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ORIGINAL ARTICLE

Nutrition and Growth

Feed fortification strategy impact on the risk of necrotizing enterocolitis in infants with complex congenital heart disease

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Abstract

Objectives: Development of necrotizing enterocolitis (NEC) in infants with complex congenital heart disease (CHD) has serious negative clinical outcomes. Unfortified expressed breast milk (EBM) is this high-risk population's enteral feed of choice. EBM often requires fortification to meet nutritional needs to prevent malnutrition. The optimal fortification strategy in this population is unclear. We hypothesize that, in infants with complex CHD at high risk of NEC, using extensively hydrolyzed formulae compared to polymeric infant formulae to fortify EBM will improve growth and reduce the incidence or severity of NEC.

Methods: A single-center, retrospective pre- and post-implementation study was conducted in a tertiary pediatric cardiac surgical center in Queensland, Australia. It observed the impact of a change in fortification strategy and formulae selection practice in infants with complex CHD at high risk of NEC.

Results: There were 133 infants eligible for study inclusion, with 69 pre-implementation and 64 post-implementation. No impact on growth outcomes was observed between pre- and post-implementation cohorts. There was a trend towards reducing the severity of NEC in the post-implementation group. Pre-implementation, 7 out of 17 infants (41%) diagnosed with NEC were classified as advanced NEC, with 0 out of 16 (0%) post-implementation.

Conclusions: The use of extensively hydrolyzed formulae instead of polymeric infant formulae, to fortify EBM in infants with complex CHD at high risk of NEC, has the potential to reduce the severity of NEC, with no impact on growth, across hospitalization.

KEYWORDS

enteral nutrition, fortify, heart defects

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1 | INTRODUCTION

Development of necrotizing enterocolitis (NEC) in infants with complex congenital heart disease (CHD) results in delays to cardiac surgical intervention, extended hospital length of stay (LOS), adverse neurodevelopmental outcomes, and increased mortality.[1–3] While the pathophysiology of NEC in CHD is not well understood, it is thought to differ from NEC in the preterm population.[1,3,4] Lower perfusion pressures, decreased systemic oxygen delivery, mesenteric hypoperfusion, ischemic re-perfusion injuries, and subsequent dysmotility are generally accepted as contributing factors to the increased risk.[1,4–6] It is thought that impaired absorption via the enteral route, secondary to dysmotility, can lead to statis of milk substrate in the bowel lumen.[6] This contributes to intestinal dilations and impairment of the epithelial barrier, causing dysbiosis and inflammation in the intestinal microbiota.[6,7]

Unfortified expressed breast milk (EBM) is the enteral feed of choice for infants with complex CHD at high risk of NEC[4,7,8]; however, it is often inadequate in providing enough calories and protein for optimal growth in this population to avoid the development of malnutrition.[8–10]

Moderate malnutrition, as defined by a weight for age (WFA) z-score < -2, is reported to be between 21% and 29% in infants with CHD at hospital admission.[9,10] Suboptimal growth parameters during cardiac surgery are associated with poorer surgical outcomes.[9,10]

As such, fortification of EBM is frequently required to meet nutritional needs in the context of elevated requirements and fluid restrictions. The addition of fortification to EBM changes its osmolality, potentially increasing the risk of developing NEC.[11–13] The optimal EBM fortification strategy, or formulae selection in the absence of EBM, in infants with complex CHD is unclear. Also, the complex relationship between enteral feeding, fortification, and the development of NEC in infants with complex CHD is scarcely described.[2] There is a lack of published literature reporting the impact of fortification on the development of NEC, as well as comparative studies between polymeric and extensively hydrolyzed formulae selection for fortification.

What is Known

- Development of necrotizing enterocolitis (NEC) in infants with complex congenital heart disease (CHD) results in negative patient outcomes.
- Unfortified expressed breast milk is the enteral feed of choice in this population; however, fortification is often required for optimal growth.
- The optimal fortification strategy for infants with CHD at high risk of NEC is unclear.

What is New

- Extensively hydrolyzed formulae in place of polymeric infant formula appear safe.
- There may be a benefit to the use of extensively hydrolyzed formulae in infants with complex CHD at high risk of NEC for fortification.

