Management of Babies born to Mothers who Seroconvert (CMV IgM positive) during Pregnancy - Paediatric Full Clinical Guideline – Joint Derby & Burton

Reference No: NIC IN 17/May 21/v001

1. Summary

This is a practical guideline and check list for assessing and managing babies born to mothers who seroconvert for Cytomegalovirus (CMV) during pregnancy (CMV IgM positive).
This guideline is based on the European Expert Consensus Statement on Diagnosis and Management of Congenital CMV, the Royal College of Obstetricians Scientific impact paper (2018).

2. Introduction

Congenital CMV is a condition that can occur when an infant is infected with a virus called Cytomegalovirus during the ante-natal period. Congenital CMV is a very common infection affecting 3-6 infants in every 1000 births in high income countries. The prevalence is 0.3-0.8% in developed countries.

The risk of transmission is higher during later stages of pregnancy though transmission during early pregnancy is more likely to be associated with severe consequences to the fetus. The rate of transmission is 30-40% with primary CMV infection in mother, but only 1% with CMV reactivation or reinfection during pregnancy.

Unfortunately, CMV is not often diagnosed in the neonatal period. This means that infected infants miss out from the benefit of early treatment or from hearing, visual or neuro developmental screening which might allow earlier intervention.

Only about 10% of affected neonates presents with symptoms at birth. The disease can be mild to severe with 5% mortality. Of the symptomatic group, two third will have long term neurological impairment.

But, 15% of infants from the group who do not have symptoms at birth (asymptomatic), may also go on to develop some complications, most commonly Sensorineural Hearing Loss (SNHL), hence the need for early action on maternal seroconversion.

Infants can easily acquire CMV infection postnatally as well; during delivery, through breast milk or close contact with body fluids. For prognosis and treatment it is essential to differentiate congenital infection from the postnatally acquired infection.

3. Aim and Purpose

This guideline is applicable to infants being cared for within Derby and Burton, for whom a diagnosis of active CMV is suspected or confirmed in pregnancy or a congenital CMV infection is suspected or confirmed in the infant.
The purpose is to provide guidance to all staff involved on the diagnosis and management of infants with congenital cytomegalovirus.

4. Definitions

CMV – Cytomegalovirus
cCMV – Congenital Cytomegalovirus
MRI – Magnetic resonance imaging
SNHL – Sensorineural Hearing Loss
CNS – Central Nervous System
NIPE – Newborn Infant Physical Examination
FBC – Full blood count
USS – Ultrasound
IUGR – Intrauterine growth restriction
PCR – Polymerase chain reaction
U& E – Urea and electrolytes
Ig – Immunoglobulin

LFT– Liver function tests

5. Diagnosis and Mangement of Congenital CMV After Birth

5.1. Confirming cCMV in babies born to a mother with CMV IgM

- Send babies urine for CMV PCR as soon as possible after birth
- Paediatric NIPES should be carried out within 24 hours - First by the SHO/GP trainee and repeated by middle- grade/Registrar looking for clinically detectable symptoms and signs of cCMV – findings which may include clinically insignificant or transient findings such as petechiae, mild hepatomegaly or splenomegaly, SGA.

Diagnostic Tests

- CMV PCR on urine. Urine for CMV does not need to be sterile. Cotton wool in nappy or bag urine is acceptable.
- Saliva swab is another possible sample for CMV PCR. In a breast fed infant, saliva swab should ideally be taken at least 1 hour after a feed. If positive need to confirm with a urine sample.
- Congenital CMV is confirmed if samples collected within first 21 days of life are positive by CMV PCR. After 21days, positive result is deemed to be acquired CMV.
- If >21 days old, retrospective testing of dried blood spot taken on day 5 can be used.

