

Profile of congenital cataract in the first year of life from a tertiary care center in South India – A modern series

Vivek Mahendrapratap Singh, Akshay Badakere, Preeti Patil-Chhablani¹, Ramesh Kekunnaya

Purpose: To report the etiology, clinical presentation, and morphology of congenital cataract in a tertiary care center. **Methods:** It is a prospective cohort study conducted at L V Prasad Eye Institute, Hyderabad. All children with congenital cataract ≤ 12 months of age that required surgical intervention between August 2015 and July 2016 were included in the study. 109 such patients were subjected to meticulous history taking, pedigree charting, ocular, and systemic examination, B-scan, TORCH testing, clinical photographs, pediatrician consult and blood tests, which included serum calcium, serum phosphorous and urine for reducing sugars. **Results:** The mean age of presentation was 4.1 months (± 2.6 months) and both the genders were equally affected ($P = 0.49$). Eighty-five patients (77.9%) presented with bilateral cataracts while 24 patients had a unilateral presentation (22.1%). The common morphological presentation was either a total or a nuclear cataract, both variants noticed in 47 patients (43.1%). TORCH infections were responsible for a maximum (37 patients, 33.4%) number of cases followed by familial (20 patients, 18%) and developmental anomalies (11 patients, 10.1%) while the total number of idiopathic cases were 24% (27 patients). Eighteen patients (16.5%) had congenital heart defects and the majority (16 patients, 88.9%) of these had positive TORCH titres. **Conclusion:** Familial cataract and those possibly due to TORCH are still the predominant cause of congenital cataract in this series-highlighting the role of vaccination and preventive measures.

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Such is the scenario of childhood blindness in the world that one child goes blind every minute.^[1] It is estimated that there are about 1.26 million children with blindness in the world, almost two-thirds of them living in developing countries.^[2] In developing countries, data on childhood blindness is limited and this hampers the development of strategies to overcome an important public health issue.

Cataract is one of the most common treatable causes of visual disability in children.^[3] The incidence of congenital cataracts during the first year of life in the United Kingdom is 2.49 per 10,000 children,^[4] while, that in the United States, it is 2.03 per 10,000.^[5] The prevalence increases from 0.2 to 0.3 per 10,000 in developed nations to 10 times in developing countries.^[6] As per the World Health Organization, this number is close to 8 per 10,000 children in India. The objective of this study is to find the various causes of congenital cataract in infants and their distinct characteristic features that can help us in early identification and appropriate management.

Methods

This is a prospective, non-comparative, descriptive study conducted at L V Prasad Eye Institute, Hyderabad, India. The study adhered to the tenets of Declaration of Helsinki and was approved by the Institutional Review Board (IRB). A total of 129 patients, with age less than or equal to 12 months, were

diagnosed to have congenital cataract from 1st August 2015 to 31st July 2016. Of these, 109 patients who were willing for further examination and follow-ups, and underwent cataract surgery were included in the study. Patients with lenticular opacities that did not require surgery, patients who underwent surgery elsewhere, and patients who did not wish to be a part of the study were excluded. Informed written consent was taken from the parents for examination and photographic documentation.

All the patients reporting to the institute underwent a complete ophthalmic evaluation by trained paediatric ophthalmologists. History was based on a standardized questionnaire to include all the relevant details (e supplement Table 1). Visual acuity was recorded based on a child's fixation as central, steady, and maintained (CSM) or as the ability to fix and/or follow the light and/or objects. When fundus examination could not be done either due to a dense cataract or because the child was very uncooperative for examination, a B scan ultrasonography was done.

The parents and siblings of the patients were examined and slit lamp findings were noted. A pedigree charting was done for all patients. A meticulous and detailed ocular and physical examination was done to rule out systemic associations. If examination revealed a possible systemic disease then an opinion was sought from a paediatrician.

