Characteristics and outcomes of infants with cytomegalovirus infection in Bloemfontein

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Background. Cytomegalovirus (CMV) infection may significantly contribute to morbidity and mortality in infancy.
Objectives. To describe the outcomes and characteristics of CMV-infected infants in an HIV-prevalent population.
Methods. A retrospective, descriptive study was conducted by reviewing hospital records of infants who had a positive CMV test and were admitted to the academic hospitals in Bloemfontein.
Results. Inpatient mortality for CMV-infected infants was 13.3% (*n*=18/135). Of those, 66.6% (12/18) of patients who died were HIV exposed and 33.3% (6/18) had CMV/HIV co-infection. The most common causes of death were sepsis (38.9%), pneumonia/pneumonitis (33.3%) and multi-organ failure (11.2%). Approximately 60.7% (82/135) of all CMV-positive infants were HIV exposed, while 20.7% (28/135) were HIV infected. More than half (55.6%) of the patients had a birth weight <2.5 kg, while 48.7% were preterm. A third (33.3%) of the patients were small for gestational age at birth, with suboptimal postnatal growth in 62.2%. Microcephaly was present at birth in 25.2%. Poor brain growth led to postnatal microcephaly in 46.6% of patients. The most common clinical presentations were CMV pneumonia/pneumonitis (60%) and hepatomegaly (50.4%). Thrombocytopenia was a common finding (41.5%). Half (50%) of the infants who died were not treated with antiviral medication.
Conclusion. CMV infection in infancy is under-appreciated in South Africa. It may contribute to morbidity and mortality, particularly in preterm and low birth weight infants and HIV-exposed or infected infants. Clinicians should have a high index of suspicion for CMV infection in infants who have postnatal growth failure and postnatal microcephaly.

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Cytomegalovirus (CMV) is a double-stranded DNA virus that forms part of the *Herpesviridae* family.[1] CMV can be transmitted in saliva, blood, secretions, urine and breast milk.[1] Infection in infants can be congenital or postnatally acquired, but the impact on morbidity and mortality in African children is under-appreciated owing to a lack of research.[2,3] Congenital CMV, generally defined as a positive nucleic acid amplification test (NAAT) before three weeks of life, has an overall mortality rate of 4 - 8% in developed countries.[3,4] Premature and very low birth weight (VLBW) infants with symptomatic infections are at higher risk of dying (8 - 10%).[5] In severe fulminant disease, mortality can be as high as 30%.[4] Postnatally acquired CMV has less clinical significance.[6] Early postnatal infection can be transmitted from maternal secretions, ingestion of breast milk or blood product transfusions.[7] Postnatal infections in term infants are typically asymptomatic or cause a mild illness. In preterm and VLBW infants, CMV can cause clinical manifestations.[8] Furthermore, immunocompromised infants with CMV can present with end-organ involvement including pneumonitis, hepatitis and myocarditis.[4] An Indian study that reviewed age-related seroprevalence reported a 92% prevalence of CMV among infants.[9]

Previous South African studies demonstrated that neonates with congenital CMV are more likely to die, particularly if they are HIV-exposed or infected.[5] A Kenyan study showed that antepartum detection of maternal CMV DNA was associated with a four-fold mortality increase in HIV-infected infants.[10] Antiretroviral treatment (ART) was not readily accessible when these studies were performed. Transplacental CMV transmission is more frequent in younger, primigravid women and later in gestation.[2] Infants with congenital or postnatally acquired HIV infection are more likely to acquire CMV than their HIV-exposed uninfected counterparts.[5] Detection of CMV DNA in breast milk is associated with postnatal acquisition of CMV in VLBW infants.[11] CMV seronegative or leucodepleted blood products minimise the risk for transfusion-related CMV infection, with a residual risk of 1 - 3%.[11]

Congenital CMV can present with petechiae due to thrombocytopenia, conjugated hyperbilirubinemia, hepatomegaly, splenomegaly, intra-uterine growth restriction (IUGR) and microcephaly. Sensorineural hearing loss is the most common sequela of congenital CMV, affecting 33 - 50% of symptomatic infants and ~25% of asymptomatic infants.[4] Lymphadenopathy, hepatitis with transaminitis and pneumonitis may occur with perinatal infection,[4] while CMV-associated colitis can develop during the neonatal period.[12] Transfusion-related CMV viraemia typically presents 20 - 60 days after fever and malaise.[4] Morbidity may also include vision loss due to chorioretinitis and non-hereditary sensorineural hearing loss.[13]

