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Long-Term Effects of Hypoxic Ischemic Encephalopathy on Feeding and Swallowing Skills of Full-Term Neonates

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Abbreviations: CP: Cerebral Palsy; MBS: Modified Barium Swallow; HIE: Hypoxic Ischemic Encephalopathy; NE: Neonatal Encephalopathy; VFSS: Video-Fluoroscopic Swallowing Study.

Abstract

Objective: The aim of this research is to find out the long-term effect of Hypoxic Ischemic Encephalopathy (HIE) in term neonates on their feeding and swallowing skills. And to estimate the prevalence and severity of feeding and swallowing problems in children with neurological impairment due to HIE.

Method: This study is a retrospective study; we collected all cases of term neonates with HIE during the period between Jan -01-2016 and Dec -31-2019 via electronic medical records. We chose the cases with varying degrees of severity of hypoxic-ischemic encephalopathy. In our study to avoid any confounding factor, we are excluding all structural lesions and only include the neurological cause (HIE). Which is suspected by signs of birth asphyxia during neonatal period (cord PH, first blood PH, and APGAR score) and then confirmed by brain MRI to exclude other structural brain lesions.

Result: showed that there is a significant difference among APGAR score 5-minute groups with *p-value<0.05* and an *F-score of 5.96*. Other than the APGAR score in 1 minute, all the other variables demonstrated no significant difference in the feeding and swallowing status of neonates

Discussion: The total sample size we considered for further analysis was 76 cases of term neonates with HIE

We discovered that approximately 16% of term neonates with hypoxic-ischemic encephalopathy would have dysphagia in childhood, regardless of the severity of HIE.

Furthermore, this study found that the sole indicator that can predict dysphagia in neonates with HIE is the APGAR score at 5 minutes, with 2/3 (66.7%) of infants with Oro motor weakness having an APGAR score at 5 minutes ranging between 0-3. Although abnormalities in brain MRI and newborn seizures indicate encephalopathy, neither has a substantial link with dysphagia in childhood.

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Introduction

Hypoxic-ischemic encephalopathy, or HIE, is a brain disease or injury caused by a lack of oxygen to the brain during the perinatal period [1]. Perinatal asphyxia can result from decreased blood flow and oxygen to a fetus or infant during the peripartum period. An impaired of placental (prenatal) or pulmonary (immediate postnatal) gas exchange results in a partial or total loss of oxygen to the vital organs. The consequences of this are progressive hypoxemia and hypercapnia. If the hypoxemia is severe enough, the muscles, liver, heart, and brain will eventually develop an oxygen debt. The consequence will be lactic acidosis and anaerobic glycolysis. Neonatal hypoxic-ischemic encephalopathy describes the neurologic consequences of perinatal hypoxia [2]. The following criteria are used to diagnose neonatal hypoxic-ischemic encephalopathy:

- Umbilical cord pH 7.0
- APGAR score of 5 at 10 minutes with ongoing resuscitation necessary;
- Multiple organ-system failures present.
- Signs of encephalopathy like seizure.
- Other causes of the neurologic disease [2]

Compared to normal newborns, the altered sensory-motor characteristics of pharynx-UES interactions and extended respiratory alterations in HIE patients indicate abnormal interactions between brain pathways and circuitry associated with swallowing and breathing. It is widely believed that newborns with HIE have variable degrees of upper and lower aerodigestive maladaptation, which can result in aspiration syndromes [3]. Early sucking and swallowing problems may be potential markers of neonatal brain injury and assist in identifying those infants at increased risk of adverse outcomes, but the relation between early sucking and swallowing problems and neonatal brain injury has not been established [4]. However, it is unclear whether hypoxic-ischemic encephalopathy has long term impacts on feeding and swallowing skills. In addition, there is limited evidence regarding whether feeding and swallowing issues, such as oropharyngeal inertia, clearing of secretions, and prolonged mealtime, will remain or improve in preschoolers due to neuroplasticity.

The review of literature mentioned above mainly focused on investigating the relationship between hypoxic-ischemic encephalopathy in different severity to the type of disability and overall outcome. Specific breastfeeding and swallowing characteristics in neonates with hypoxic-ischemic encephalopathy (HIE) have not yet been well described in the literature [5]. Early identification of feeding problems in neonates with HIE by speech-language therapists (SLTs) may prevent secondary complications of OPD such as aspiration pneumonia and death [6]. Therefore, we aimed to investigate the long-term impact of hypoxic-ischemic encephalopathy on the feeding and swallowing skills of term neonates over time.