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Pediatric Ophthalmology and Strabismus Services, LVPEI, Hyderabad, ¹UPMC Childrens, Pittsburgh, USA

Correspondence to: Dr. Ramesh Kekunnaya, Head, Child Sight Institute, Jasti V Ramanamma Children's Eye Care Center, L V Prasad Eye Institute, Banjara Hills, Road No 2, Hyderabad, TS, India. E-mail: rameshak@lvpei.org

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Mothers and infants who had cataracts other than familial or developmental anomalies like persistent hyperplastic primary vitreous (PHPV), were subjected to TORCH infection testing. TORCH infections were diagnosed as per the definitions laid by the Center for Disease Control and Prevention, 2015 (e supplement Tables 2–4).^[7-9] All patients also underwent investigations like blood sugar, complete blood count, serum bilirubin, serum calcium and phosphorus, and urine examination for the presence of reducing substances.

The child’s intraocular pressure (with Perkins tonometer), axial length (A-scan biometry AL-100, Tomey), corneal curvature (NIDEK hand-held keratometer), corneal thickness (pachymeter, SP100, Tomey), and diameter (Castroviejo callipers) were measured under general anesthesia in the operating room just before the cataract surgery. All the patients were analysed for the nature of presentation, morphology and etiology of the cataracts, and associated ocular and systemic conditions.

Microsoft Excel (Microsoft Work Professional 2013) was used to manage the data-sheet and for graphical and diagrammatic representations. Appropriate measures for central tendency, proportions, standard deviations (SD), 95% confidence interval (CI), sensitivity, specificity, and positive predictive values were calculated using Microsoft Excel wherever deemed necessary. Chi-square test was used for the categorical data and *P* value less than 0.05 was considered statistically significant.

Results

A total of 109 patients under the age of 12 months underwent surgery for congenital cataract from August 2015–July 2016. The mean age of presentation was 4.1 months (SD ± 2.6 months; 95% CI ± 0.489). There was a near-normal distribution of males and females (males 57/109, females 52/109) (*P* = 0.49). It was also noted that only 17% of patients (19 out of 109) presented early (≤1 month), while the remaining 90 patients presented after 1 month. Sixty-one patients (55.9%) belonged to the lower socio-economic status (*P* = 0.07).

Detailed history revealed contributory prenatal risk factors in 26 mothers (23.8%). Of these, 9 mothers (8.2%) tested positive for TORCH titres. Other significant risk factors included fever without rash (4.5%), fever with rash (2.7%), hypothyroidism (1.8%), gestational hypertension (1.8%), hyperthyroidism (0.9%), post-partum haemorrhage (0.9%), pre-eclampsia (0.9%), oligohydramnios (0.9%), and sickle cell trait (0.9%). History of consanguinity was present in 30 (27.5%) patients. Of these, only 9 (8.2%) had a family history of congenital cataract.

The most common presenting complaint was the presence of white reflex in these eyes (67 eyes, 61.4%) followed by the inability to follow the mother’s face and/or objects in 12 eyes (11%), inward or outward deviation of the eye in 8 eyes (7.3%), and shaking of eyes in 2 eyes (1.8%). Two patients were diagnosed to have cataracts during their retinopathy of prematurity (ROP) screening while the remaining 18 patients (16.5%) were diagnosed to have cataract elsewhere and were referred to our center for further management.

Eighty-five patients (77.9%) had bilateral cataracts while 24 patients (22.1%) had unilateral cataracts [Table 1]. The common morphological variants [Fig. 1] reported were either a total or a nuclear cataract (reported in 47 eyes each). Table 2 describes the various morphological types in the study patients. TORCH infections (37 patients, 33.4%) were the commonest cause responsible for these cataracts [Table 3] followed by familial (20 patients, 18.3%), and developmental anomalies (11 patients, 10.1%) while the total number of

idiopathic cases were 24.7% (27 patients). Amongst familial cataracts, the most common pattern of inheritance was found to be autosomal dominant. It was reported in 13 patients while the remaining 7 were found to have an autosomal recessive pattern of inheritance [Table 4]. Fifteen patients presented with yellow to dirty brown colour hue on the lens. Thirteen such patients tested positive for Rubella infections (72% sensitive, 98% specific, 87% positive predictive value).