Extensively hydrolyzed formulae are increasingly used in complex diseases where tolerance and absorption via the enteral route are affected.[14,15]

The standard practice at our tertiary cardiac surgical center for infants with complex CHD was to fortify EBM with polymeric—whole protein—infant formulae (hereafter termed polymeric infant formulae). From January 2021, in the Pediatric Intensive Care Unit (PICU) and cardiac ward, we piloted the use of extensively hydrolyzed formulae instead of polymeric infant formulae, to fortify EBM or in the absence of EBM.

The objective of this study was to observe the impact of this change of practice, using extensively hydolyzed formulae instead of polymeric infant formulae for fortification. Impact was measured by comparison of changes to growth across admission, incidence, and severity of NEC diagnoses pre- and post-implementation. We hypothesized that using extensively hydrolyzed formulae compared to using polymeric infant formulae would improve nutritional status at hospital discharge and reduce the incidence and/or severity of NEC in infants with complex CHD at high risk of NEC.

2 | METHODS

2.1 | Ethics statement

The Children's Health Queensland Hospital and Health Service Human Research Ethics Committee provided ethical approval for the study (HREC/22/QCHQ/87851), with a waiver of consent for access to patient records.

2.2 | Study setting and design

This was a single-center, retrospective pre- and post-implementation study, conducted in a tertiary pediatric cardiac surgical center in Queensland, Australia. The study compared data pre- and post-change in fortification strategy and formulae selection practices in infants with complex CHD at high risk of NEC. Standard breast milk fortification practices used in our institution were followed, with the only change being the type of formulae selected for fortification—extensively hydrolyzed formulae, rather than polymeric infant formulae. A single clinical dietitian was responsible for making the fortification and formula selection across hospital admissions in this cohort. The pre-implementation period was January–December 2020, and the post- implementation period was January–December 2021.

2.3 | Study population and data collection

Data were retrospectively collected for all inpatients from birth to 6 months of age at the time of admission, planned to undergo cardiac surgery and identified as at high risk of developing NEC.[1] High NEC risk was based on cardiac anatomy, cardiac surgical intervention, and pre-term status at admission[1,3,5] (Table S1). Infants with CHD, not identified a priori as high risk but who were subsequently diagnosed with NEC by pediatric surgeons during their hospital admission, were also included. Eligible patients were identified from the Queensland Pediatric Cardiac Research (QPCR) database.

The study sourced data from the QPCR database for demographic data, including primary cardiac anatomical diagnosis, primary surgical procedure received, pre-term status at admission, comprehensive Aristotle score,[16] hospital LOS, cardiopulmonary bypass (CPB) status, and duration of CPB. This data was supplemented with manually extracted nutrition status and feeding data from the clinical record. Further data included admission and discharge weight, day during admission enteral nutrition (EN) was commenced, type of first EN commenced, categorization as higher or lower malnutrition risk[10] (Table S2), whether fortification of EN was commenced during admission, and type of fortification received. WFA *z*-score on admission and discharge was calculated from admission and discharge weights using the World Health Organization (WHO) growth charts for 0–2years of age[17] or Fenton growth charts for pre-term infants <37 weeks of gestation.[18]

For patients diagnosed with NEC, additional feeding data were manually extracted, including the temporal association of NEC diagnosis to cardiac surgery, the type of nutrition intake at the time of NEC diagnosis, the number of days of parenteral nutrition (PN), and gut rest.

All episodes of NEC were diagnosed by a pediatric surgeon. Depending on the severity of symptoms and signs, general initial recommendations were for 2-, 5- or 7-day course of treatment with antibiotics, gut rest, and PN. The stage of NEC was retrospectively manually evaluated and scored by two assessors (one a junior pediatric surgical doctor, the other a consultant surgeon) and classified using the Modified Bell's Criteria[19] as Suspected (IA and IB), Definite (IIA and IIB) or Advanced (IIIA and IIIB)[19] (Table S3). All elements of Modified Bell's criteria—systemic parameters, radiology, and abdominal examination—were used to score NEC severity retrospectively.

The primary outcome of the study was the change in WFA *z*-score from hospital admission to hospital discharge. The secondary outcomes were the incidence and severity of NEC episodes.