Method

This retrospective study aims to find out the long-term effect of Hypoxic Ischemic Encephalopathy (HIE) in term neonates on their feeding and swallowing skills. And to estimate the prevalence and severity of feeding and swallowing problems in children with neurological impairment due to HIE. This study will be carried out at the pediatric rehabilitation feeding and swallowing clinic at Qatar Rehabilitation Institute Hospital in collaboration with the NICU in Women's Wellness and Research Center (WWRC, Hamad Medical Corporation). We analyze not only feeding and swallowing at birth but also beyond one year of age when the hypoxic-ischemic lesion manifests in the form of spasticity and neurological deficiency. As well as follow up with the child till he or she reaches preschool-age.

We collected all cases of term neonates with HIE during the period between Jan -01-2016 and Dec -31-2019 via electronic medical record (Cerner) of pediatric rehabilitation feeding and swallowing clinic in the Children Rehabilitation Department, Qatar Rehabilitation Institute, and the neonatal intensive care unit in the women's hospital, Hamad Medical Corporation. We did not use ICD-10 codes to collect information regarding the primary diagnosis of HIE; rather, we used CERNER documents. We chose the cases with varying degrees of severity of hypoxic-ischemic encephalopathy that were diagnosed at the NICU in WWRC. These cases were also seen at the pediatric rehabilitation feeding and swallowing clinic for an MDT clinical and /or instrumental evaluation of feeding and swallowing and received therapy at this clinic. We were assessing the children for oral pharyngeal dysphagia (OPD) through observations of signs suggestive of oropharyngeal impairment, and impaired saliva control and assessing pharyngeal dysphagia by Video-fluoroscopic swallowing study (VFSS).

In our study to avoid any confounding factor, we are excluding all structural lesions and only include the neurological cause (HIE). which was suspected by signs of birth asphyxia during the neonatal period (cord PH, first blood PH, and APGAR score) and then confirmed by brain MRI to exclude other structural brain lesions. HIE severity classification will be based on the cord blood PH and first blood PH investigations, APGAR score and MRI Brain changes. To establish the correlation between the severity of HIE and swallowing difficulties, the children will also be assessed for oral pharyngeal dysphagia (OPD) through observations of signs suggestive of oropharyngeal impairment, impaired saliva control and assess pharyngeal dysphagia by Video-fluoroscopic swallowing study (VFSS).

Results

The total sample size we considered for further analysis was 76 cases of term neonates with HIE during the period between 01 Jan 2016 and 31 Dec 2019. The result also depicted that in most of the neonates with normal feeding status 34/62 (54.8%) were First Blood Gas PH 7-7.27, whereas 7/11 (63.6%) of Oropharyngeal dysphagia were among First Blood Gas PH <6.9. Table (1).

The result also showed that 43/76 (56.6%) of neonates had NO cooling required, whereas 2/3 (66.7%) of neonates with Oro motor weakness were under the category that needed cooling. The chi-square result indicated that there is no significant difference between different categories of current feeding and swallowing status and cooling (see Table 6 for details).

Table 3 showed that most of the neonates with normal feeding 46/42 (74.2%) did not have neonatal Seizures. On the other hand, neonates with oropharyngeal dysphagia were almost equal among Neonatal Seizures 5/11 with neonatal seizure and 6/11 without neonatal seizure. The chi-square result indicated that there is no significant difference among current feeding and swallowing status categories with respect to Neonatal Seizure.

Table 1: Cross-tabulation of First Blood Gas PH and Current feeding and swallowing status.

Crosstab						
			Current feeding and swallowing status			Total
			Normal feeding	Oro motor weakness	Oropharyngeal dysphagia	
First Blood Gas PH	<6.9	Count	28	0	7	35
		% within Current feeding and swallowing status	45.2%	0.0%	63.6%	46.1%
	7-7.29	Count	34	3	4	41
		% within Current feeding and swallowing status	54.8%	100.0%	36.4%	53.9%
Total		Count	62	3	11	76
		% within Current feeding and swallowing status	100.0%	100.0%	100.0%	100.0%

Table 2: Cross-tabulation of Cooling and Current feeding and swallowing status.

