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Feeding practices and growth of infants with Pierre Robin Sequence

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ABSTRACT

Objectives: To assess the impact of feeding practices on growth in infants with Pierre Robin Sequence (PRS) during their inpatient stay in a neonatal intensive care unit in a large tertiary paediatric hospital setting.
Methods: A retrospective review of feeding practices in infants with PRS was conducted between January 2006 and September 2017. Baseline demographics, nutrition-related and general outcomes were collected. Feeding difficulties, length of stay (LOS) and malnutrition were the primary outcome measures. Feeding difficulties included absence or poor-quality suck, episodes of aspiration, use of proton pump inhibitors or multiple episodes of vomiting. Malnutrition was classified as a weight-for-age Z score of $<$ -1.
Results: Analysis was conducted on 49 infants with PRS that met eligibility criteria. Feeding difficulties correlated with a longer LOS (24.1 vs 6.8 days ($p = 0.001$)) Z-scores differed significantly between birth and discharge (0.21(1.84) vs -1.27(2.14)) ($p < 0.001$*) with malnutrition being evident in 26 infants of which only 17 infants were seen by a dietitian. Presence of intrauterine growth restriction (IUGR) increased the likelihood of malnutrition (OR 1.40(CI-1.11–1.77)).
Conclusion: Infants with PRS are highly likely to have feeding difficulties and malnutrition. Early intervention by a dietitian is recommended to reduce the impacts of feeding difficulties, meet elevated energy requirements and facilitate growth. Infants with a longer inpatient stay or presence of IUGR should have their growth and feeding routinely monitored.

1. Introduction

Pierre Robin Sequence (PRS) is characterised by a combination of micrognathia, glossoptosis and upper airway obstruction. Antenatally, there is an absence of outgrowth of the mandible [1]. In 70–90% of cases a wide U-shaped cleft palate presents [2]. The prevalence of PRS varies in the population between 1 in every 8000 to 14000 of live births [3,4], It can occur as an isolated anomaly or as a component of a syndrome [1]. Respiratory distress occurs secondary to upper airway obstruction, with interventions to assist ranging from non-surgical modalities that include continuous positive airway pressure, nasopharyngeal intubation and/or prone positioning to surgical procedures for severe cases such as jaw distraction, tongue-lip adhesion and tracheostomy [4,5].

Feeding difficulties occur in approximately 40–70% of paediatric patients with chronic medical conditions [6], and in the PRS population, it is reported that 50–100% have feeding difficulties [4,5]. These difficulties are associated with either respiratory compromise or neuromotor disorders that affect swallow-suck coordination [4,5]. Nutritional requirements increase secondary to respiratory difficulty, as well as varying degrees of swallowing dysfunction, aspiration and gastro-oesophageal reflux disease (GORD) resulting in limited nutritional intake [5]. Studies suggest additional feeding interventions utilised by the multidisciplinary team which have proven beneficial in optimising growth include the introduction of small amounts of bottle feeds to encourage sucking and improve neuromuscular coordination thus helping to further develop feeding skills and optimise nutrition intake [4]. A Habermann feeder, calorie-fortified nutrition, nasogastric tube-feeding or a gastrostomy are likely to be required until the respiratory and feeding difficulties alleviate [5]. Long-term reliance on tube-feeding can result in oral aversion, further posing risk of poor nutrition status later in infancy and childhood [6].

Malnutrition is defined as an imbalance between nutrient needs and intake, resulting in cumulative deficits of macronutrients or micronutrients that may result in failure to thrive and poor developmental outcomes [7]. Substantial evidence links malnutrition to reduced immunity and poor physical, cognitive development and clinical outcomes [8]. Malnutrition is present in 15% of the Australian paediatric

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inpatient population [8], however the rate of malnutrition in infants with Pure.

We aimed to identify the feeding practices of infants with PRS during their inpatient stay and at discharge, and to assess the impact of these feeding practices on growth.