2.4 | Data analysis

Patient characteristics, feeding practices, and outcomes are described using appropriate descriptive statistics: frequency with percentage for categorical variables and mean with standard deviation or median with IQR for continuous variables. Bivariable and multivariable linear regression analysis was performed to assess whether the study period, after adjustment for clinical and demographic characteristics, was associated with the primary outcome, absolute change in WFA *z*-score, calculated as WFA *z*-score at discharge minus WFA *z*-score at admission. Four infants were not included in the regression analysis: two infants who died during their admission and only had an admission weight and WFA *z*-score, and two infants with a cardiac defect, who received venovenous ECMO for respiratory failure, but no other cardiac surgery during their admission, did not have a comprehensive Aristotle score. Variables selected for investigation were those that had a clinically relevant difference between periods or, from the literature, are known to have an association with the outcome. The following variables were chosen: study period (key exposure of interest), admission WFA

z-score, comprehensive Aristotle score[16] (accounting for differences in primary diagnosis and primary procedure between groups), PICU LOS, higher malnutrition risk, and those diagnosed with NEC. The coefficient and associated 95% confidence interval are reported. As a convenience sample was used, and as such, the analyses are not adequately powered, no p-values are reported. R-studio (version 2023.06.0+421; Posit PBC) was used for statistical analysis.

3 | RESULTS

Of 625 cardiac surgical patients admitted over the study period, 133 infants (21%) met eligibility criteria for the study. There were 69 infants in the pre-implementation group and 64 infants in the post-implementation group (Table 1). The median age at admission was 7.0 days for both groups (IQR of 3.0, 22.0 for pre-implementation and 4.0, 13.5 for post-implementation).

Table 1 summarizes the patient characteristics pre- and post- implementation in terms of primary cardiac diagnosis and cardiac surgical intervention. Pre-implementation, the median PICU LOS was 9.4 days (4.9, 19.7), with median hospital LOS at 25.0 days (19.0, 47.9). Post- implementation, median PICU LOS was 13.9 days (7.2, 21.4), with hospital LOS at 31.0 days (19.8, 52.0). All preterm infants were between 34 and 36 weeks at hospital admission.

3.1 | Nutrition risk and initial feed

EN was commenced on a median of Day 1 for both groups (IQR of 1, 3 pre-implementation, and 1, 2 in post-implementation). EBM (mother's own, or donor breast milk) was the first EN commenced in 60 patients (87%) pre-implementation and 56 patients (88%) post-implementation. The pre-implementation group had 27 (39%) patients with a cardiac diagnosis, with a higher association with malnutrition,[10] with the post-implementation group at 30 (47%). One patient in each group received no EN during their admission.

3.2 | Use of fortification

Breast milk fortification or concentrated formulae were provided to 37 (54%) patients pre-implementation with 39 (61%) post-implementation. Pre-implementation, polymeric infant formulae were the predominant fortification used in 16 (43%) patients. Post-implementation, extensively hydrolyzed formulae were used to fortify breast milk in 16 (41%) of patients (Table 1).

3.3 | Impact on incidence of NEC

Seventeen patients (25%) developed NEC pre-implementation, of which seven (41%) were in the post-operative period. Post-implementation, 16 patients (25%) developed NEC, with 10 (62%) cases in the post-operative period. Pre-implementation, two patients had multiple episodes of NEC, with three patients post-implementation. Of these, one patient in the pre-implementation group developed NEC in both pre- and post-operative periods.

At the time of NEC diagnosis, 14 (82%) patients were receiving EN in the pre-implementation group and 15 (94%) patients in the post-implementation group. The predominant type of EN, at the time of NEC diagnosis, pre-implementation was unfortified breast milk (six [43%]), followed by breast milk fortified with polymeric infant formulae or concentrated polymeric infant formulae (four [29%]). Post-implementation, 11 patients (73%) were receiving unfortified breast at the time of NEC diagnosis.

Pre-implementation, two (12%) NEC diagnoses were classified, using the Modified Bell's criteria[17] as suspected (IA and IB), eight (47%) classified as definite (IIA and IIB), and seven (41%) classified as advanced (IIIA and IIIB) using modified Bell's criteria. Post-implementation, seven (44%) were classified as suspected, nine (56%) as definite, and zero cases classified as advanced (Table 2).

3.4 | PN use in NEC cohort

The median number of days of PN post NEC diagnosis was 4.8 days (2.0, 11.6) pre-implementation and 6.8 days (1.5, 9.6) post-implementation. Median number of days of gut rest post NEC diagnosis was 5.9 days (3.6, 8.0) pre-implementation and 4.8 days (2.5, 6.4) post-implementation.