Crosstab						
			Current feeding and swallowing status			Total
			Normal feeding	Oro motor weakness	Oropharyngeal dysphagia	
Cooling	Yes	Count	25	2	6	33
		% within Current feeding and swallowing status	40.3%	66.7%	54.5%	43.4%
	No	Count	37	1	5	43
		% within Current feeding and swallowing status	59.7%	33.3%	45.5%	56.6%
Total		Count	62	3	11	76
		% within Current feeding and swallowing status	100.0%	100.0%	100.0%	100.0%

Table 3: Cross-tabulation of Neonatal Seizure and Current feeding and swallowing status.

Crosstab						
			Current feeding and swallowing status			Total
			Normal feeding	Oro motor weakness	Oropharyngeal dysphagia	
Neonatal Seizure	Yes	Count	16	1	5	22
		% within Current feeding and swallowing status	25.8%	33.3%	45.5%	28.9%
	No	Count	46	2	6	54
		% within Current feeding and swallowing status	74.2%	66.7%	54.5%	71.1%
Total		Count	62	3	11	76
		% within Current feeding and swallowing status	100.0%	100.0%	100.0%	100.0%

Table 4: Cross-tabulation of APGAR score at 5min and Current feeding and swallowing status.

Crosstab						
			Current feeding and swallowing status			Total
			Normal feeding	Oro motor weakness	Oropharyngeal dysphagia	
APGAR score at 5min	0-3	Count	60	2	6	68
		% within Current feeding and swallowing status	96.8%	66.7%	54.5%	89.5%
	4-7	Count	2	0	3	5
		% within Current feeding and swallowing status	3.2%	0.0%	27.3%	6.6%
	8-10	Count	0	1	2	3
		% within Current feeding and swallowing status	0.0%	33.3%	18.2%	3.9%
Total		Count	62	3	11	76
		% within Current feeding and swallowing status	100.0%	100.0%	100.0%	100.0%

Additionally, the APGAR score at 5 minutes ranging between 0-3 with normal feeding and swallowing status was 60/62(96.8 %). 2/3 (66.7%) of neonates with Oro motor weakness were APGAR scores at 5 min ranging between 0-3 and 6/11 (54.5%) of neonates with Oropharyngeal dysphagia also had APGAR scores at 5 min ranging between 0-3 see Table 5 for details. The chi-square result indicates a significant difference between the APGAR score at 5 mins and the current feeding and swallowing status of neonates with a *p-value<0.05. Table (4).*

Table 5: ANOVA table.

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
Age (years)	Between Groups	4.744	2	2.372	2.440	0.094
	Within Groups	69.027	71	0.972		
	Total	73.771	73			
Actual PH Value	Between Groups	0.084	2	0.042	1.503	0.229
	Within Groups	2.048	73	0.028		
	Total	2.132	75			
Actual APGAR score 1 min	Between Groups	9.067	2	4.534	1.076	0.346
	Within Groups	307.604	73	4.214		
	Total	316.671	75			
ABGAR 5 min	Between Groups	25.481	2	12.740	5.956	0.004
	Within Groups	156.151	73	2.139		
	Total	181.632	75			

The ANOVA table (Table 5) showed that there is a significant difference among APGAR score 5-minute groups with *p-value<0.05* and an *F-score of 5.96*. Other than the APGAR score in 1 minute, all the other variables demonstrated no significant difference in the feeding and swallowing status of neonates. See details in Table 5.

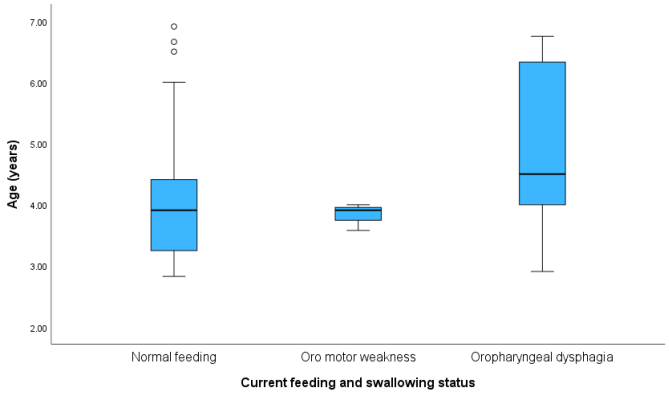

Figure 1: Box plot of Age distribution among current feeding and swallowing status.

Figure 1 shows that there are outliers among Normal feeding neonates the mean age in years lies between the lower quartile of 3 and the upper quartile of 4.5 years. The figure also shows that neonates with oropharyngeal dysphagia age ranges higher than those of neonates with normal feeding and Oro motor weakness. See Figure 1 for details.

