Evolution of swallowing and feeding abilities of neonates with hypoxic-ischaemic encephalopathy during hospitalisation: A case series

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Abstract

Purpose: To describe the evolution of swallowing and feeding abilities of neonates with hypoxic-ischaemic encephalopathy (HIE) during hospitalisation.

Method: A longitudinal cohort study was used. Twenty-nine participants (median age 39.0 weeks [IQR = 2.0 weeks]) with mild ($n = 7$), moderate ($n = 19$) and severe ($n = 3$) HIE were included. Clinical swallowing and feeding assessments were conducted at introduction of oral feeds and at discharge using the Neonatal Feeding Assessment Scale (NFAS).
Videofluoroscopic swallow studies (VFSS) supplemented the NFAS before discharge.

Result: Approximately two thirds of participants showed symptoms of oropharyngeal dysphagia (OPD) during initial NFAS and VFSS. Significantly fewer OPD symptoms occurred at discharge NFAS ($p = 0.004$). Endurance during non-nutritive sucking ($p < 0.001$) and nutritive sucking ($p < 0.001$) significantly improved. Nine participants (31.0%) demonstrated penetration or aspiration. Most aspiration events were silent (60%). Instrumental assessment identified pharyngeal phase dysphagia more effectively than bedside evaluation. High proportions of participants displayed OPD symptoms regardless of HIE severity. The correlation between OPD severity and the length of hospitalisation ($p = 0.052$) was not significant.

Conclusion: All grades of HIE should be considered for early intervention by speech-language pathologists before discharge. Findings may be valuable to neonatal feeding teams.

Keywords: hypoxic-ischaemic encephalopathy; mild, moderate and severe hypoxic-ischaemic encephalopathy; neonate; dysphagia; pediatric; swallowing

Introduction

Neonatal hypoxic-ischaemic encephalopathy (HIE) is a central nervous system disorder that occurs in approximately 1–20/1000 live births in high-income and lower- and middle-income countries (LMICs) respectively (Acun et al., 2022; Montaldo et al., 2015; Shipley et al., 2021). Not only does the condition have a profound burden of disease due to high rates of mortality and long-term neurodevelopmental disability, but it commonly also results in oropharyngeal dysphagia (OPD) among affected neonates (Arvedson et al., 2020; Ballot et al., 2020). This may be caused by disturbances of muscle tone, poor coordination of movement, impaired function of neuromuscular units, poor state regulation, and/or reduced feeding endurance (Arvedson et al., 2020; Genna et al., 2013; Krüger et al., 2017). A recent study found that 89% of neonates with HIE dis- played at least one symptom of OPD (Krüger et al., 2019). Another study reported that one-third of infants with HIE required long-term feeding tubes due to severe feeding difficulties (Martinez-Biarge et al., 2012). This proportion increased to 91% when injuries to the basal ganglia, thalamus, and pons existed (Martinez-Biarge et al., 2012).

HIE can be graded as mild, moderate, or severe (Sarnat & Sarnat, 1976; Shalak et al., 2003). The numerous health concerns associated with HIE may lead to complicated feeding profiles in affected neo- nates with all grades of the condition, prompting healthcare professionals such as speech-language path- ologists (SLPs) working with OPD to require specialist knowledge of this population (Lefton-Greif & Arvedson, 2016). Consequences of OPD may include malnutrition, aspiration, difficulties administering medication, behavioural abnormalities, reduced health status, and poor quality of life for neonates and their families (Arvedson et al., 2020; Martinez-Biarge et al., 2012). OPD also places strain on health care resources by increasing the length of hospital stay, number of emergency room visits, and increased costs of medical equipment and treatment (Dziewas et al., 2017). Evidence-based early intervention contributes to improved progression of swallowing and feeding skills and may assist in mitigating the negative effects associated with OPD (Jadcherla et al., 2017; Leder et al., 2016). However, research on OPD in both typical and high-risk infants remains limited (Arvedson et al., 2020). Some research on OPD among neonates with HIE is emerging, but studies using validated and standardised assessment tools are lacking, and gold-standard instrumental evaluations of this population are needed (Audag et al., 2017; Krüger et al., 2019). Importantly, videofluoroscopic swallow studies (VFSS) may recognise subtle symptoms of OPD, including silent aspiration, resulting in earlier management and possible prevention of associated negative consequences (Arvedson et al., 2020; Audag et al., 2017). Serial assessment of OPD is rarely found in the relevant research, even though neonates present with rapidly changing anatomical and physiological subsystems that continue to mature throughout hospitalisation (Jensen et al., 2017; Krüger et al., 2019; Lau, 2015). A deeper understanding of the evolution of swallowing and feeding among neonates with HIE, from introduction of oral feeds to discharge, may increase efficacy of speech-language pathology service delivery and may facilitate timely development of dis- charge feeding plans for this vulnerable population.