5.2. If Urine CMV PCR comes as positive (cCMV confirmed) - Screen for other features of congenital CMV – Symptomatic disease

- Blood tests
    - FBC (Neutropenia, thrombocytopenia)
    - LFTs (increased transaminases, conjugated hyperbillirubinaemia)
    - U&E (as base line prior to treatment)
    - Baseline CMV viral load
- Cranial USS - If abnormalities in USS (calcifications) or clinical concerns consider early MRI. All infants with confirmed cCMV should have an MRI but treatment should not be delayed till it is done.
- Refer for formal auditory assessment, in addition to new born hearing screening (OAE, ABR)
- Notify audiology department as infants need long term follow up until 5-6 years of age
- Ophthalmic assessment for chorioretinitis, optic atrophy or cataracts

6. Treatment

6.1. All infants with cCMV should be discussed with the Paediatric infectious disease team;

Dr Scott Hackett or a member of infectious disease team at Heartlands Hospital #6166

6.2. Treatment indicated

- Evidence of CNS disease by USS or MRI
- Severe disease (life threatening or severe single organ or multi-organ non-CNS disease)

6.3 Treatment Considered

- Isolated Sensorineural hearing deficits
- Moderate disease(eg multiple minor findings consistent with CMV disease)

6.4 Treatment not normally indicated

- Mildly symptomatic infants (isolated IUGR, Hepatomegaly with normal liver enzymes, mild and transient thrombocytopenia, isolated elevation of liver enzymes)
- No clinical or biochemical findings of the disease
- Diagnosis of congenital CMV after 1st Month of life (treat normally as only as part of research

6.5 Treatment Guideline

- Treatment should be initiated in the first month of life after discussing benefits and the side effects of the medication with parents
- Valganciclovir oral solution 16mg/kg/dose PO BD, or
- Ganciclovir 6mg/kg/dose IV BD if not fully enterally fed
- Complete 6 months of antiviral treatment
- Adjust dose 2 weekly for the first month and then monthly based on weight and blood results
- Monitor FBC, U&Es, LFTs, 2 weekly for the first month and then monthly. Monitor them weekly when on IV Ganciclovir
- Urine CMV viral load and therapeutic drug monitoring not routinely required –as directed by infectious disease team at Heartlands Hospital #6166
- If results are abnormal, discuss with infectious disease team
- Provide National CMV support group details to all parents of infants with cCMV for information and support: http://cmvaction.org.uk

7. Follow up

7.1. Paediatric Follow up

- All infants diagnosed with cCMV infection should be followed up irrespective of symptoms apparent at birth.
- All infants diagnosed with congenital CMV infection should be followed up, irrespective of symptoms apparent at birth
- **Infants NOT treated**: General Pediatric review with Pediatric Infectious Disease input for a minimum of 2 years.
- **Infants treated**: Paediatric Infectious Disease clinic at Heartland at diagnosis, then as required 6-12 monthly**.** Local follow-up monthly for 6 months, then annually for a minimum of 2 years

7.2. Audiology Follow up – All infants

- Audiology assessment as soon as possible following diagnosis
- Audiology assessment every 3-6 months in the first year, then every 6 months until 3 years of age, then every 12 months until 6 years of life

7.3. Ophthalmology follow up – All infants

- Ophthalmic assessment as a baseline at diagnosis and then as recommended by the ophthalmologist (ideally annually until 5 years

7.4. Developmental follow up

- All infants – at 12 months
- For treated infants – as with other infants requiring developmental follow up at 6, 12, 24 and 48 months of corrected gestational age

8. References

1. https://www.piernetwork.org/congenital-cmv
2. Shah T, et al. Arch Dis Child Educ Pract Ed 2016;101:232–235
3. Management of babies born to mother who seroconvert for CMV during pregnancy (CMV IgM positive) Burton Guideline (2017)
4. Staffordshire, Shropshire and Black Country Neonatal Operational Delivery Network
5. Southern West Midlands Neonatal Operational Delivery Network

Documentation Controls

Development of Guideline:	Dr Sujeeva Sukumar (Specialty Doctor in Paediatrics) Dr Martins Iwunze (GP trainee)
Consultation with:	Dr Muogbo (Consultant Paediatrician) Dr Bala Subramaniam (Consultant Paediatrician)
Approved By:	*Paediatric Business Unit Guidelines Group, Women and Children's Division – 25th May 2021*
Review Date:	May 2024
Key Contact:	Dr Sujeeva Sukumar