3.5 | Growth outcomes

Changes to our enteral feeding regimens did not lead to an appreciable change in WFA *z*-scores across the two cohorts in this study (Figure 1); a smaller reduction in change in WFA *z*-score of 0.3 was observed in the post-implementation group. Bivariate analyses revealed evidence of an association between a smaller negative change in WFA *z*-score with a higher WFA *z*-score at admission (Table 3).

4 | DISCUSSION

This study compared the use of extensively hydrolyzed formulae to polymeric infant formulae, with or without EBM, and evaluated the impact on nutritional

TABLE 1 Patient and nutrition characteristics.

Variable	Pre-implementation *N* = 69	Post-implementation *N* = 64	All patients *N* = 133
Age at admission (days), median (IQR)	7.0 (3.0, 22.0)	7.0 (4.0, 13.5)	7.0 (3.0, 18.0)
Weight on admission (kg) (mean)	3.3 (0.9)	3.4 (0.6)	3.4 (0.7)
Weight for age *z*-score on admission, median (IQR)	−0.7 (−2.1, −0.2)	−0.5 (−1.2, 0.1)	−0.6 (−1.5, −0.02)
Pre-term at admission (born < 36 + 6 weeks gestation), *n* (%)	4 (6%)	2 (3%)	6 (4%)
Primary diagnosis, *n* (%)			
Hypoplastic left heart syndrome/single ventricle physiology	6 (9%)	9 (14%)	15 (11%)
Aortic arch hypoplasia/aortic stenosis/interrupted arch/coarctation of the aorta	20 (29%)	21 (32%)	41 (31%)
Atrioventricular septal defect/atrioventricular canal	5 (7%)	3 (5%)	8 (6%)
Pulmonary atresia/pulmonary stenosis/tricuspid atresia/tricuspid stenosis/Ebstein anomaly	3 (4%)	5 (8%)	8 (6%)
Transposition of the great arteries	12 (17%)	18 (28%)	30 (23%)
Truncus arteriosus	1 (1%)	3 (5%)	4 (3%)
Tetralogy of Fallot/double outlet right ventricle	10 (15%)	3 (5%)	13 (10%)
Other	12 (17%)	2 (3%)	14 (11%)
Primary procedure, *n* (%)			
Norwood	3 (4%)	8 (13%)	11 (8%)
Modified Blalock-Taussig shunt/central shunt	9 (13%)	11 (17%)	20 (15%)
Pulmonary artery band	7 (10%)	5 (8%)	12 (9%)
Arch repair/coarctation repair/interrupted aortic arch repair/aortic stenosis repair	22 (32%)	20 (31%)	42 (32%)
Truncus repair	1 (1%)	3 (5%)	4 (3%)
Tetralogy of Fallot repair/double outlet right ventricle repair	2 (3%)	0 (0%)	2 (2%)
Arterial switch operation/Ross procedure	12 (17%)	12 (19%)	24 (18%)
Other	13 (19%)	5 (8%)	18 (14%)
Comprehensive Aristotle Score, mean (SD)	13.2 (4.9)	13.1 (4.3)	13.1 (4.6)
Cardiopulmonary bypass (CPB), *n* (%)	38 (55%)	44 (69%)	82 (57%)
CPB time (min), median (IQR)	138 (98.5, 168.5)	140 (120.3, 194.5)	138 (111.3, 184.0)
PICU length of stay (days), median (IQR)	9.4 (4.9,19.7)	13.9 (7.6,21.4)	11.0 (6.0,20.9)
Hospital length of stay (days), median (IQR)	25.0 (19.0,47.0)	31.0 (19.8,52.0)	29 (19.0,48.0)
Day of admission enteral nutrition started, median (IQR)	1 (1,3)	1 (1,2)	1 (1,2)
First feed type on admission to hospital			
Breast milk	60 (87%)	56 (88%)	116 (87%)
Polymeric infant formulae	6 (9%)	6 (9%)	12 (9%)
Extensively hydrolyzed formulae	1 (1%)	0 (0%)	1 (1%)
Other	1 (1%)	1 (2%)	2 (2%)
Nil enteral feed	1 (1%)	1 (2%)	2 (2%)
Higher malnutrition risk (9), *n* (%)	27 (39%)	30 (47%)	57 (43%)
Change to weight for age *z*-score across admission, median (IQR)	−1.0 (−1.7, −0.4)	−0.8 (−1.7, −0.4)	−0.9 (−1.7, −0.4)