Figure 2 on the other hand shows that the average Actual APGAR score of 5 min is a significant outlier for Normal feeding neonates and it ranges from 2-8 for neonates with Oro motor weakness (most of them in the third quartile) and ranges from 2-4.7 for neonates with Oropharyngeal dysphagia (most of them in the fourth quartile).

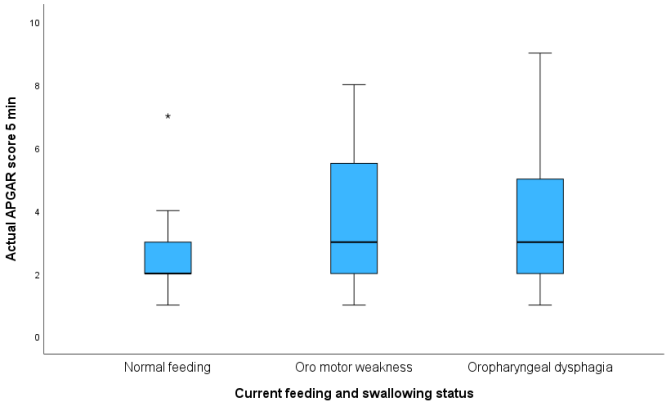

Figure 2: Box plot of current feeding and swallowing status and Actual APGAR score 5 min.

Discussion

We discovered that approximately 16% of term neonates with hypoxic-ischemic encephalopathy would have dysphagia in childhood, regardless of the severity of HIE. Furthermore, this study found that the sole indicator that can predict dysphagia in neonates with HIE is the APGAR score at 5 minutes, with 2/3 (66.7%) of infants with Oro motor weakness having an APGAR score at 5 minutes ranging between 0-3. Although abnormalities in brain MRI and newborn seizures indicate encephalopathy, neither has a substantial link with dysphagia in childhood. The study found a relationship between the first blood gas PH and current feeding and swallowing status, with most neonates with normal feeding status having a first blood gas PH of 7-7.27. In contrast, most neonates with Oropharyngeal dysphagia had a first blood gas PH of <6.9. However, it also found no significant difference between the categories. The study also found a high incidence of oropharyngeal dysphagia and Oro motor weakness in male neonates (81.8% and 66.7%, respectively) and a lower incidence of these conditions in female neonates (18.2% and 33.3%, respectively). However, it also found no significant difference between gender in terms of current feeding and swallowing status.

It is also interesting to note that about half of HIE infants were on exclusive oral feeds at discharge and remained to be on exclusive oral feeds at 1 yr. of age. This indicates that despite neurological injury, neuroplasticity may allow for the fast-developing brain of an infant to adapt to injury to allow for organism survival. Additionally, radiological markers of neurological injury do not necessarily correlate with functional feeding milestones [3]. The results suggested that there is no statistically significant difference between the categories of feeding and swallowing status in childhood and neonatal F&S assessment, which may explain the effect of neuroplasticity on brain development and maturation. Brain damage does not inhibit or hinder endogenous neurogenesis; exactly the reverse is true. Neurogenesis is maintained or even enhanced following seizures [7]. Migration of proliferating cells from the SVZ or enhanced potential of local progenitors to proliferate in response to injury-triggered environmental alterations [8]. The endogenous regenerative capacity of the damaged newborn brain: boosting neurogenesis with mesenchymal stem cell treatment [9]. Overall, the study provides insight into the relationship between the first blood gas PH and APGA score at 5 min with current feeding and swallowing status.

Limitation

In this retrospective investigation, we relied on electronic records to determine current feeding and swallowing status. Furthermore, research on the long-term effects of hypoxia ischemic encephalopathy with just feeding and swallowing status is limited. There is no standardized scale used in new-born units, such as the Sarnat scale, to help us classify HIE into severity groups.

Recommendation

Sarnat Stage I is considered "mild," HIE, Stage II "moderate," and Stage III "severe" [10]. Surviving neonates with stage 3 HIE, as well as those with stage 2 HIE and feeding and swallowing difficulties, should be referred directly to a developmental therapist, and, if severe, to a feeding team [11].

We require a more in-depth prospective study to monitor neonates with HIE in the feeding and swallowing clinic, and to evaluate the efficacy of early intervention therapy on the outcome and how to accelerate the neuroplasticity process.

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