Congenital CMV is diagnosed by molecular detection of CMV present in urine or saliva within the first 3 weeks of birth.[1] The sensitivity for PCR (urine and saliva) ranges from 97.4 - 100%, with a specificity of 99.9%.[4] Urine PCR is preferred as saliva may have a high false negative rate due to sampling error.[4] Conversely, saliva PCR can be falsely positive in breastfeeding infants, if the mother is CMV-positive.[4] To minimise false positives, saliva PCR should be done 2 hours after breastfeeding.[1] If urine PCR is unavailable, saliva PCR is recommended.[1]

There is limited literature on the use of blood CMV PCR and CMV viral load (CMVVL) for diagnosing congenital CMV.[4] These tests have sub-optimal sensitivity and are not advised for screening.[6] CMVVL is instead used to monitor infants during therapy.[14] Serology tests are also not recommended for diagnosing congenital or postnatally acquired CMV owing to low sensitivity.[4] CMV serology can remain positive for protracted periods and cannot differentiate between primary and secondary disease.[1] The presence of CMV immunoglobulin G (IgG) in neonates indicates placental transfer of maternal antibodies, while its absence suggests infection is unlikely.[4] A Japanese study showed that CMV IgM at birth had a 96.4% positive predictive value, which may be useful in resource-constrained settings where alternative tests are unavailable.[15]

Perinatal CMV testing is not routinely performed on all South African neonates[16] and is typically done if congenital infection is suspected. During the study period, urine and saliva CMV PCR were not available at the study institute, and the unit policy was to use CMV blood PCR, CMVVL or serology.

Neuroimaging may reveal significant brain abnormalities that predict adverse neurodevelopmental outcomes.[17] Current recommendations support antiviral treatment for infants with central nervous system (CNS) involvement, life-threatening infections, severe single-organ disease or multiple-organ involvement.[6,14] Treatment with ganciclovir or valganciclovir for 6 months is suggested.[1]

Methods

A retrospective, descriptive, cross-sectional study was performed. The study population included all infants with a positive CMV test (either CMV IgM, CMV blood PCR or detectable CMVVL) admitted to Universitas Academic and Pelonomi Tertiary Hospital Complex in Bloemfontein, South Africa (SA), from 01 January 2017 to 31 December 2019. Patients were identified through the National Health Laboratory Service (NHLS) database, and hospital records were obtained for data extraction. Patient outcomes were captured to determine the inpatient mortality, causes of death and morbidity. Demographic data included maternal and infant characteristics, birth parameters and postnatal growth. Information was collected on potential risk factors for CMV infection, such as HIV exposure or co-infection, along with clinical and biochemical features of infant CMV infection and related complications. Details regarding CMV testing and antiviral management were also recorded. The study was approved by the Health Sciences Research Ethics Committee of the University of the Free State, the Free State Department of Health and the NHLS (ref. no. UFS-HSD2020/0097/3006). Statistical analysis was done by the Department of Biostatistics at the University of the Free State.

Results

During the 3-year study period, 156 infants tested positive for CMV. Fifteen patients were duplicated owing to changes in names or hospital numbers, and six additional patients were excluded for the following reasons: four were outpatients, one transferred to a private hospital and one had undergone a liver transplant and was on valganciclovir prophylaxis. Therefore, 135 patients were included in the final data analysis. The median age of the patients was 75 days. Of these, 94.1% (*n*=127/135) tested positive after 3 weeks of age and were likely congenital CMV cases based on the clinical and biochemical features, while 5.9% (*n*=8/135) were classified as true congenital CMV, having tested positive within 3 weeks of birth.

Mortality and causes of death

The inpatient mortality rate for CMV-infected infants was 13.3% (*n*=18/135). The most common causes of death were sepsis (38.9%), pneumonia/pneumonitis (33.3%) and multi-organ failure (11%). Less common causes were liver failure (5.6%), colitis (5.6%) and severe gastro-oesophageal reflux (5.6%). Among the infants who died, 66.7% (*n*=12/18) were HIV exposed and 33.3% (*n*=6/18) had CMV/HIV co-infection.

Maternal characteristics of infants with CMV infection

Owing to the study design, maternal risk factors for infant CMV infection could not be calculated. However, 60.7% of the mothers were HIV-positive during pregnancy. Among these, 90.2% received ART, 4.9% had not yet initiated treatment and 4.9% had defaulted. HIV viral loads (HIVVL) were available for all but three mothers. Of the HIV-positive mothers, 53.7% had an HIVVL lower than detectable levels (<1 000 copies/mL), while 42.7% had an HIVVL >1 000 copies/mL. Virological failure in women exceeding 12 weeks of ART was documented in 18.6%. Further maternal characteristics are detailed in Table 1.