(Continues)

TABLE 1 (Continued)

Variable	Pre-implementation *N* = 69	Post-implementation *N* = 64	All patients *N* = 133
Fortification/concentrated formulae received in hospital, *n* (%)	37 (54%)	39 (61%)	76 (57%)
Type of fortification/concentrated formulae, *n* (%)[a]			
Polymeric infant formulae	16 (43%)	9 (23%)	25 (33%)
Extensively hydrolyzed formulae	5 (14%)	16 (41%)	21 (28%)
Pre-nan (breast milk fortifier)	15 (41%)	7 (18%)	22 (29%)
Other[b]	1 (3%)	7 (18%)	8 (11%)

Abbreviations: IQR, interquartile range; PICU, Pediatric Intensive Care Unit; SD, standard deviation.

[a]Denominator for this calculation based on patients who received fortification.

[b]Other formulae include low long-chain triglyceride formulae and amino acid formulae.

TABLE 2 Characteristics of necrotizing enterocolitis diagnoses.

Variable	Pre-implementation *N* = 17	Post-implementation *N* = 16	All patients *N* = 33
Post-operative diagnosis, *n* (%)	7 (41%)	10 (63%)	17 (52%)
Modified Bell's stage (18), *n* (%)			
Suspected: stage IA and stage IB	2 (12%)	7 (44%)	9 (27%)
Definite: stage IIA and stage IIB	8 (47%)	9 (56%)	17 (52%)
Advanced: stage IIIA and stage IIIB	7 (41%)	0 (0%)	7 (21%)
Receiving enteral nutrition at NEC diagnosis (%)	14 (82%)	15 (94%)	29 (88%)
Type of enteral nutrition at NEC diagnosis (%)[a]			
Breast milk	6 (43%)	11 (73%)	17 (52%)
Polymeric infant formulae	2 (14%)	1 (7%)	3 (9%)
Extensively hydrolyzed formulae	0 (0%)	1 (7%)	1 (3%)
Fortified breast milk with pre-nan breast milk fortifier	0 (0%)	1 (7%)	1 (3%)
Fortified breast milk with polymeric infant formulae/concentrated polymeric infant formulae	4 (29%)	1 (7%)	5 (15%)
Fortified breast milk with extensively hydrolyzed formulae/concentrated extensively hydrolyzed formulae	2 (14%)	0 (0%)	2 (6%)
Parenteral nutrition for NEC, median (IQR) (days)	4.8 (2.0, 11.6)	6.75 (1.5, 9.6)	6.5 (1.7, 10.0)
Gut rest for NEC, median (IQR) (days)	5.9 (3.6, 8.0)	4.8 (2.5, 6.4)	5 (3.1, 6.8)

Abbreviations: IQR, interquartile range; NEC, necrotizing enterocolitis.

[a]Denominator based on the number of patients who were receiving enteral nutrition at the time of NEC diagnosis.

outcomes. There was a similar change to the WFA *z*-score across hospitalization between cohorts. This is despite a higher proportion of patients post-implementation having a cardiac diagnosis associated with malnutrition.[10] We observed an increased number of patients receiving fortification of breast milk, or concentrated formulae, post-implementation, with no increase in the overall incidence of NEC. For those diagnosed with NEC, there was a reduction in severity post-implementation, where extensively hydrolyzed formulae were more commonly used.

Development of malnutrition in the first months of life is common in infants and children with CHD.[4] This is consistent with our study observations, with a worsening WFA *z*-score across hospitalization in both cohorts. Reasons for growth restriction in this population are multifactorial, with poor enteral feed tolerance secondary to impaired systemic perfusion and subsequent reduced nutritional intake a contributing factor.[4] The use of extensively hydrolyzed formulae in infants with digestive dysfunction and dysmotility, secondary to complex disease, has