This study set out to describe the evolution of swallowing and feeding abilities of neonates with HIE during their hospital stay, using a validated and standardised assessment tool and VFSS. Specifically, the following sub-aims were developed: (1) to describe and compare the swallowing and feeding abilities of neonates at introduction of oral feeds and at dis- charge from hospital; (2) to describe the swallowing and feeding abilities of affected neonates according to HIE severity; and (3) to explore the relationship between OPD severity and the length of hospitalisation among affected neonates.

Method

Study design and setting

A longitudinal cohort study described the swallowing and feeding abilities of neonates with HIE consecutively admitted to the 29-bed neonatal unit of an urban tertiary academic hospital in South Africa during the course of their hospitalisation. The study was conducted between October 2018 and October 2020.

Ethical considerations

All preapprovals and permissions were obtained from the University of Pretoria Faculty of Health Sciences Research Ethics Committee (protocol number 380/ 2018). The study did not change any aspect of participants' routine care. Written informed consent was obtained from the legal guardian of each participant prior to the start of data collection.

Participants and recruitment

Neonates independently diagnosed with HIE by a neonatologist according to hospital protocol were recruited for the study. Eligible participants had to be born ≥ 37 weeks' gestation as confirmed by a neonatologist, using the most reliable information available. Early ultrasound is considered the most accurate method of determining gestational age; where this information was not available due to a lack of resources, sure dates or the new Ballard score were used (Lee et al., 2017). The new Ballard score estimates gestational age by examining and rating physical and neuromuscular maturity characteristics in the neonate (Ballard et al., 1991).

Neonatal encephalopathy was suspected to be secondary to an acute peri- or intrapartum event if participants presented with encephalopathy (disturbed neurological function manifested as an abnormal level of consciousness or seizures, possibly accompanied by respiratory difficulties and decreased tone and/or primitive reflexes), in addition to at least one of the following criteria: (1) APGAR scores < 5 at 5 and 10 min, or (2) evidence of foetal acidemia (arterial umbilical cord blood gas or radial artery blood gas done within 60 min of delivery with a pH < 7.0 or a base deficit 2:12 mmol/L; American Academy of Pediatrics [AAP], 2014; Shankaran et al., 2005). Encephalopathy grading was performed by a neonatologist using the modified Sarnat stages (Shalak et al., 2003). The modified Sarnat stages were scored according to six categories related to encephalopathy (Shalak et al., 2003; Shankaran et al., 2005). Each category was scored as normal, mild, moderate, or severe according to predefined signs (Shalak et al., 2003). Mild encephalopathy was defined as ≥ 1 abnormal category (Prempunpong et al., 2018). Moderate or severe encephalopathy was defined as ≥ 3 abnormal categories; the number of moderate or severe signs determined the extent of encephalopathy (Shankaran et al., 2005). If moderate and severe signs were equally distributed, the participant's staging was based upon the level of consciousness (Shankaran et al., 2005). Modified Sarnat scores were performed during the first six hours of life. If there was progression of the disease among mild participants within this time frame, the worse staging was assigned to participants to determine eligibility for therapeutic hypothermia (TH).

All participants with moderate and severe HIE received TH, as it is the standard of care for these grades of severity (Table I; Goswami et al., 2020). One participant with mild HIE inadvertently received TH; this mimics a recent therapeutic drift towards offering TH to mildly affected neonates, despite there being insufficient evidence for the use of TH in this population (Goswami et al., 2020). Depending on the avail- ability of TH equipment, high-cost devices (servo-controlled methods) or low-cost devices (cloth-covered ice packs) were offered to participants under intensive care. Low cost devices such as ice packs have proven to be plausible substitutes for servo-controlled devices, as similar outcomes have been found among neonates receiving the two treatment modalities previously (Kinoshita et al., 2021; Rossouw, 2015).

Participants were excluded if they presented with genetic syndromes or major congenital abnormalities, metabolic disease, meningitis, structural brain abnormalities, intracerebral or intraventricular hemorrhage, congenital hydrocephalus, or perinatal stroke (see Figure 1 for CONSORT flow diagram). Neonates were not excluded based on HIV exposure, due to a current lack of evidence that this affects neo- natal swallowing and feeding abilities (Krüger et al., 2019). All participants received daily oral sensory-motor intervention by the same SLP since the introduction of oral feeds.

Data collection

Once participants were deemed medically ready for introduction of oral feeds by the treating pediatrician (see Supplemental File 1 for criteria), they were referred for speech-language pathology services and assessed using the

Neonatal Feeding Assessment Scale (NFAS; Viviers, 2016) on the same day. The NFAS was re-administered on the day each participant was discharged to allow for serial assessment.