Infant characteristics

Among CMV-infected infants, 54.8% were born prematurely and 55.5% had a birthweight <2.5 kg. IUGR was noted in 33.3% of CMV-infected infants. Postnatal growth was suboptimal in 62.2%, with 25.2% being underweight and 37% experiencing failure to thrive. Microcephaly was present at birth in 25.2%, but poor brain growth increased the frequency of postnatal microcephaly to 46.6%. HIV co-infection occurred in 28 infants (20.9%). During admission, blood products were administered to half of the patients, with 66.2% receiving packed red blood cells (PCs) and 26.5% receiving both PCs and platelets. Further infant characteristics are detailed in Table 2.

Clinical characteristics and laboratory parameters

Infants mostly presented with signs of pneumonia/pneumonitis (60%). Hepatomegaly was noted in half of the patients, but only 20.7% had transaminitis and 23.7% had conjugated hyperbilirubinemia. Thrombocytopenia was present in 41.5% (*n*=56/135) of patients, with 39.3% (*n*=22/56) experiencing severe thrombocytopenia. Further clinical characteristics are detailed in Table 3.

Special investigations

Cranial ultrasound examinations were performed on 54.8% (*n*=74/135) of patients, with 36.5% (*n*=27/74) showing normal results. The imaging revealed haemorrhage, periventricular calcifications and cystic lesions. Only 6.6% of patients underwent MRI and 2% underwent CT brain imaging. Hearing screening results were documented for 17.7% of patients, with hearing loss confirmed in 41.7% of those screened. Otoacoustic emission (OAE) tests were the most commonly performed (62.5%). Regarding ophthalmology screening, 11.1% (7/63) of screened infants had vision loss. Developmental assessments were documented for 43.7% of cases, with 74.6% of evaluated infants showing delayed milestones. Further details of special investigations are provided in Table 3.

Management of CMV

A significant CMVVL (>3 000 copies/mL) was documented in 61.6% of cases, with a median CMVVL of 7 394 copies/mL. Diagnosis was based on a positive CMV IgM test in 17% (*n*=23/135) of patients. Antiviral treatment was administered to 52.6% (*n*=71/135) of infants, with 54.9% (*n*=39/71) receiving both ganciclovir and valganciclovir. Most treated patients received 4 weeks or less of treatment (49.3%). Post hoc analysis showed that infants not treated for CMV infection were more likely to experience developmental

Table 1. Maternal characteristics

Characteristics	*n* (%)
Maternal age, years	
<20	15 (11.1)
20 - 29	64 (47.4)
30 - 34	25 (18.5)
35 - 39	8 (5.9)
≥40	2 (1.5)
Unknown	21 (15.6)
Gravidity	
Primigravid	27 (20.0)
G2	54 (40.0)
G3	28 (20.7)
G4	8 (5.9)
>G4	5 (3.7)
Unknown	13 (9.7)
Delivery method	
Vaginal	82 (60.3)
Caesarean section	45 (33.3)
Unknown	8 (6.0)
HIV status during pregnancy	
Positive	82 (60.7)
Negative	53 (39.3)
HIV viral load in positive patients	
Lower than detectable/ ≤1 000 copies/mL	44 (53.7)
>1 000 copies/mL	35 (42.7)
Unknown	3 (3.6)
CD4 count in HIV-positive mothers (cells/mm^3)	
<200	24 (29.3)
>200	32 (39.0)
Unknown	26 (31.7)
Received HIV treatment during pregnancy	
Yes	74 (90.2)
No	8 (9.8)
Duration of HIV treatment	
Never initiated treatment	4 (4.9)
≤12 weeks of treatment (high risk of vertical transmission)	17 (20.4)
>12 weeks of treatment (low risk of vertical transmission)	42 (51.2)
>12 weeks of treatment (virological failure/poor adherence)	15 (18.6)
Defaulted treatment	4 (4.9)

G = gravida (2,3,4).

delay, with this association being significant according to the χ^2 test (p=0.0067). Further details of management are provided in Table 4.