The most common ocular association was nystagmus (41/109). Nine patients had esotropia, while 5 patients presented with exotropia. Congenital nasolacrimal duct obstruction was

Table 1: Laterality of cataract and relationship to etiology

Laterality	Number of patients
Bilateral	
Hereditary	19 (16.5%)
TORCH	27 (24.7%)
Others	15 (13.7%)
Idiopathic	24 (22.0%)
Total	85 (77.9%)
Unilateral	
Hereditary	1 (0.9%)
TORCH	10 (9.1%)
Others	10 (9.1%)
Idiopathic	3 (2.7%)
Total	24 (22.1%)
Total	109

Table 2: Various cataract morphologies and their aetiologies

Morphology of cataract	Etiology	
Total cataract	Hereditary	8 (7.3%)
	TORCH	17 (15.5%)
	Others	9 (8.2%)
	Idiopathic	13 (11.9%)
	Total	47 (43.1%)
Nuclear	Hereditary	9 (8.2%)
	TORCH	17 (15.5%)
	Others	9 (8.2%)
	Idiopathic	12 (11.1%)
	Total	47 (43.1%)
PHPV	Total	4 (3.6%)
Lamellar	Hereditary	1 (0.9%)
	TORCH	1 (0.9%)
	ROP	1 (0.9%)
	Idiopathic	1 (0.9%)
	Total	4 (3.6%)
Anterior polar cataract	Anterior segment dysgenesis	1 (0.9%)
	TORCH	1 (0.9%)
	Idiopathic	1 (0.9%)
	Total	3 (2.7%)
Anterior capsular cataract	Smith-Lemli-opitz syndrome	1 (0.9%)
Anterior sub-capsular cataract	Hereditary	1 (0.9%)
Posterior sub-capsular cataract	TORCH	1 (0.9%)
Cortical cataract	Hereditary	1 (0.9%)



Figure 1: Various morphological variants of congenital cataract reported in the study. (a, d and g) total cataract, (b) child with Down syndrome and total cataract, (c) typical dirty yellow Rubella cataract, (e) asymmetrical cataract with exotropia, (f) Lamellar cataract, (i) Sutural cataract (h) Posterior lenticonus (Bilateral)

Table 3: Congenital cataract patients with TORCH infections and their laterality

Etiology	Bilateral presentation	Unilateral presentation	Total
Rubella			
Confirmed Congenital rubella syndrome	8 (7.3%)	6 (5.5%)	14 (12.8%)
Probable Congenital rubella syndrome	3 (2.7%)	1 (0.9%)	4 (3.6%)
Total	11 (10.1%)	7 (6.4%)	18 (16.5%)
Cytomegalovirus			
Congenital Cytomegalovirus	6 (5.5%)	1 (0.9%)	7 (6.4%)
Possible Cytomegalovirus	9 (8.2%)	1 (0.9%)	10 (9.1%)
Total	15 (13.7%)	2 (1.8%)	17 (15.5%)
Neonatal Herpes simplex virus	1 (0.9%)	1 (0.9%)	2 (1.8%)
Total	27 (24.7%)	10 (9.7%)	37 (33.4%)

found in 6 (5.5%) patients. Posterior lenticonus was also seen in a similar number of patients. Less common ocular findings included ROP, microspherophakia, vitreous haemorrhage, retinal detachment, and choroidal coloboma [Fig. 2].

Micro-cornea (corneal diameter <9.5 mm) was seen in approximately one third (71 out of 218) of the eyes. Of these, 39 eyes tested positive for either Rubella or CMV infections. Salt and pepper retinopathy was present in 10 patients (9.1%). All the patients with salt and pepper retinopathy were later diagnosed to have congenital rubella syndrome after TORCH screening. B-scan ultrasonography revealed few positive findings in the form of Persistent hyperplastic primary vitreous (3.6%), retinal detachment (1.8%), disc excavation (0.9%), choroidal coloboma (0.9%), and vitreous haemorrhage (0.9%).

Eighteen patients (16.5%) had congenital heart disease (CHD), and patent ductus arteriosus (PDA) was the most common CHD in the study patients (13 patients). Few patients with PDA also had other heart defects like ventricular septal defect (VSD), atrial septal defect (ASD), pulmonary stenosis (PS), tricuspid regurgitation (TR), and coarctation of the aorta (CoA). Other isolated heart defects noted were patent foramen ovale, ASD, and pulmonary stenosis. Of the 18 patients with CHD, 16 patients were positive for TORCH infections (13 Rubella, 3 CMV). Fig. 3 describes the systemic conditions present in these patients.