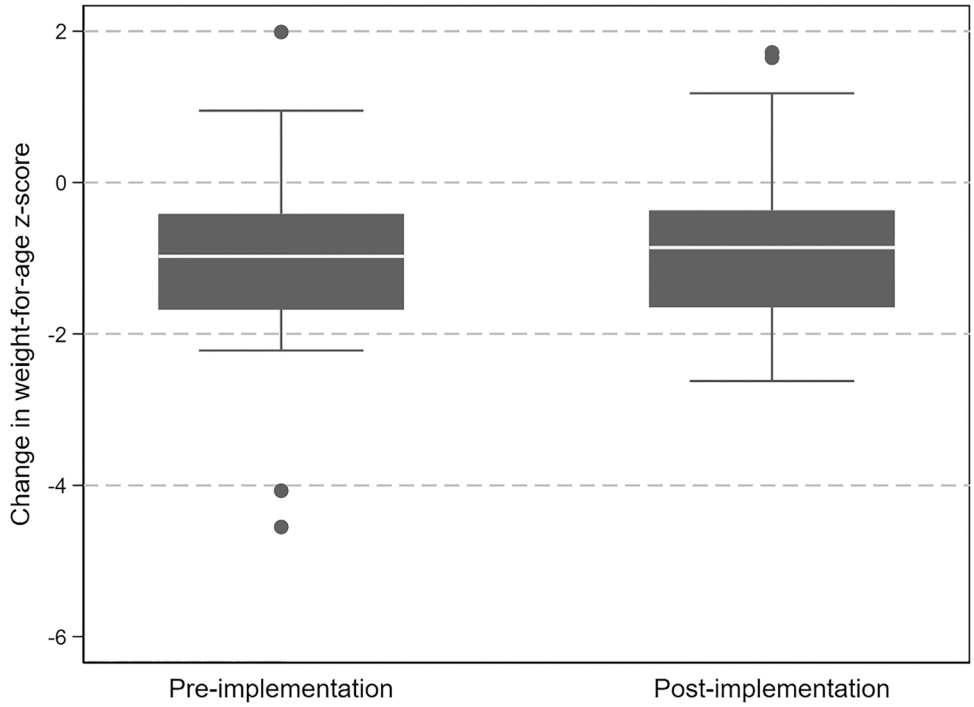

FIGURE 1 Change to weight for age *z*-score across hospital admissions.

TABLE 3 Regression modeling for change to weight for age (WFA) *z*-score across admission ($N = 128$).

Characteristic	Category	Change in WFA *z*-score Mean (SD)	Bivariate analysis Coefficient (95% confidence interval)	Multivariate analysis Coefficient (95% confidence interval)
Study period	Pre	−1.06 (0.93) ($N = 66$)	1 (reference)	1 (reference)
	Post	−0.89 (0.94) ($N = 62$)	0.17 (−0.16, 0.50)	0.30 (−0.011, 0.60)
Admission weight for age *z*-score[a]		rho = −0.398	−0.30 (−0.42, −0.18)	−0.30 (−0.43, −0.18)
Comprehensive Aristotle score[a]		rho = −0.236	−0.048 (−0.083, −0.013)	−0.024 (−0.062, 0.014)
Risk of malnutrition	Lower risk	−1.03 (0.84) ($N = 75$)	1 (reference)	1 (reference)
	Higher risk	−0.89 (1.06) ($N = 53$)	0.14 (−0.19, 0.47)	0.12 (−0.21, 0.44)
PICU LOS[b]		rho = −0.128	−0.11 (−0.26, 0.041)	−0.042 (−0.21, 0.13)
Necrotizing enterocolitis diagnosis	No NEC	−0.92 (0.88) ($N = 97$)	1 (reference)	1 (reference)
	NEC	−1.16 (1.09) ($N = 31$)	−0.24 (−0.62, 0.14)	−0.28 (−0.65, 0.085)

Abbreviations: LOS, length of stay; PICU, Pediatric Intensive Care Unit; SD, standard deviation.

[a]Correlation coefficient (rho) presented.