Discussion

There are limited studies on infant mortality due to CMV infection, particularly among premature infants who were HIV-exposed or HIV infected. Our study findings suggest that CMV infection in infants may contribute to mortality and morbidity, with an inpatient mortality rate of 13.3%. This was high compared with other countries. Studies in high-income countries have reported a low overall mortality of congenital CMV, ranging from 5 to 10%.[18] Some studies suggest that in cases of severe fulminant disease, the mortality rate can reach as high as 30%.[4] Additionally, congenital symptomatic CMV has a mortality rate of 10% during the neonatal period.[14]

Of the 18 patients who died, 12 were HIV-exposed, while six had CMV/HIV co-infection. A previous SA study showed that neonates with congenital CMV were more likely to die than CMV-negative neonates (42% v. 18%, p=0.01), especially if they were HIV exposed (47% v. 15%, p=0.02) or HIV infected (62% v. 11%, p=0.02).[5] Another study examined the impact of CMV/HIV co-infection in infancy and found that CMV infection contributed to the progression of HIV disease and increased mortality, especially when both infections were acquired during infancy.[19] That study highlighted CMV as a significant pathogen independently associated with poor outcomes in individuals with HIV. However, that research was conducted in 1999, an era when ART was not accessible to maternal and infant populations.[19] In the current study, 60.7% of mothers were HIV positive before or during pregnancy, with 90.2% receiving ART, indicating the effectiveness of prevention of mother-to-child transmission (PMTCT) programmes. Despite this, high HIVVLs (42.7%) were observed during pregnancy, and documented virological failure after 12 weeks of treatment was significant (18.6%). An observational SA study hypothesised that ART efficacy might be compromised by physiological changes during pregnancy, such as increased blood volume and body mass index, as well as altered drug metabolism. While these physiological changes could explain the high HIVVL during pregnancy, social determinants negatively impacting adherence to drug regimens should also be considered.[20]

Although a study conducted in the Eastern Cape, SA, did not find a higher prevalence of CMV infection in HIV-exposed compared with unexposed infants, the literature suggests possible associations between maternal HIV and congenital CMV, particularly when the maternal CD4 count is <200 cells/μL.[21] A lower maternal CD4 count has also been shown to correlate with a higher CMVVL in the infant.[22] In our study, 29.3% of women had an antepartum CD4 count <200 cells/μL and 20.7% of infants had HIV/CMV co-infection. Exclusive breastfeeding rates were high, with 84.4% continuing beyond 1 month. The literature suggests that any detectable CMV DNA in maternal breast milk has a risk for postnatal infection, especially in preterm infants.[7] Despite this, the American Academy of Paediatrics still supports breastfeeding, even in preterm infants, as the benefits generally outweigh the risks. Pasteurisation of expressed breast milk may help minimise risks in preterm infants.[23]

In the current study, a history of prematurity and low birth weight was prevalent, with IUGR noted in 33.3% of patients. Poor postnatal growth was observed in 62.2% of infants. Documented microcephaly was present in 25.2%, while poor brain growth increased the incidence of postnatal microcephaly to 46.6%. These findings align with those from other studies that reported a 36 - 53% incidence of microcephaly.[24] Jaundice was noted in 26.6%, which is slightly lower than the 38 - 67% reported in another study.[4] Hepatomegaly was present in 50.4% of patients, and splenomegaly in 22.2%, consistent with another study that found hepatosplenomegaly in 39 - 60% of cases.[6] CMV hepatitis with transaminitis and conjugated hyperbilirubinemia was less common in this study compared with literature reports (21 - 24% v. 50 - 83%).[4] Thrombocytopenia, commonly described in patients with CMV (48 - 77%),[4] was present in 41.5% of infants in this study, with 39.3% experiencing severe thrombocytopenia. Colitis was suspected in 11.9% of patients, though it was not histologically confirmed as surgical intervention was not indicated in all cases. CMV enterocolitis is not well documented in the literature, indicating a need for a heightened index of suspicion and efforts to confirm the diagnosis.[12]

