NCMD

National Child Mortality Database

Knowledge, understanding and learning to improve young lives

Deaths of children due to neonatal Herpes Simplex Virus

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HQIP

Healthcare Quality Improvement Partnership

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We thank all Child Death Overview Panels (CDOPs) who submitted data for the purposes of this report and all child death review professionals for submitting data and providing additional information when asked.

Background

Herpes Simplex Virus (HSV) infection is a rare but serious illness in neonates. Babies can become infected in three ways[1]:

- Perinatal: through contact with HSV in the birth canal (85%)
- Postnatal: through direct exposure to active herpes infection from anyone in close contact with the baby (10%)
- Congenital: in-utero transmission (5%).

The British Paediatric Surveillance Unit (BPSU) found that the incidence of neonatal HSV infection in children younger than 90 days of age, from 2019 to 2022, has almost doubled, from 3.6 per 100,000 live births to 6.9 per 100,000 live births, when compared to the previous report for the years 2004 to 2006. Disseminated disease, lower gestational age at birth, and higher admission and peak blood alanine transaminase (ALT) concentrations were factors associated with increased mortality. The overall mortality was 24%[2].

A single tertiary centre in Nottingham, United Kingdom (UK), found an incidence of 17.5 cases per 100,000 live births, from January 2006 to December 2013, in infants up to 28 days of life[3]. 47% of infants died, most of whom presented at five to ten days of life.

The aim of this briefing is to describe the demographics and characteristics of deaths due to neonatal HSV, including clinical features, diagnosis and treatment.

Deaths of children who died due to neonatal HSV

- Between 1 April 2019 and 31 December 2024 there were 39 child deaths following confirmed HSV presenting within the first 28 days of life. 35 were of infants (children aged under 1 year).
- A third (34%, n=13/38) were born prematurely (<37 weeks' gestation).
- There were 32 (82%) deaths of children from a white ethnic background, and 7 (18%) deaths of infants from black, Asian, mixed, or other ethnic backgrounds.
- 15 (38%) of the deaths were of children living in the most deprived areas, compared to 5 (13%) in the least deprived areas.

Four children died of long-term complications years later, therefore further analysis of those cases was not possible due to limited neonatal admission information.

Deaths of infants due to neonatal HSV

Age at presentation and age at death

- Of the 35 infant deaths, the majority of infants presented between days four and ten of life (69%, n=24) with a median of 7 days. The median age at death was 11 days, and most died by day 14 of life (77%, n=27). For infants who were born at 37 weeks' gestation or later, the median time between presentation and death was 2 days.

Presentation and exposure

- Non-specific symptoms, such as apnoea, poor feeding, lethargy, respiratory distress and temperature instability, were reported in 24 (69%) deaths. 2 (6%) presented with seizures or liver dysfunction.

- For infants born below 28 weeks' gestation (n=2), both presented with skin lesions at birth. In one case, the mother had cold sores in the perinatal period.
- Very few cases specified the likely source of infection:
    - There was a history of cold sores in the parents of 4 infants.
    - In another 4 cases, the mothers either had a reactivation of genital infection or were diagnosed with HSV using virological testing.

Clinical course

- 91% (n=32) had disseminated HSV. One infant (3%) had skin, eye and mouth disease, and another 2 (6%) presented with central nervous system disease.
- 66% (n=23) died within four days, and of these, at least 17 were started on treatment within one day of presentation. All 23 had liver failure during the course of their hospital admission.
- Where information was available, 28 neonates were commenced on aciclovir at some point after presentation (median= the day of presentation), 22 of whom were commenced within the first day after presentation.

Discussion

Neonatal HSV is rare, but can be very serious and cause death or long-term neurological problems. Bacterial and fungal infections are much more common in neonates, and diagnosing neonatal HSV remains challenging.

For children who died due to neonatal HSV, most children presented between day four to ten of life and died a few days later. In those who presented with liver failure (n=23), all died within four days, despite most (74%, n=17) having commenced aciclovir within one day of presentation. Symptoms and signs at presentation were often non-specific and in keeping with late-onset sepsis.

The presence of liver failure was universal in those who died within a few days. This demonstrates that an early recognition of liver dysfunction may be crucial in the diagnosis of neonatal HSV. The UK Paediatric Antimicrobial Stewardship (UK-PAS) Guide was updated in February 2025 and recommends using liver function tests (LFTs) and clotting studies to determine the need for high-dose aciclovir. Criteria for considering the addition of high-dose aciclovir have been clearly laid out in the UK-PAS guide.

Routine testing of LFTs is not currently recommended in the NICE guidelines[4] for neonatal infection.

A history of cold sores in parents was present in at least 4 of the deaths. The high risk of neonatal infection following primary genital infection of the mother is well accepted, but rates of postnatal transmission may be underestimated. The Lullaby Trust[5] have strong messaging for 'Think Hands And No KisseS (THANKS) to prevent infections by discouraging kissing of newborn infants by those other than parents or main carers.