NFAS findings were supplemented with VFSS prior to discharge from hospital. VFSS could not be conducted on the same day as NFAS administration due to challenges surrounding the availability of equipment, staff shortages, and high patient loads, which commonly occur in LMICs such as South Africa (Ostrofsky & Seedat, 2016). During the VFSS, participants were positioned supine at 20° and commercially prepared non-ionic contrast solution was administered via a Tommee Tippee 260 mL 0m + bottle with standard wide-neck teat. If participants were unable to extract the solution from the teat due to sucking difficulties, it was administered via a syringe or cup. The lateral view was first used. Participants were initially screened for a series of up to 20 suck–swallow–breath cycles and were then screened intermittently during continued drinking to conduct fatigue testing (Weir et al., 2011). The anterior-posterior view was then used to assess symmetry and to scan the esophagus for bolus transit. Views were first assessed in real time, followed by frame-by- frame analysis. Total radiation time did not exceed two minutes (Arvedson, 2008). A VFSS checklist and the Penetration Aspiration Scale (PAS; Rosenbek et al., 1996) were completed by two SLPs registered with the Health Professions Council of South Africa (HPCSA), having experience in assessment and management of pediatric OPD. VFSS were independently reviewed by two radiologists also registered with the HPCSA. All professionals were blinded to participants' NFAS results and participant characteristics such as HIE severity. There was 100.0% agreement between the SLPs' and radiologists' findings.

Materials and apparatus

The NFAS assesses the following areas related to swallowing and feeding: physiological functioning; neonatal state; stress cues; motor performance; oral anatomy and primitive reflexes; and signs and symptoms of OPD (Viviers et al., 2019). It also provides a composite score that indicates whether OPD is pre- sent (Viviers et al., 2019). Preliminary investigations into the psychometric properties of the NFAS have proven that it is a valid tool for describing neonatal feeding skills and that it shows acceptable interrater reliability (Viviers et al., 2017; Viviers et al., 2019).

VFSS were conducted using the CombiDiagnost R90 remote controlled fluoroscopy system (Koninklijke Philips N.V., Netherlands). A data collection sheet based upon guidelines by Arvedson and Brodsky (2002) was used with the PAS for VFSS interpretation. The PAS was created for reliable quantification of penetration or aspiration during VFSS (Rosenbek et al., 1996).

Table 1. Participant characteristics

Participant characteristics	**Overall (*n* = 29)**	**Mild (*n* = 7)**	**Moderate (*n* = 19)**	**Severe (*n* = 3)**
Male, *n* (%)	18 (62.1)	5 (71.4)	12 (63.2)	1 (33.3)
Gestational age (weeks), median (IQR)	39.0 (2.0)	40.0 (1.5)	39.0 (2.0)	39.0 (1.5)
Birth weight (grams) median, (IQR)	3143.0 (779.0)	3300.0 (367.5)	3140.0 (796.5)	3100.0 (271.0)
Mode of delivery:				
Normal vaginal delivery, *n* (%)	11 (37.9)	2 (28.6)	7 (36.8)	2 (66.7)
Assisted delivery, *n* (%)	5 (17.2)	0 (0.0)	4 (21.1)	1 (33.3)
Caesarean section, *n* (%)	13 (44.8)	5 (71.4)	8 (42.1)	0 (0.0)
Maternal age (years), median (IQR)	28.0 (10.0)	28.0 (1.0)	27.0 (9.5)	33.0 (2.5)
Neonatal seizures[a] *n* (%)	4 (13.8)	0 (0.0)	1 (5.3)	3 (100.0)
Therapeutic hypothermia[b] *n* (%) of which:	23 (79.3)	1 (14.3)	19 (100.0)	3 (100.0)
Servo-controlled methods, *n* (%)	18 (78.3)	1 (100.0)	14 (73.7)	3 (100.0)
Frozen gel packs, *n* (%)	5 (21.7)	0 (0.0)	5 (26.3)	0 (0.0)

[a]*Participants who demonstrated seizures during hospitalisation were placed on anticonvulsant medications. The severe participants (n = 3) were discharged home on these medications. The moderate participant (n = 1) no longer required these medications by discharge.*

[b]*Core body temperature was maintained at 33.5–34.5 °C for 72 h. Thereafter, rewarming occurred at rates of 0.5 °C per hour until normal ranges of 36.5–37.5 °C were achieved.*