Table 2. Infant characteristics and laboratory parameters

Characteristics	*n* (%)
Sex	
Male	74 (54.8)
Female	61 (45.2)
Gestational age	
Preterm	74 (54.8)
Term	60 (44.4)
Unknown	1 (0.8)
HIV status	
HIV exposed	82 (60.7)
HIV unexposed	53 (39.3)
HIV infected	28 (20.7)
HIV uninfected	107 (79.3)
Weight category	
<1 kg	13 (9.6)
1 - 1.499 kg	25 (18.5)
1.5 - 2.499 kg	37 (27.4)
≥2.5 kg	60 (44.5)
Type of feeding	
Exclusive breastfeeding	125 (92.6)
Exclusive formula feeding	1 (0.7)
Mixed feeding	9 (6.7)
Duration of breastfeeding	
≤1 month	7 (5.2)
>1 month	114 (84.4)
Unknown	14 (10.4)
Fetal growth	
Small for gestational age (symmetrical)	15 (11.1)
Small for gestational age (asymmetrical)	30 (22.2)
Appropriate for gestational age	81 (60.0)
Large for gestational age	4 (2.9)
Unknown	5 (3.8)
Head circumference at birth	
Microcephaly	34 (25.2)
Normal	90 (66.7)
Macrocephaly	3 (2.2)
Unknown	8 (5.9)
Length at birth	
<10th centile	23 (17.0)
10th - 90th centile	103 (76.3)
>90th centile	0
Unknown	9 (6.7)
Postnatal growth	
Underweight	34 (25.2)
Normal	45 (33.3)
Overweight	1 (0.7)
Failure to thrive	50 (37.0)
Not applicable	2 (1.5)
Unknown	3 (2.3)
	(continued)

Table 2.(continued) Infant characteristics and laboratory parameters

Characteristics	*n* (%)
Head circumference growth	
Microcephaly	63 (46.6)
Normal	61 (45.2)
Macrocephaly	2 (1.5)
Not applicable	2 (1.5)
Unknown	7 (5.2)
Received blood products	
Yes	68 (50.3)
No	67 (49.7)
Blood products received	
Packed red blood cells	45 (66.2)
Platelets and packed cells	18 (26.5)
Unknown	5 (7.3)
Number of transfusions	
1	16 (23.5)
2 - 5	43 (63.2)
5 - 10	5 (7.4)
>10	0 (0.0)
Unknown	4 (5.9)
Presence of clinical characteristics	
Petechiae	12 (8.8)
Jaundice	36 (26.6)
Hepatomegaly	68 (50.4)
Splenomegaly	30 (22.2)
Colitis	16 (11.9)
Pneumonitis	81 (60.0)
Lethargy	15 (11.0)
Hypotonia	11 (8.1)
Poor neonatal sucking reflex	17 (13.0)
Convulsions	6 (4.4)
Fever	20 (14.8)
Lymphadenopathy	14 (10.4)
Laboratory characteristics	
Hepatitis	28 (20.7)
Elevated liver enzymes	28 (20.7)
Elevated direct bilirubin	32 (23.7)
Elevated indirect bilirubin	32 (23.7)
Thrombocytopenia	56 (41.5)
Severity of thrombocytopenia (x109/L)	
Mild (100 - 150)	11 (19.6)
Moderate (50 - 100)	23 (41.1)
Severe (<50)	22 (39.3)

Exposure to blood products was common during admission. Neonates received leucodepleted packed cells as standard of care, but details on the type of packed cells administered to older infants were not provided. Clinical presentations of CMV seroconversion post-transfusion, such as fever, lymphadenopathy and malaise, were well documented in 14.8%, 10.4% and 8.1% of post-transfusion cases, respectively.

Central nervous system involvement significantly impacts morbidity and mortality.[25] MRI and CT brain scans were performed in only 6.6% and 2% of cases, respectively, likely owing to resource limitations. Cranial ultrasound was performed in 55% of patients, with 63.5% showing abnormal findings. Periventricular calcifications were noted in 16.2% of those scanned. Neurosensory hearing deficits were identified in 10 patients, but hearing screens were documented in only 18% of patients.

During the study period, CMVVL or serum IgM was routinely performed to confirm CMV infection in infants at the study

Table 3. Special investigations

Characteristics	*n* (%)
Cranial ultrasound performed	74 (54.8)
Cranial ultrasound findings	
Normal	27 (36.5)
Periventricular calcifications	12 (16.2)
Periventricular cysts	5 (6.6)
Multi-cystic lesions	2 (2.7)
Interventricular haemorrhage	19 (25.7)
Periventricular calcifications and cysts	1 (1.4)
Hydrocephalus and periventricular cysts	2 (2.7)
Periventricular leukomalacia	1 (1.4)
Hydrocephalus	2 (2.7)
Periventricular flaring	1 (1.4)
Ventriculitis	2 (2.7)
MRI brain performed	5 (6.6)
MRI brain findings	
Normal scan	3 (60.0)
Periventricular cysts	1 (20.0)
Poor myelination	1 (20.0)
CT brain performed	3 (2.0)
CT brain findings	
Normal	2 (66.6)
Ventriculomegaly	1 (33.3)
Hearing screen done	24 (17.7)
Hearing loss diagnosed	10 (41.7)
Type of hearing screen	
OAE	15 (62.5)
BERA	8 (33.3)
Unknown	1 (4.2)
Ophthalmology screen done	63 (46.6)
Vision loss diagnosed	7 (11.1)
Developmental assessment	59 (43.7)
Delayed milestones in assessment	44 (74.6)

CT = computed tomography; OAE = otoacoustic emission; BERA = brainstem evoked response audiometry.