NICE guidelines[6] recommend that HSV infection should be discussed with all pregnant women; in particular, the risk of neonatal transmission if the first episode of genital herpes is during pregnancy, especially in the third trimester. All women with a first episode of genital herpes should also be advised to inform a healthcare professional if they are, or as soon as they become, pregnant. There should be further analysis of data collected by the BPSU and NCMD to improve understanding of the outcomes and impact of neonatal HSV.

Summary of improvements needed in clinical practice in keeping with existing guidance[4,6,7]

1. Neonatal HSV should be considered in infants presenting with features of late-onset infection (>72 hours).
2. A thorough history of herpes exposure, including cold sores in any caregiver, should be taken.
3. Local guidance should reflect recent updates regarding management of neonatal HSV in the UK-PAS Guide. This may include adding LFTs when investigating late-onset sepsis in a neonate.
4. Local units should ensure that the risks of herpes in pregnant women are shared. This education needs to be done in the antenatal period so pregnant women are empowered to share any history of symptoms.
5. Continue to raise awareness and education regarding exposure to herpes, including cold sores, in healthcare staff and expectant parents and caregivers.

Data tables

Table 1. Number of child deaths due to neonatal Herpes Simplex Virus between 1 April 2019 and 31 December 2024, by sex, ethnicity and gestational age

	N (%)
Sex (N=39)	
Male	22 (56%)
Female	17 (44%)
Ethnicity (N=39)	
White	32 (82%)
Black, Asian, Mixed or Other	7 (18%)
Gestational age (weeks) at birth (N=38)	
<28	2 (5%)
28-31	4 (11%)
32-36	7 (18%)
37+	25 (66%)

Table 2. Number of child deaths due to neonatal Herpes Simplex Virus between 1 April 2019 and 31 December 2024, by region and social deprivation (N=39)

	N (%)
Region	
East Midlands	5 (13%)
East of England	4 (10%)
London	6 (15%)
North East	1 (3%)
North West	5 (13%)
South East	4 (10%)
South West	7 (18%)
West Midlands	3 (8%)
Yorkshire and Humber	4 (10%)
Social deprivation	
1 (most deprived)	15 (38%)
2	11 (28%)
3	5 (13%)
4	3 (8%)
5 (least deprived)	5 (13%)

Table 3. Number of infant (children aged under 1 year) deaths due to neonatal Herpes Simplex Virus between 1 April 2019 and 31 December 2024, by age at presentation and death (N=35)

	N (%)
Age at presentation	
0 – 3 days	5 (14%)
4 – 10 days	24 (69%)
11 – 14 days	4 (11%)
Over 14 days	2 (6%)
Age at death	
0 – 14 days	27 (77%)
15 – 27 days	4 (11%)
28 – 364 days	4 (11%)
Median (IQR) age at presentation (days)	7 days (4 - 9)
Median (IQR) age at death (days)	11 days (9 - 14)
Median (IQR) days between presentation and death	3 days (1 - 7)
Median (IQR) days between presentation and death (babies born over 37 weeks gestation only (N=23)	2 days (1 - 7)

Table 4. Number of infant (children aged under 1 year) deaths due to neonatal Herpes Simplex Virus between 1 April 2019 and 31 December 2024, by HSV type, exposure, presentation and classification (N=35)

	N (%)
HSV type (N=31)	
HSV-1	17 (55%)
HSV-2	14 (45%)
Exposure (N=8)	
Cold sores	4 (50%)
Genital reactivation or unspecified HSV in mothers	4 (50%)
Signs and symptoms of presentation (N=35)	
Non-specific symptoms	24 (69%)
Skin lesions	6 (17%)
Shocked/critically unwell	3 (9%)
Seizures	1 (3%)
Liver dysfunction	1 (3%)
Classification (N=35)	
Disseminated HSV	32 (91%)
Central nervous system HSV	2 (6%)
Skin, eye and mouth HSV	1 (3%)

Methodology and limitations

Cohort identification

All child (0 – 17 years, inclusive) deaths between 1 April 2019 and 31 December 2024 with "HSV" or "Herpes Simplex" recorded as a cause of death in the statutory analysis form by the Child Death Overview Panel were identified, where they were notified to the National Child Mortality Database by a Child Death Overview Panel (CDOP) in England. The cases were then clinically validated retrospectively to ensure appropriate case inclusion of deaths with laboratory-confirmed HSV within the first 28 days of life, and to code information around HSV type, exposure and presentation.

Clinical information about the neonatal admission was reviewed and was available in 35 cases.

Exclusions

Cases identified where HSV was not the cause of death, and cases of older children who had contracted HSV outside the neonatal period, were excluded.

Data extraction

The data used for deaths that occurred between 1 April 2019 and 31 December 2024 within this briefing was extracted on 17 January 2025.

Limitations

This work is based on statutory data reported to NCMD, and previous work has shown good validation and coverage. However, this work relied on the completion of the cause of death within the statutory analysis form by the CDOP to identify the cases, meaning that child deaths that had not yet been reviewed by a CDOP would not be included in this work. In total, 73% of infant deaths between 1 April 2019 and 31 December 2024 had been reviewed before 17 January 2025. This means that there would be an underestimation of the total number of deaths that occurred during the time period, particularly in the later years. The identification of deaths for this work is dependent on the key words being recorded in the cause of death fields.

References

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