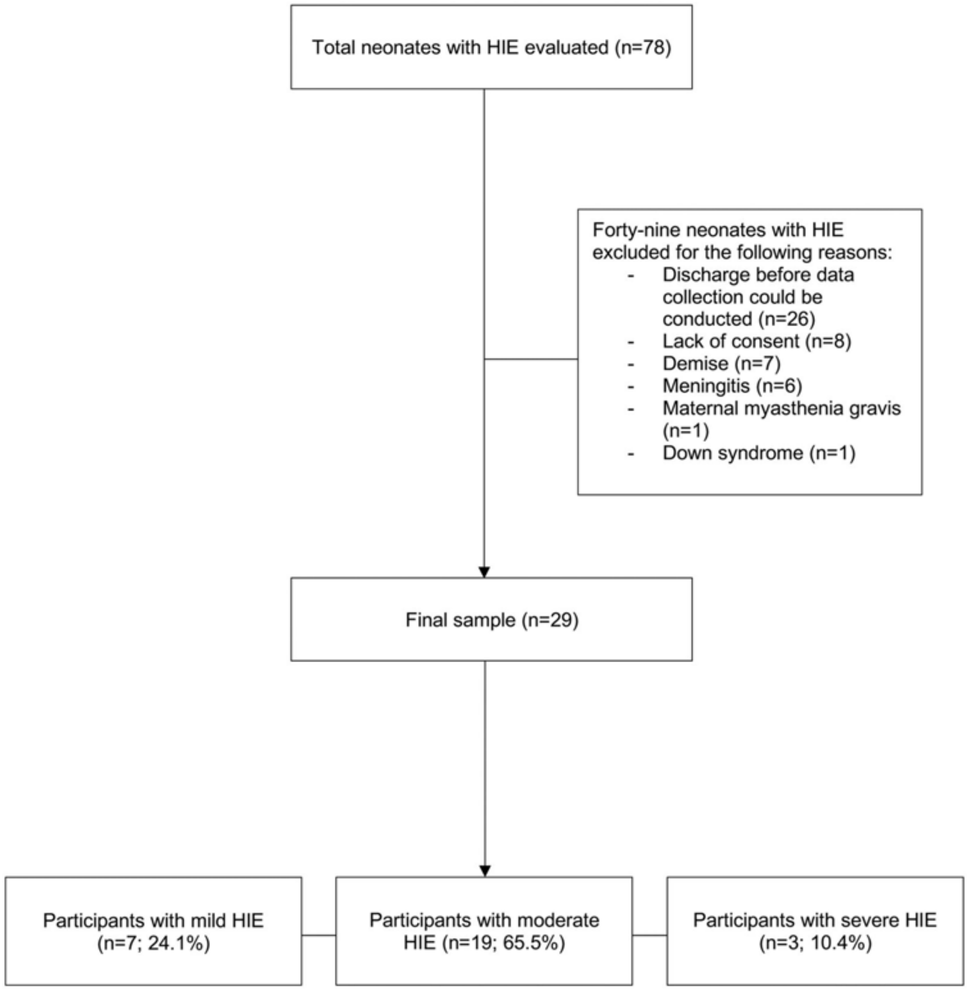

Figure 1. CONSORT flow diagram indicating the inclusion and exclusion of participants.

Data analysis

The NFAS and VFSS were both scored using a binary yes/no system. All items were scored "yes" if symptoms were present and "no" if symptoms were absent. Composite scores were obtained. In the NFAS, the composite score indicated whether OPD was present. In the VFSS, the composite score determined how many symptoms of OPD were evident, reflecting OPD severity. A PAS score was assigned to participants during VFSS, reflecting the amount of penetration or aspiration found (Rosenbek et al., 1996). A score of 1 indicated no penetration or aspiration; scores of 2–5 indicated penetration; and scores of 6–8 indicated aspiration (Rosenbek et al., 1996).

IBM Statistical Package for the Social Sciences (SPSS), Version 26.0 (IBM Corp, 2019) was used for all statistical analyses. Descriptive statistics were obtained. McNemar's test for paired nominal binary data compared participants' performance on the NFAS initially versus discharge. Nonparametric Spearman's rank-order correlations investigated correlations between the number of combined OPD symptoms and the length of hospital stay. In the study, p values less than 0.05 indicated statistical significance. However, Bonferroni adjustments were applied where variables were tightly related and adjusted levels of significance were indicated where relevant. As is appropriate when using nonparametric tests, medians and inter- quartile ranges (IQR) were reported as measures of location and spread.

Result

Twenty-nine participants were included in the study, of which 24.1% had mild HIE (n = 7), 65.5% had moderate HIE (n = 19) and 10.4% had severe HIE (n = 3). Table 1 displays participant characteristics. The median age at initial NFAS assessment and introduction of oral feeds was 5.0 days (IQR = 4.0 days; see Supplementary File 1 for more information). Most participants were assessed during breastfeeding (n = 13; 44.8%), cup feeding (n = 8; 27.6%), or breastfeeding supplemented with cup (n = 7; 24.1%). Bottle feeding was assessed once (3.5%) due to early maternal decision to formula feed exclusively.

The discharge NFAS was conducted on the day participants went home. The median age at discharge was 12.00 days (IQR = 7.0 days). As all participants were born in hospital, age at discharge equalled the length of hospitalisation. Everyone went home on full oral feeds when they were feeding safely and efficiently, as well as demonstrating appropriate growth patterns for their age. Twenty participants (69.0%) were discharged on exclusive breastfeeding; five participants (17.2%) had breastfeeding supplemented with expressed breast milk (EBM) via cup; one participant (3.5%) had cup feeding of EBM; and three participants (10.3%) were discharged on bottle feeding. Among all three participants, reasons for bottle feeding included maternal decision to formula feed exclusively.

The NFAS divides symptoms of OPD into six diagnostic areas. It is possible for neonates to have symptoms of OPD in more than one area. Eighteen participants (62.1%) initially presented with OPD in at least one NFAS diagnostic area, but an overall diagnosis of OPD was only given to three participants (10.3%). Upon discharge, five participants (17.2%) presented with OPD symptoms in at least one NFAS diagnostic area, but an overall diagnosis of OPD was only given to one participant (3.4%). There were significantly fewer signs and symptoms of OPD among participants at discharge compared to initial assessment ($p = 0.004$). Table 2 displays the frequency with which OPD symptoms occurred within the diagnostic areas, across HIE grades initially and at discharge.