Table 4. Management of cytomegalovirus

Characteristics	*n* (%)
Viral load at diagnosis (copies/mL)	
200 - 3 000	43 (38.4)
>3 000	69 (61.6)
Other CMV tests done	
CMV IgM	23 (17.0)
Infants treated for CMV	71 (52.6)
Antiviral medication used in treated patients	
Ganciclovir only	28 (39.4)
Valganciclovir only	4 (5.6)
Ganciclovir and valganciclovir	39 (54.9)
Duration of treatment	
< 4 weeks	35 (49.3)
4 - 6 weeks	16 (22.5)
6 weeks - 3 months	14 (19.8)
3 months - 6 months	6 (8.4)
Viral load done at follow-up	29 (21.5)
Viral load value at follow-up (copies/mL)	
200 - 3 000	24 (82.8)
≥3 000	5 (17.2)

CMV = Cytomegalovirus; IgM = immunoglobulin M.

facilities. Although the literature suggests that blood CMV PCR and CMVVL are not ideal for screening congenital CMV, CMVVL is useful for monitoring therapy response.[4] This is because CMVVL has a higher sensitivity and specificity than serology.[14] Additionally, CMVVL is more useful in immunocompromised patients, as a high CMVVL often correlates with clinical symptoms and disease presence.[26] In this study, a significant CMVVL was noted in 61.6% of patients, and CMV IgM was positive in 22.2%.

The literature generally agrees that infants with symptomatic CMV benefit from treatment,[6] especially HIV-infected infants with severe pneumonia.[26] Some studies advocate for CMV treatment in cases of two or more end-organ involvement.[1] However, the benefit of treating postnatally acquired CMV in asymptomatic neonates, infants with asymptomatic congenital CMV, and HIV-exposed but uninfected infants with pneumonia remains unclear.[6,27] An individualised approach and discussion with a paediatric infectious disease specialist is recommended.[6] In the current study, 52.6% of patients were treated for CMV, usually with ganciclovir and transitioning to valganciclovir. Despite the expectation that critically ill infants requiring admission would receive CMV antiviral medication,[6] only half of those who were demised received such treatment. Additionally, most patients were treated for less than 4 weeks, whereas current guidelines recommend a 6-month treatment course for patients with CNS involvement, life-threatening infection, severe single-organ disease or multiple-organ involvement.[6] Infants not treated for CMV infection were more likely to have developmental delays. A post hoc analysis revealed a statistically significant association between lack of treatment and developmental delay (p=0.0067). These untreated infants likely had congenital CMV, and current guidelines suggest that such patients may benefit from antiviral treatment.

Limitations

This study used a retrospective descriptive design and focused on a selected population of hospitalised infants who tested positive for CMV. Consequently, comparisons between CMV-positive and CMV-negative patients could not be made, nor could the mortality risk among HIV-exposed or HIV-co-infected patients be assessed. The study did not include information on whether HIV-infected infants were receiving ART. Additionally, HIVVL results for infants were also not captured. During the study period (2017 - 2018), the OAE machine was out of order, which may explain the limited screening results. Data from outpatient records were also unavailable, possibly leading to underreporting of BERA tests. At the time of the study, the only available tests for congenital CMV at the study facilities were blood CMV PCR and CMVVL. These tests are not recommended for screening owing to their low sensitivity; however, their high specificity (99%) suggests that the study population likely had CMV.[14] Since patients were selected based on a positive CMV blood test, the study population is not representative of the general infant population. This selection may reflect a subset of the larger disease burden, as testing may have been prompted by severe disease.

Conclusion

CMV infection in infancy is often under-recognised in SA, and a higher index of suspicion is warranted. CMV infection contributes to morbidity and mortality in infancy, particularly in preterm and low birth weight infants. CMV/HIV co-infection is particularly concerning and can be associated with adverse outcomes. Early diagnosis of CMV infection in infants, timely special investigations and appropriate antiviral management can potentially improve prognosis.

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Data availability statement. The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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