2. Methods

2.1. Eligibility

A retrospective review was conducted on feeding practices in infants diagnosed with PRS admitted to a surgical Neonatal Intensive Care Unit (NICU) at a large tertiary paediatric centre in Sydney, Australia. Infants were included if they had a diagnosis of PRS and were excluded if they were born less than 34 weeks gestation, diagnosed with Sticklers disease or a major congenital anomaly. The Human Research Ethics Committee of the institution approved the study (LNR/17/SCHN/325).

2.2. Data extraction

Infants admitted to the NICU between January 2006 and September 2017 with PRS were identified from the unit's neonatal database. Demographic and surgical data, along with additional information on nutrition, feeding and growth were collated from the database, medical records and discharge summaries.

2.3. Outcomes

Nutrition-related outcomes included feeding difficulties, malnutrition and length of stay. Feeding difficulties were defined as absence or poor suck, episodes of aspiration diagnosed clinically or radiologically, use of proton pump inhibitors or 5 or more episodes of vomiting. To calculate weight-for-age, World Health Organisation growth standards for patients from 0 to 2 years of age [9] (www.who.int/childgrowth/standards/en) were used for term infants and Intergrowth 21st Standards [10] were used for preterm infants (< 37 weeks gestation). Malnutrition was classified as a weight-for-age Z-score of ≤ -1, with mild being categorised as −1 to −1.99, moderate −2 to −2.99 and extreme ≤ -3. Intrauterine Growth Restriction (IUGR) was defined as light for gestational age (weight below but length above the 10th centile for gestational age) or small for gestational age at birth (weight and length below 10th centile for gestational age) [11]. Calorie fortification was classified as use of a breast-milk fortifier or a calorie dense formula (greater than 0.67kCal/mL).

2.4. Statistics

Normality was checked using Shapiro-Wilk test and visual inspection of normality plots. Variables were summarised using mean ± standard deviation or median ± interquartile range if data were not normally distributed, frequency and percentage were also used where appropriate. All associations between categorical variables were conducted using Fisher's exact tests (Type of milk on admission vs type of milk on discharge). Between-group differences on continuous variables were conducted using Mann-Whitney U tests (including jaw distraction with first oral feed age, caloric fortification with first oral feed age, feeding difficulties with length of stay, Weight-for-age Z score on admission vs discharge and gestational age and birthweight with presence or absence of IUGR). Binomial proportions test was used to test differences in categorical groups at baseline (IUGR and gender). Subgroup analyses was conducted after significant differences presented between those with IUGR and those without, risk ratios were calculated to identify likelihoods of outcomes. Exact Odds Ratio (OR) and 95% Confidence Intervals (CI) were used to correct for the small sample size. IBM SPSS (V.24) (IBM Corporation, New York) was used to analyse the data. A significance level of $p < 0.05$ were used throughout.

3. Results

3.1. Patient demographics

A total of 55 infants were included in this study, six infants were excluded due to a diagnosis of Sticklers syndrome, Williams syndrome, diatrophic dysplasia or a congenital cardiac condition and two infants were born at a gestational age less than 34 weeks. After exclusion, analysis was conducted on a total of 49 infants with PRS. Jaw distraction technique was used in nine of the infants and 2 received tongue lip adhesions. Significant differences presented between presence and absence of IUGR ($p < 0.001$), further sub-group analysis revealed gestational age (37.5(3) vs 39.0(2) weeks) ($p = 0.045$) and birth weight (2520(1237) vs 3355(1880) grams) ($p < 0.001$) were where these differences exist.