NFAS assessment of physiological functioning included observing respiratory status. Initially, abnormal respiratory patterns occurred among six participants (20.7%). Stridor persisted in one participant upon discharge home (3.4%). Eight participants (27.6%) presented with non-optimal states of alert- ness at introduction of oral feeds. This number decreased to five participants (17.2%) at discharge. Four participants (13.8%) were on anticonvulsant medications but displayed adequate alertness for oral feeding during both NFAS assessments. Table 3 presents the oral reactions elicited and OPD symptoms evaluated as part of the NFAS initially and at discharge. Since the variables per subscale in Table 3 are tightly related, Bonferroni adjustments were applied. The “oral reactions elicited”, “non-nutritive sucking skills”, “nutritive sucking skills”, “behavioural responses”, and “symptoms of OPD” subscales have 7, 8, 6, 9, and 14 items respectively. The adjusted levels of significance to which the p-value was compared were therefore 0.007, 0.006, 0.008, 0.006, and 0.004 respectively. At discharge, significant improvement was observed in endurance during non-nutritive sucking (NNS; $p < 0.001$) and nutritive sucking (NS; $p < 0.001$).

The median age at VFSS was 10.5 days (IQR = 4.5 days). Twenty participants (69.0%) presented with OPD symptoms during VFSS. Supplementary File 2 displays the frequency with which OPD symptoms occurred during VFSS across HIE grades. Nine participants (31.0%) demonstrated penetration or aspiration during VFSS (penetration $n = 4$, 13.8%; aspiration $n = 5$, 17.2%). All participants who aspirated presented with moderate HIE. Three out of five participants (60.0%) displayed silent aspiration. Causes of penetration/aspiration included disorganisation of the participant at the beginning of the VFSS ($n = 1$; 3.4%), and excessive drowsy or crying states ($n = 2$; 6.9%). Four participants (13.8%) demonstrated aspiration during the swallow due to reduced endurance during fatigue testing. Disorganised tongue movements ($n = 1$; 3.4%) and delayed pharyngeal swallows ($n = 3$; 10.3%) also emerged during fatigue testing. Compensatory techniques were beneficial for two out of nine cases (22.2%) where penetration/aspiration occurred; for one participant, slow external pacing of liquid presentation eliminated penetration and for another, thickening liquids to a slightly thick consistency (International Dysphagia Diet Standardisation Initiative Level 1) eliminated aspiration.

Difficulties in the esophageal phase of swallowing were found among 23 participants (79.3%). Slow oesophageal clearance and retrograde movement of the bolus from lower to upper esophagus were noted among 14 (48.3%) and 20 (69.0%) participants respectively. VFSS composite scores reflecting the number of combined OPD symptoms within individual participants were obtained. Overall, the median composite score was 2.0 (IQR = 3.0). The median composite score for mild participants was 3.0 (IQR = 3.0), for moderate participants was 1.0 (IQR = 2.0), and for severe participants was 4.0 (IQR = 1.0). Using the VFSS composite score as a reflection of OPD severity, no statistically significant correlations were found between OPD severity and the length of hospitalisation ($p = 0.052$).

Table 2. Frequency of oropharyngeal dysphagia symptoms within the Neonatal Feeding Assessment Scale diagnostic areas across hypoxic-ischaemic encephalopathy grades: Initial vs. discharge assessment (*N*=29).

	Initial assessment				Discharge assessment				p-values of the McNemar test
Diagnostic area	Mild participants (*n*=7) frequency (%)	Moderate participants (*n*=19) frequency (%)	Severe participants (*n*=3) frequency (%)	Overall (*N*=29) frequency (%)	Mild participants (*n*=7) frequency (%)	Moderate participants (*n*=19) frequency (%)	Severe participants (*n*=3) frequency (%)	Overall (*N*=29) frequency (%)	(Overall: initial vs discharge)
Physionogical function	0 (0.0)	5(26.3)	2 (66.7)	7 (24.1)	0 (0.0)	2 (10.5)	0 (0.0)	2 (6.9)	*p*=0.063
Neonatal state	2 (28.6)	6 (31.6)	0 (0.0)	8 (27.6)	0 (0.0)	3 (15.8)	0 (0.0)	3 (10.3)	*p*=0.063
Stress cues	0 (0.0)	1 (5.3)	0 (0.0)	1 (3.4)	0 (0.0)	1 (5.3)	0 (0.0)	1 (3.4)	*p*=1.000
Motor performance	0 (0.0)	2 (10.5)	2 (66.7)	4 (13.8)	0 (0.0)	2 (10.5)	1 (33.3)	3 (10.3)	*p*=1.000
Oral anatomy and primitive reflexes	1 (14.3)	1 (5.3)	2 (66.7)	4 (13.8)	0 (0.0)	1 (5.3)	0 (0.0)	1 (3.4)	*p*=0.250
Signs and symptoms of OPD	2 (28.6)	5 (26.3)	3 (100.0)	10 (34.5)	0 (0.0)	1 (5.3)	0 (0.0)	1 (3.4)	***p*=0.004**[a]
Overall diagnosis of OPD	0 (0.0)	1 (5.3)	2 (66.7)	3 (10.3)	0 (0.0)	1 (5.3)	0 (0.0)	1 (3.4)	*p*=0.611