[b]Log-transformed.

been suggested as a potential intervention to improve nutritional intake.[14,15]

A 2018 study of infants with complex disease, attributed improved nutritional intake through reduction in vomiting and diarrhea, as well as improved growth, through increased volume of intake, with use of extensively hydrolyzed formulae.[19] Extensively hydrolyzed formulae are more easily absorbed due to the pre-digested protein and a higher proportion of medium chain triglyceride-based fat compared to

whole protein and long chain fats in polymeric infant formulae.[15,20]

Infants with complex CHD have the potential for poor bowel perfusion for an extended period, from weeks to months, depending on their underlying cardiac anatomy and surgical pathway.[21] This is compared to the pre-term population, where the incidence of NEC is inversely proportional to gestational age and weight, with immature gut function improving, and NEC risk decreasing, as pre-term infants progress in age.[22] Therefore, while there is no published evidence in either population, we hypothesize that infants with CHD who have bowel hypoperfusion for an extended period may benefit from the use of extensively hydrolyzed formulae over polymeric formulae.

Median PICU and hospital LOS appeared higher in the post-implementation group. Studies have found an association between suspected NEC (Bell's stages 1A and 1B) and increased hospital LOS.[23,24] With a higher incidence of Bell's stages 1A and 1B in the post-implementation group, this could explain the increased LOS in this cohort. This could also be accounted for by the higher number of staged procedures (Norwood, systemic-pulmonary shunt procedures, pulmonary artery banding) in the post-implementation group. It is not uncommon for these patients to remain as inpatients between stages. The increased LOS may impact growth outcomes across admission, as longer admissions give more time for nutritional correction. Equally, this could be offset by the increased malnutrition risk, and associated poorer growth, of patients who undergo staged cardiac procedures.[10]

The incidence of NEC within our study was 5.3%, with literature reporting an incidence of approximately 5% in the CHD population.[2] While the incidence of NEC did not appear to change appreciably, we did observe a decrease in the severity of NEC in the post-implementation group, with increased use of extensively hydrolyzed formulae and reduction of polymeric, cow's milk protein, infant formulae. A case series hypothesized that infants with impaired intestinal perfusion, secondary to reduced cardiac output, are at higher risk of food protein-induced allergic proctocolitis.[25] Cow's milk protein is thought to be the most common trigger.[25] Symptoms present similarly to NEC and can be resolved using extensively hydrolyzed formulae.[25] This may explain the reduction in severity of NEC diagnosis observed in our study, with increased use of extensively hydrolyzed formulae.

Days of PN use were increased in the post-implementation group, which may have influenced growth outcomes. It also possibly reflects variation in practice within our center, where PN down-titration post NEC is clinician-driven and not protocolised. There was a reduction in the number of days of gut rest received for a NEC diagnosis. This supports the finding of less severe NEC, with a shorter period of nil enteral intake, in the post-implementation group. There was no change in the group of pediatric surgeons consulting on these patients during the time of this study. No other active interventions to manage this patient cohort occurred during the study period. However, we acknowledge that reduction in NEC severity may have related to other contributing factors that were not captured in this study.

This study, based on a strong scientific rationale, observed the outcomes of a change to feeding practices. It is the first of its kind to study nutritional outcomes based on fortification or formula selection in this high-risk population.

The change of practice was feasible and sustainable due to strong support and involvement from multidisciplinary stakeholders, ensuring robust implementation. Our clinical practice could be translated and adopted in similar PICU and cardiac ward settings due to its simplicity. Our center's pragmatic clinical diagnosis of NEC was based on surgical review from a single, unchanged group of pediatric surgeons. While there is inherent variability in practice, as with most hospital clinical care, it is translatable to other settings.

There are limitations in our study. It is a single-center study with a small cohort. This impacts the generalizability of the study results. Because of the retrospective nature of our study, other potential mediators that precipitate NEC and its severity may not have been accounted for. A single clinical dietitian was responsible for making the fortification and formula selection across hospital admissions in the PICU and cardiac ward. A standardized feed and fortification selection protocol would strengthen standardized implementation processes, rather than relying on clinician-led decision-making.

This study is a snapshot of nutrition practices in our center, with nutrition intake data, including volume and concentration, not collected for the entire admission. Differences in caloric density, protein content, and osmolality between the fortification selections were not captured. A cost analysis comparison between interventions and the financial implications of outcomes was not completed for this study, but would add value to the impact.

5 | CONCLUSION

The results of our observational study indicate that the use of extensively hydrolyzed formulae compared with polymeric infant formulae appears to be safe. While this study was not adequately powered to deliver a conclusion to direct clinical practice, there seems to be a signal that fortification with extensively hydrolyzed formulae may benefit infants with complex CHD at high risk of NEC. Further larger studies to explore this, in addition to the cost implications of such a change, should be considered.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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