


**Figure 1 - Results overview**

## Conclusion

Non-invasive management of maternal CMV infection during pregnancy by US/MRI seems to be a valid option to detect severe cases of congenital CMV infection. We suggest a non-invasive prenatal management by detailed US every 4 weeks and a fetal MRI at around 32 weeks and the use of amniocentesis in a second line if anomalies are detected by US/MRI.
This method has to be approved by a larger cohort of patients primo-infected with CMV and longer follow-up of newborns.

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## Conflicts of interest

None conflicts of interest