3.2. Feeding type & difficulties

In this study, Infants who underwent jaw distraction surgery took significantly longer to commence oral feeds (40.19(41.19) vs 9.63 (13.00) days) ($p < 0.010$) than those who didn't have jaw distraction. Infants who required caloric fortification took longer to commence oral feeding (18.8(25) vs 8.8(13) days) although this was not significant ($p > 0.05$). Of the participants who demonstrated feeding difficulties (78%) there was a statistically significant difference in LOS (24.1(24) vs 6.8(15) ($p = 0.001$) when compared to those who didn't. The type of milk used on admission (breast milk or formula) was the same on discharge ($p < 0.001$). There was a statistically significant association between feeding difficulties and accessing speech pathology ($p = 0.008$) with 91% of those with feeding difficulties accessing a speech pathologist. Of those classified with IUGR, 88% presented with feeding difficulties (see Table 1).

3.3. Growth and malnutrition

Weight-for-age Z Scores differed significantly between birth and discharge 0.21(1.84) vs −1.27(2.14) ($p < 0.001$). Of the 28 infants that were malnourished, 9 (32%) received no dietetic input. An association was present between IUGR and malnutrition ($p = 0.015$), presence of IUGR significantly increased odds of 1.40 (CI-1.11–1.77) of being malnourished at discharge. Male infants were more likely to have malnutrition than female infants (OR 1.63 (CI 0.51–5.14)). Infants were more likely to suffer from malnutrition if feeding difficulties were present (OR 1.40 (0.36–8.66)).

4. Discussion

The present study has identified feeding practices of infants with PRS during their admission in NICU and at discharge, as well as

Table 1
Baseline characteristics (n = 49).

Gender, n(%)	
Male	22(45)
Female	27(55)
Gestational age, weeks, mean (SD)	38(2)
Birth Weight, mean (SD)	3152(600)
Admission Age, median(IQR)	7(10)
Length of Stay, median(IQR)	22(25)
Weight-for-age Percentile, median(IQR),%	58(32)
Weight-for-age Z score, median (IQR), %	0.21(1.84)
IUGR**, n(%)	
Yes	8(16)
No	41(81)

SD, standard deviation; IQR, interquartile range; IUGR, intrauterine growth restriction.
**$p < 0.001$.

Table 2
Surgical versus non-surgical outcomes.

	Non-surgical (n = 38)	Surgical (n = 11)	*p* value
Discharge age, days, median (IQR)	21(34)	52(52)	0.359
Discharge weight, grams, median (IQR)	3564(1033)	3960(1075)	0.497
Discharge Z-Score, median (IQR)	−0.94(1.98)	−2.01(1.67)	0.147
Malnutrition, n(%)	18(47.4)	10(90.9)	0.014*
LOS, days, median (IQR)	20(11)	43(24)	0.002*
IUGR, n(%)	5(13.2)	3(27.3)	0.355
Polysomnography, n(%)	38(100)	10(90.9)	0.224
Feeding Difficulties, n (%)			
Aspiration	2(5.3)	0(0)	NA
Absence/poor sucking	14(36.8)	7(63.6)	0.169
PPIs	8 (22.2)	2 (25)	NA
Vomiting	17(44.7)	7(63.6)	0.321
Milk route, n(%)			0.967
Bottle	4(10.8)	2(18.2)	
Gastric tube	8(21.6)	1(9.1)	
Combination (bottle & tube)	25(67.6)	8(72.7)	
Milk type, n(%)			0.168
Breast Milk	10(27.0)	1(9.1)	
Formula	14(37.8)	5(45.5)	
Combination (breast milk & formula)	13(35.1)	5(45.5)	

IQR interquartile range, LOS length of stay, IUGR intrauterine growth restriction, PPIs *proton pump inhibitors*.
*$p < 0.05$.

assessed the impact of these practices on growth. Feeding difficulties and malnutrition were highly prevalent in the PRS cohort studied, with the presence of IUGR increasing susceptibility.