[a]*Significant at 5% level of significance.*

Table 3. Oral reactions elicited, and signs and symptoms of oropharyngeal dysphagia: Initial vs. discharge Neonatal Feeding Assessment Scale assessment (*N* = 29)

Domain	Initial assessment, frequency (%)	Discharge assessment, frequency (%)	*p* values of the McNemar test (initial vs discharge)
Oral reactions elicited (7 items)[a]			
Transverse tongue	27 (93.1)	28 (96.6)	p = 1.000
Strong sucking	25 (86.2)	27 (93.1)	p = 0.500
Jaw clenching	23 (79.3)	26 (89.7)	p = 0.250
Tongue protrusion	21 (72.4)	28 (96.6)	p = 0.025
Rooting	27 (93.1)	29 (100.0)	p = 0.500
Santmyer reflex	24 (82.8)	25 (86.2)	p = 1.000
Palmomental (Babkin) reflex	23 (79.3)	26 (89.7)	p = 0.250
Signs and symptoms of OPD			
Non-nutritive sucking (NNS) skills (8 items)[b]			
<10–20 sucks per burst cycle	8 (27.6)	6 (20.7)	p = 0.500
Reduced endurance	17 (58.6)	3 (10.3)	**p < 0.001***
Reduced lip closure	2 (6.9)	2 (6.9)	p = 1.000
Reduced tongue cupping	3 (10.3)	2 (6.9)	p = 1.000
Reduced anterior–posterior tongue movement	3 (10.3)	2 (6.9)	p = 1.000
Reduced sucking strength	5 (17.2)	2 (6.9)	p = 0.250
Uncoordinated suck–swallow–breathe (SSB) rhythm	6 (20.7)	2 (6.9)	p = 0.125
Abnormal breathing pattern	6 (20.7)	2 (6.9)	p = 0.125
Nutritive sucking (NS) skills (6 items)[c]			
<10–20 sucks per burst cycle	11 (37.9)	8 (27.6)	p = 0.453
Reduced endurance	19 (65.5)	2 (6.9)	**p < 0.001[A]**
Reduced lip closure	5 (17.2)	2 (6.9)	p = 0.250
Lack of timely initiation of sucking	5 (17.2)	0 (0.0)	p = 0.063
Reduced sucking strength	5 (17.2)	1 (3.4)	p = 0.125
Uncoordinated suck–swallow–breathe (SSB) rhythm	7 (24.1)	2 (6.9)	p = 0.031
Behavioural responses (9 items)[d]			
Refusal of nipple/teat/ syringe/cup	2 (6.9)	0 (0.0)	p = 0.500
Refusal of finger/pacifier	3 (10.3)	0 (0.0)	p = 0.500
Tongue thrusting	2 (6.9)	0 (0.0)	p = 0.500
Jaw clenching	0 (0.0)	0 (0.0)	Not applicable
Jaw thrusting	1 (3.4)	0 (0.0)	p = 1.000
Lip retraction	1 (3.4)	0 (0.0)	p = 1.000
Arching of back and neck	0 (0.0)	0 (0.0)	Not applicable
Turning head away	0 (0.0)	0 (0.0)	Not applicable
Emesis	1 (3.4)	0 (0.0)	p = 1.000
Symptoms of OPD (14 items)[e]			
Lack of timely initiation of sucking	5 (17.2)	1 (3.4)	p = 0.125
Weak sucking	5 (17.2)	1 (3.4)	p = 0.125
Absent sucking	1 (3.4)	1 (3.4)	p = 1.000
Uncoordinated	3 (10.3)	1 (3.4)	p = 0.500
tongue movement			
Poor lip closure resulting in excessive anterior spillage	3 (10.3)	2 (6.9)	p = 1.000
Multiple attempts to initiate pharyngeal swallow	1 (3.4)	0 (0.0)	p = 1.000
Gurgling during/ after swallow	3 (10.3)	0 (0.0)	p = 0.250

Coughing during/ after swallow	3 (10.3)	0 (0.0)	p = 0.250
Choking during/after swallow	1 (3.4)	0 (0.0)	p = 1.000
Teary eyes during/ after swallow	0 (0.0)	0 (0.0)	Not applicable
"Wet" respiratory sounds	3 (10.3)	0 (0.0)	p = 0.250
"Wet" vocal sounds	2 (6.9)	0 (0.0)	p = 0.500
Suspected delayed pharyngeal swallow	5 (17.2)	2 (6.9)	p = 0.250
Absent pharyngeal swallow	0 (0.0)	0 (0.0)	Not applicable