Discussion

This study showed that congenital TORCH infections were the leading cause (33%) for congenital cataracts while in one-fourth

of patients the cause could not be determined. Intrauterine infections were found to be present in 25% of patients in a study by Vijayalakshmi *et al.*,^[10] while it was as low as 3% in the Danish study.^[11] As per the studies carried out across the globe, in the majority of cases, the cause remains undetermined. In both Indian and western studies, the number of idiopathic cases

range from 46-63%.^[10-12] In our study, the percentage is 25%. This reduction maybe due to the fact that the earlier studies were carried out almost two decades ago when the diagnostic modalities and investigations available to detect underlying etiology were limited.

Table 4: Etiology of the patients with congenital cataract

Etiology	Number of patients
Hereditary	
Autosomal dominant	13 (11.9%)
Autosomal recessive	7 (6.4%)
Total	20 (18.3%)
TORCH	
Confirmed Congenital rubella syndrome	14 (12.8%)
Probable Congenital rubella syndrome	4 (3.6%)
Congenital Cytomegalovirus	7 (6.4%)
Possible Cytomegalovirus	10 (9.1%)
Neonatal Herpes simplex virus	2 (1.8%)
Total	37 (33.4%)
Metabolic	
Neonatal hypoglycemia	2 (1.8%)
Hypercalcemia	1 (0.9%)
Galactosemia	1 (0.9%)
Total	4 (3.6%)
Trauma	19 (0.9%)
Developmental	
Posterior lenticonus	5 (4.5%)
Persistent hyperplastic primary vitreous	4 (3.6%)
Anterior segment dysgenesis	2 (1.8%)
Total	11 (10.1%)
Others	
Retinopathy of prematurity	2 (1.8%)
Pierre Robin syndrome	1 (0.9%)
Coats disease	1 (0.9%)
Smith-Lemli-Opitz syndrome	1 (0.9%)
Lowe syndrome	1 (0.9%)
Warburg micro-syndrome	1 (0.9%)
Cri-du-chat with muscular dystrophy	1 (0.9%)
Down syndrome	1 (0.9%)
Total	9 (8.1%)
Idiopathic	27 (24.7%)
Total	109

India has implemented the Universal immunization programme (UIP) in 1985,^[13] however, Rubella vaccine fails to find a place in the mandatory immunization schedule but it can be taken as an optional vaccination in two divided doses in combination with measles and mumps as a part of the MMR vaccine.^[13] The total number of patients positive for rubella was quite significant (17%) in our study. Congenital rubella syndrome can result not only in cataracts but is also associated with systemic comorbidities such as congenital heart disease and sensorineural hearing deficit highlighting the role of mandatory vaccination against it and the importance of public awareness. In our study, out of the 18 patients with rubella, 13 had congenital heart diseases. As per one of the studies conducted in the United States, one-half of the patients of CRS are associated with congenital heart diseases.^[7]

Apart from Rubella, the second most common organism associated with congenital cataract reported in our study was Cytomegalovirus (16%). Hence, it becomes mandatory to screen all TORCH positive patients for the presence of deafness, petechial haemorrhages, jaundice, microcephaly, and other systemic abnormalities associated with CMV infections.^[8] Ante-natal history of fever and rash especially in the first trimester, when organogenesis takes place, should be elicited in all mothers of infants with congenital cataracts. The majority of the TORCH infections were reported in patients with a lower socio-economic status. The community has to be made aware of the importance of healthy and clean environment through awareness programmes.

Less than one-fifth of the patients had hereditary cataract (18%). This is similar to other studies in which the hereditary cases ranged from 12-23%.^[10-12] All the siblings and parents of the patients with hereditary cataracts have to be screened by a dilated slit-lamp examination to look for lenticular opacities. Genetic counselling aids in providing information to parents regarding the risk of cataracts in subsequent pregnancies.

All the patients where etiology cannot be determined should be subjected to blood testing such as complete blood examination, serum calcium and phosphorus, blood sugar levels, and urine for reducing sugars. In our study one patient tested positive for reducing sugars in urine and was later diagnosed to have galactosemia. Two patients had neonatal hypoglycaemia and one patient was found to have high levels of serum calcium.