Our findings suggest that 78% of infants with PRS suffer from feeding difficulties, comparatively within the previously described range of 50–100% of the PRS population [4,5], although this is slightly higher than the prevalence of 40–70% found in children with chronic medical illness [6]. Understandably, LOS was significantly longer in infants with feeding difficulties than in those who did not present with feeding difficulties which may also be related to the severity of upper airway obstruction and if surgery occurred. Utilising jaw distraction surgery resulted in a longer time taken to commence oral feeding ($p < 0.01$), Paes et al. similarly found surgical intervention resulted in the prolonged use of nasogastric feeding (72 vs 21 days, $p = 0.011$) [4]. Positively, 91% of those who presented with feeding difficulties accessed a speech pathologist for intervention. This is of importance as feeding-facilitated techniques recommended by speech pathology can assist in orofacial and tongue stimulation through the introduction of small amounts of bottle-feeding [4].

Malnutrition was present in 57% of the PRS population at discharge in this study, which was significantly higher than the rate described in the paediatric inpatient population at 15% [8]. The significant increase in malnutrition in the surgical group ($p = 0.014$) was anticipated as these cases were higher in severity of PRS and upper airway obstruction (Table 2). Z scores in our cohort, significantly reduced between birth and discharge ($p < 0.001$) which is similar to the findings of Daniel et al. [12]. This reduction is attributable to the increase in energy requirements secondary to respiratory distress as well as complications with feeding [5]. Alarmingly, 32% of this population received no dietetic assessment or intervention. While these infants were in the mild malnutrition category, lack of intervention leaves them susceptible to ongoing malnutrition and its consequences. Improvements in weight have been previously observed as a result of calorie fortification in infants with PRS who present with malnutrition, though it's impact on growth is dependent on the severity of the sequence [12]. A dietetic referral currently occurs at the judgement of the attending neonatologist at our institution. An automatic referral system to a dietitian or early nutritional assessment may be warranted to meet energy requirements and reduce catabolic effects. A uniform guideline with a recommendation to refer infants with PRS to a dietitian early in admission may also assist in facilitating a change in practice. Male infants with PRS had higher odds (1.6) of being malnourished than females, however, the reason for this is unclear as gender does not predispose infants to PRS.

Presence of IUGR at birth increased the odds of an infant with PRS having feeding difficulties (OR 2.26) and malnutrition (OR 1.40), leaving these 8 infants highly susceptible to poor outcomes. IUGR can result due to a combination of maternal, placental, fetal or genetic factors [13]. These infants are particularly disadvantaged having been growth restricted before birth, making birth and using their respiratory system independently a distressing experience. Infants with IUGR and PRS require frequent monitoring of feeding difficulties and growth due to their increased susceptibility.

Infants who underwent surgery were likely to be at the severe end of the spectrum of PRS and may have skewed the increased incidence of feeding difficulties, malnutrition and longer LOS, however presence of IUGR may have also influenced these results. Surgery for PRS and IUGR presence predispose the infants in this cohort to poorer growth outcomes.

The main limitation of this study was the small sample size of infants (n = 49), a similar study conducted previously had a sample size of 48, reflecting the same difficulties with data analysis within this population due to its rare nature [4]. Retrospective studies are limited by the quality of data collection and missing or incomplete data, in particular, management of feeding difficulties and the intensity of the dietetic or speech pathology intervention data was difficult to determine. Defining feeding difficulties may be subjective and varies between practitioners. As this study was conducted within a tertiary paediatric hospital, the clinical case presentation is higher in severity, making statistical interpretation challenging. Finally, weight-for-length could not be calculated to identify chronic malnutrition and stunting as length is not measured routinely within the NICU.

5. Conclusion

Infants with PRS are highly likely to have feeding difficulties, poor growth and malnutrition. Early intervention by a dietitian is recommended to reduce the impacts of feeding difficulties, meet elevated energy requirements and facilitate growth. A uniform guideline with the recommendation to refer infants with PRS to a dietitian could facilitate a change in practice. Infants with IUGR should have their growth and feeding regularly monitored due to their high risk of feeding difficulties and malnutrition.

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Declarations of interest

None.

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