[a]*Bonferroni adjusted level of significance = 0.007.*
[b]*Bonferroni adjusted level of significance = 0.006.*
[c]*Bonferroni adjusted level of significance = 0.008.*
[d]*Bonferroni adjusted level of significance = 0.006.*
[e]*Bonferroni adjusted level of significance = 0.004.*
[A]*Statistically significant at the specified Bonferroni adjusted level of significance.*

Discussion

Approximately two thirds of participants displayed swallowing and feeding difficulties in at least one area at the introduction of oral feeds ($n = 18$; 62.1%) and during VFSS ($n = 20$; 69.0%), reinforcing OPD as a concern among neonates with HIE. Fortunately, participants' swallowing and feeding skills generally improved during hospitalisation and, by discharge, significantly fewer signs and symptoms of OPD occurred ($p = 0.004$). Specifically, endurance during NNS ($p < 0.001$) and NS ($p < 0.001$) significantly improved. Improvements may be due to neonates' dynamic anatomical and physiological subsystems, neurological recovery, and early speech-language pathology intervention during admission (Jensen et al., 2017; Lau, 2015). All participants went home on full oral feeds, with most receiving either exclusive breastfeeding or EBM feeds. This is positive as oral feeding may have stimulatory effects on neurodevel- opment and because breastfeeding and breast milk have significant benefits for infant health and development (Binns et al., 2016; Jadcherla et al., 2017).

Common initial difficulties identified during NFAS assessment included reduced sucking endurance, short sucking bursts, and uncoordinated SSB rhythm. These findings correspond with previous observations of infants with neurological impairment (Arvedson et al., 2020; Krüger et al., 2019). Abnormal breathing patterns and reduced tongue reactions were also found. Breathing difficulties may have implications for successful oral feeding, increasing the neonate's risk for aspiration (Arvedson, 2008). Diminished oral reactions and reflexes may indicate neurological immaturity (Modrell & Tadi, 2021). Non-optimal states of alertness for oral feeding commonly occurred at initial assessment and persisted among five participants (17.2%) at discharge. These states included light sleep, drowsy, and crying states, with three participants (10.3%) falling asleep during feeding. Drowsiness during oral feeds may be attributed to neurological compromise (Genna et al., 2013; Krüger et al., 2019). Although the participants who received anticonvulsant medications displayed adequate states of alertness for oral feeding, it is important to note that these medications may have a sedation effect, consequently impacting neonatal swallowing and feeding. More research in this area may be needed.

Despite significant changes in participants' swallowing and feeding, five participants (17.2%) still presented with OPD in at least one NFAS diagnostic area at discharge. Persistent OPD symptoms mostly included short sucking bursts. This relates to previous findings that neonates with HIE had significantly more single sucks and short sucking bursts than healthy controls (Krüger et al., 2019). Persistent OPD symptoms at discharge have the potential to impact upon feeding, possibly resulting in reduced health and nutritional status, reduced quality of life, and increased chance of hospital readmissions (Arvedson et al., 2020; Dziewas et al., 2017; Martinez-Biarge et al., 2012). This highlights the need for continuous monitoring by SLPs to prevent secondary complications.

Although contextual limitations existed, a benefit of this study included the instrumental evaluation of OPD among neonates with HIE. Delayed swallows occurred among all three grades of HIE and constitute one of the most common abnormalities observed in infants with dysphagia (Arvedson et al., 2020). The fact that the VFSS identified considerably more delayed swallows than the NFAS shows that clinical evaluation alone may be insufficient. Nine participants demonstrated penetration or aspiration (31.0%) and most aspiration events (60.0%) occurred without participant response. This concurs with findings that aspiration in infants with neurologic impairment is typically silent and highlights the importance of con- ducting gold-standard VFSS (Audag et al., 2017; Velayutham et al., 2018; Weir et al., 2011). Causes of penetration and aspiration included disorganisation of the neonate at the beginning of the VFSS, as well as excessive drowsy and crying states. Additionally, four participants (13.8%) demonstrated aspiration due to reduced endurance during fatigue testing, underscoring the need for this manner of assessment during VFSS.