There are very few studies on the epidemiology of congenital cataract and most of these studies are from

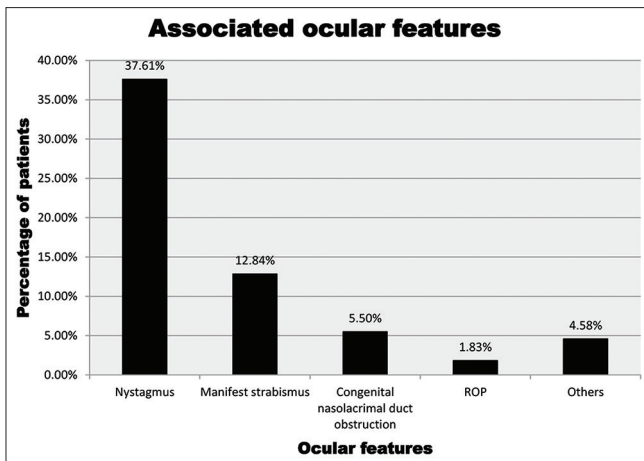


Figure 2: Bar diagram showing associated ocular features in patients with congenital cataract

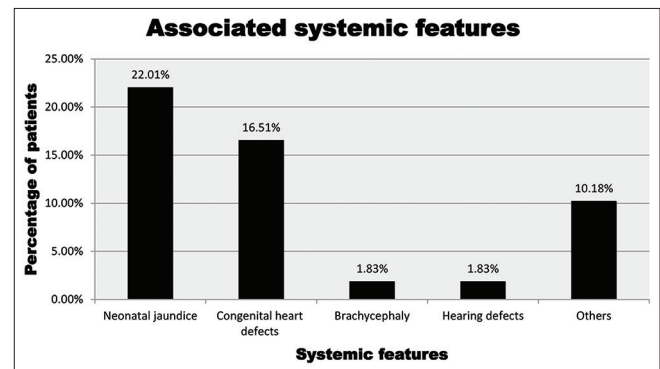


Figure 3: Bar diagram showing associated systemic features in patients with congenital cataract

developed countries.^[3-4,6,10-12,14-22] The magnitude of the problem and the importance of early intervention to restore normal binocular vision mandates public awareness of the necessity. Ours is a society, where gender bias has always been rampant and the girl child has been ignored for her medical conditions and denied the necessary medical care. The fact that no gender predilection was noted in this study is a good sign that we as a society are moving towards eliminating gender bias. The male to female ratio in our study was 1:1 while it was 3:2 in a study conducted by Vijayalakshmi *et al.*^[10] in 1996.

Nuclear and total cataracts were found most commonly in our study. It is important to do B-scan ultrasonography especially in patients with dense nuclear cataracts and total cataracts as they obscure the view of the fundus. Such patients at times might harbour retinal pathologies like retinal detachment, retinoblastoma, or persistent fetal vasculature and therefore it is, imperative to make B-scan as a mandatory screening protocol in all such patients to avoid intra-operative or post-operative surprises.

Six (6%) patients were reported to have congenital nasolacrimal duct obstruction in this study. The lacrimal sac area should be carefully examined for any swelling or fistula and regurgitation of clear or mucoid fluid from the punctum on compression. The tear film height should be checked and fluorescein dye disappearance test should be done in patients with suspicion.

Previous studies show that congenital cataract can be a part of a generalized syndrome and systemic associations can be present in 6-7% of the patients.^[3-4,6,10-12,14-21] Hence a detailed physical and general evaluation is mandatory. Should any doubt arise, the patient should be referred to a paediatrician to rule out any systemic abnormalities. We came across six (4.8%) such syndromic patients in our study. These were Pierre Robin syndrome, Smith-Lemli-Opitz syndrome, Down syndrome, Lowe syndrome, muscular dystrophy with cri du chat syndrome, and Warburg syndrome.

Every seventh patient was found to be associated with congenital heart disease. Almost all of them were associated with TORCH infections. We recommend that all patients of TORCH infections should undergo further assessment by a paediatrician and a cardiologist to rule out underlying heart disorders. As ophthalmologists, we may be the first point of contact for these families and would be doing them a great service by looking for systemic anomalies and appropriately referring them to a paediatrician or a cardiologist.

There are a few limitations to the study. Firstly, the genetic analysis could not be done in patients where the cause was undetermined. Although we referred our patients to a genetic counsellor, parents were unwilling to undergo genetic testing due to the costs involved. Secondly, patients with hereditary and developmental cataracts were not subjected to the TORCH profile. Testing the entire cohort could have possibly given higher number of TORCH positive patients. The number of patients with idiopathic cataracts remains high. Prevention strategies have to be planned with the help of available data on etiology. Management of these patients is a challenge, and it requires a dedicated team effort by the parents, paediatricians, ophthalmologists, and community health workers.

Conclusion

In one year of the study period, a total of 129 patients under the age of 12 months were diagnosed to have a congenital cataract and 109 (84%) of these patients underwent surgical management. Most (78%) of the patients diagnosed with familial cataract and TORCH infections presented with bilateral cataracts. 17% of patients had congenital heart defects and the majority (89%) of these tested positive for TORCH Infections.

Both total and nuclear cataracts were the predominant morphology (43%). TORCH infections were responsible for the maximum (33%) number of cases followed by familial cataracts and developmental anomalies. The total number of cases with unknown etiology was noted to be 24%. Our study highlights the important role of vaccination and public awareness to counter this crucial problem.

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Conflicts of interest

There are no conflicts of interest.

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E Supplementary Table 1: Questionnaire for history taking

Standardized questionnaire for history:

Presenting complaints

Age of presentation

Onset, duration and course of the presenting complaints

Birth history (Vaginal delivery or cesarean section, full term or pre-term, birth weight, history of incubation, history of jaundice, any other significant birth history)

General health, growth and developmental history

Immunization history

History of any exposure (treatments - medical or surgical, trauma, radiation, etc.) to both mother and the child

Maternal drug or infection history

History of any associated ocular or systemic feature.

Any significant family history (Pedigree charting)

E Supplementary Table 2: Congenital rubella syndrome (CRS) as per the definition given by the Centers for Disease Control and Prevention, 2015

Congenital rubella syndrome (CRS) was diagnosed as per the definition given by the Centers for Disease Control and Prevention, 2015.

Clinical case definition

An illness, usually manifesting in infancy, resulting from rubella infection in utero and characterized by clinical findings from the following categories

- a. Category A: Cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, pigmentary retinopathy
- b. Category B: Purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease

Laboratory criteria (any one of the following)

- a. Isolation of rubella
 - b. Demonstration of rubella-specific immunoglobulin M (IgM)
 - c. Infant rubella antibody level (immunoglobulin G, IgG) that persists at a higher level and for a longer time than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a twofold dilution per month)
-

Classification	Criteria
Suspected CRS	An infant that does not meet the criteria for a probable or confirmed case but has one of more of the above clinical findings
Probable	An infant without an alternative etiology that does not have laboratory confirmation of rubella infection but has either: At least two clinical findings from category A above, or One finding from category A and one or more from category B
Confirmed	An infant with at least one of the above clinical findings that is clinically consistent with congenital rubella syndrome; and laboratory evidence of congenital rubella infection as demonstrated by any of the above laboratory criteria
Infection only	An infant without any clinical symptoms or signs but with laboratory evidence of infection as demonstrated by any of the above laboratory criteria

E Supplementary Table 3: Congenital Cytomegalovirus infection as per the definition given by the Centers for Disease Control and Prevention, 2015

Confirmed congenital CMV:

IgM CMV antibody positive

High titres of IgG CMV antibody - Although IgG beyond 3 weeks suggest passive transfer from mother. This usually starts decreasing from 3 months of age and completely disappears anywhere between 6 months to 12 months. High titres which are not decreasing beyond 3 months and are high for that respective age are considered to be significant.

Presence of 3 or more clinical signs of CMV:

Petechiae

Jaundice at birth

Hepatosplenomegaly

Short for age

Microcephaly

Sensorineural hearing loss

Hypotony

Failure to thrive

Seizures

Pneumonia

MRI findings: Periventricular calcifications, Periventricular leukomalacia, Ventriculomegaly, Polymicrogyria

Possible case of congenital CMV:

One or more signs of congenital CMV

Other causes have been excluded

High titres of CMV IgG after 3 weeks of life

E Supplementary Table 4: Neonatal Herpes simplex virus infection as per the definition given by the Centers for Disease Control and Prevention, 2015

Neonatal HSV was diagnosed on basis of positive IgM HSV antibody or HSV PCR positive.