Neonates with different grades of HIE demonstrated diverse swallowing and feeding abilities. Initial OPD symptoms occurred most frequently for severe participants. This is unsurprising, since neonates with severe HIE have the highest risk for adverse outcomes (Schreglmann et al., 2020). OPD severity was also greatest for neonates with severe HIE. They had a median VFSS composite score of 4.0 (IQR = 1.0). Only one persistent difficulty was noted among the severe group at discharge: this occurred in the motor performance area. These findings may indicate the potential for neonates with severe HIE to recover neurologically and respond to early intervention. However, only participants with severe HIE who survived hospitalisation were included in the study; findings may not be representative of all severely affected neonates. More research in this field is required. Participants with mild HIE also experienced OPD symptoms during the initial NFAS administration. However, by discharge, no mild participants displayed OPD signs. Although neonates with mild HIE are generally considered lower risk than their moderate and severe counterparts, these findings highlight that they do remain at risk for adverse outcomes, especially in the short-term (Krüger et al., 2017; Prempunpong et al., 2018). Participants with moderate HIE demonstrated OPD symptoms across the greatest variety of areas. This group had the fewest OPD symptoms during VFSS but constituted the bulk of participants dis- playing penetration/aspiration. Moderate participants also had persistent difficulties across all NFAS areas at discharge. Evidently, the current research supports the notion that the outcomes of neonates with moderate HIE are variable and may be difficult to predict (De Vries & Jongmans, 2010). The high proportions of participants with HIE displaying OPD symptoms regardless of severity indicate that neonates with all grades of HIE should be considered for early speech- language pathology intervention. It is important to note that the way neonates with different grades of HIE are managed may independently impact swallowing and feeding. This may include intubation and ventilation, which are associated with an increased risk for OPD (Tutor, 2022). Additionally, neonates with mild HIE do not usually receive TH. As restrictions on oral feeding are often implemented during TH, this group may subsequently be introduced to oral feeds sooner than their moderate and severe counterparts (Craig et al., 2020; Goswami et al., 2020).

Earlier research has consistently found that the presence of OPD is associated with extended the length of hospital stay (Attrill et al., 2018; Dziewas et al., 2017). This link has also been described among neonates with HIE, although studies did not make statistical inferences about the associations (Gupta et al., 2018; Krüger et al., 2017). The current study appeared to be the first to investigate the correlation between OPD severity and the length of hospitalisation among neonates with HIE. However, a significant correlation was not found between these variables ($p = 0.052$). Although it is possible that the mere presence of OPD is related to the length of hospital stay and that OPD severity plays a lesser role, it was previously suggested that early identification and management of OPD may decrease the length of hospitalisation (Attrill et al., 2018). Therefore, the early introduction of oral feeding and involvement of the SLP as soon as participants were medically stable may have played a role in mitigating the effect of OPD severity on the length of hospital stay. In settings where outpatient support is available to complete transition to oral feeding, OPD severity may also have a smaller association with the length of hospitalisation. Findings may be limited by a small sample size and should be further explored in future research using more participants.

Limitations

Common resource limitations in LMICs were highlighted in the study. These included a lack of availability of equipment such as early ultrasound, a lack of trained medical personnel, and poor maternal access to healthcare, which in some cases necessitated the use of sure dates or the new Ballard score to determine gestational age (Lee et al., 2017). Although a qualified neonatologist oversaw the administration of the new

Ballard score, which may improve the validity of this clinical assessment, it should be noted that the Ballard score may over- or underestimate gestational age and may therefore affect interpretations of swallowing and feeding (Lee et al., 2017). Neuroimaging tools such as magnetic resonance imaging are also costly and were not available for all participants. The relationship between patterns of brain injury and OPD could therefore not be determined.

Additional study limitations include a small sample size and unequal distribution of participants with mild, moderate, and severe HIE in the study sample. Neonates with mild HIE who were discharged from the hospital before data collection could be completed, or neonates with severe HIE who demised, were not included in the study. Future research should include more equally distributed grades of HIE and a larger sample size, to allow for more effective comparisons.

Clinical implications

A high proportion of neonates displayed OPD regard- less of HIE severity. Neonates with all grades of HIE should be considered for early intervention by SLPs, who are uniquely equipped to manage swallowing and feeding difficulties in a neonatal feeding team. Although significantly fewer signs and symptoms of OPD were found among neonates with HIE at discharge compared to initial assessment, 17.2% of neo- nates still presented with OPD when they went home. SLPs should thus optimally use opportunities during hospitalisation for early intervention and parent coaching before families are discharged and dispersed to areas where early intervention services may be scarce. Using VFSS identified symptoms of pharyngeal phase dysphagia more effectively than clinical evaluation alone. Most aspiration events among participants were silent and may have been missed otherwise. The value of instrumental dysphagia evaluation is therefore highlighted. The role of early speech-language pathology intervention in mitigating the effect of OPD severity on the length of hospitalisation remains important.

Conclusion

This study provided a comprehensive description of the evolution of swallowing and feeding abilities of neonates with HIE during hospitalisation, using a validated and standardised assessment tool and instrumental evaluation. Findings may be beneficial to neonatal feeding teams. Further well-designed experimental studies on neurological recovery, early establishment of oral feeds, and the length of hospitalisation are also warranted, since the ideal early feeding regime for neonates with HIE on TH has not yet been described (Chandrasekaran et al., 2021). Intervention for OPD among neonates with HIE should similarly be investigated, since this was not included in the current study.

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Conceptualisation (R.M., J.V., A.K. and E.K.); method (R.M., J.V., A.K., E.K., Z.L. and K.K.); formal analysis and investigation (R.M. and M.G.); writing (R.M.); supervision (J.V., A.K. and E.K.).

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Data availability statement

All data are stored securely in the University of Pretoria repository. Due to the nature of the research, data cannot be made publicly available to ensure privacy of participants.

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