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ORIGINAL ARTICLE

IMPACT OF TIME TO ACHIEVE FULL ENTERAL NUTRITION ON INTRAVENTRICULAR HEMORRHAGE RISK IN PRETERM INFANTS: A STUDY IN A RESOURCE-LIMITED SETTING

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ABSTRACT

Background: Intraventricular hemorrhage (IVH) is a serious complication in preterm infants, particularly in low-resource settings where total parenteral nutrition (TPN) is unavailable. This study explores the relationship between early enteral feeding with partial parenteral nutrition and IVH incidence in a resource-limited neonatal intensive care unit (NICU).

Methods: A retrospective cohort study was conducted on 88 preterm infants admitted to a NICU without TPN access. IVH was classified by cranial ultrasound. Early feeding was defined as achieving full enteral nutrition (≥150 mL/kg/day) by day 7 of life. Statistical analysis included chi-square tests and binary logistic regression to identify independent predictors of IVH.

Results: The mean gestational age was 28.4 ± 2.1 weeks, and the mean birth weight was 1.15 ± 0.32 kg. The overall incidence of IVH was 23.9%, with 17.0% of infants experiencing Grade II or higher. IVH occurred in 18.8% of the early feeding group and 25.0% of the delayed group ($p = 0.837$). While this difference was not statistically significant, it trends toward protective effect ($\chi^2 = 5.20$, $p = 0.268$). However, the longer time to reach full feeds was significantly associated with increased odds of developing intraventricular hemorrhage (IVH) (OR = 1.13, 95% CI: 1.01–1.26, $p = 0.030$).

Conclusion: While early achievement of full enteral feeding showed a trend toward reduced IVH incidence, it was not statistically significant. Future multicenter studies with larger sample sizes and a control group receiving TPN are needed to determine the impact of early feeding on IVH risk, particularly in low-resource settings.

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preterm infants, intraventricular hemorrhage (IVH), parenteral nutrition, enteral feeding, resource-limited settings, neonatal care.

ABBREVIATIONS

GA Gestational Age

IVF Intravenous Fluids

IVH Intraventricular Hemorrhage

NEC Necrotizing Enterocolitis

NICU Neonatal Intensive Care Unit

NIV Non-Invasive Ventilation

PDA Patent Ductus Arteriosus

TPN Total Parenteral Nutrition

Introduction

Intraventricular hemorrhage (IVH) contributes to significant morbidity and mortality in preterm infants less than 32 weeks of gestation. The pathogenesis of IVH involves the fragility of the germinal matrix vasculature and fluctuations in cerebral blood flow, with multiple interconnected mechanisms contributing to cerebral injury in vulnerable preterm infants.[1]

The overall incidence of severe IVH is around 10% in preterm infants <28 weeks GA and may reach as high as 45% in extremely low birth weight infants depending on gestational age and neonatal care quality.[2,3] However, the incidence in low-middle resource settings is around 20-30%.[4,5]

In high-resource NICU units, total parenteral nutrition (TPN) is commonly used in the early postnatal period to provide stable and adequate nutritional support.[6] However, in limited resource neonatal intensive care units (NICUs), including our unit at Ibri Hospital, TPN is not available. Instead, intravenous fluids (IVF) combined with amino acids are used for initial parenteral nutrition. The outcome of this approach on IVH is still unclear. In recent studies, early nutritional deficiency, electrolyte imbalances, and variable osmolarity may contribute to the development or worsening of IVH.[7,8]

Methods & Materials

Study Design and Setting

This is a retrospective cohort study conducted at the Neonatal Intensive Care Unit (NICU) of Ibri hospital analyzing medical records of preterm infants admitted between January 2022 and December 2024. The study aimed to evaluate the association between early partial parenteral nutrition practices (IVF and amino acids, in the absence of Total Parenteral Nutrition [TPN])

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Figure 1. IVH incidence by gestational age. Incidence of intraventricular hemorrhage (IVH) decreases with increasing gestational age, from 100% at 23 weeks to 0% at 31 weeks.

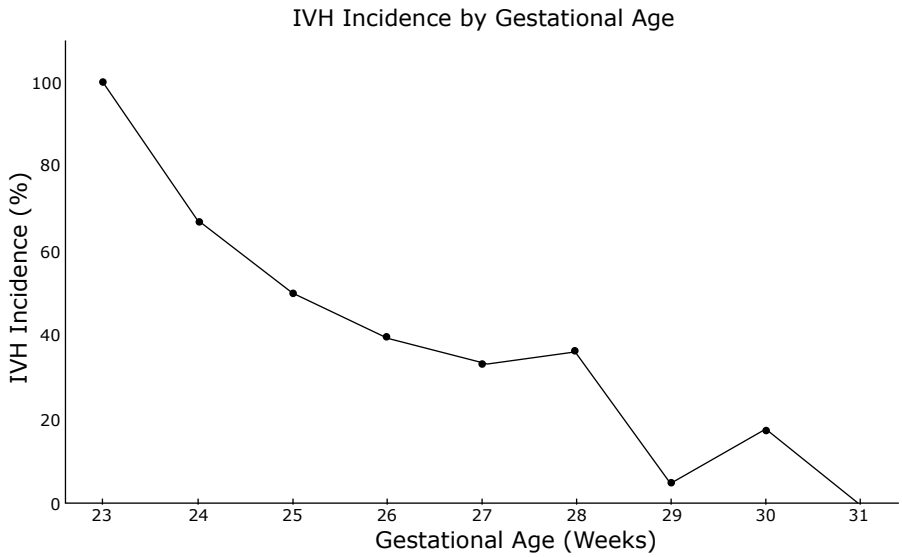
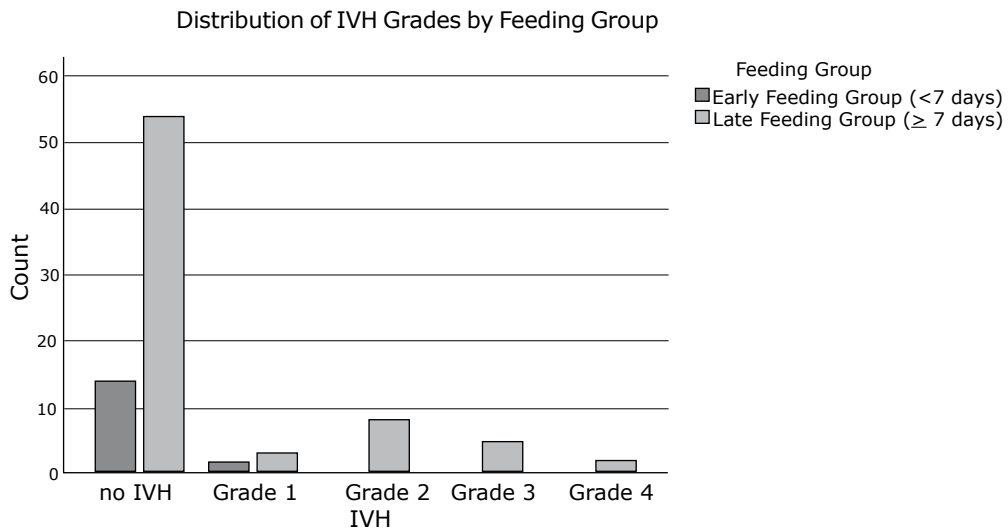


Figure 2. Distribution of IVH grades by feeding group. The bar chart compares the incidence of different grades of intraventricular hemorrhage (IVH) between two feeding groups: early feeding group (less than 7 days) and late feeding group (more than 7 days). A higher count of IVH, particularly Grades II–IV, is observed in the late feeding group.



and the risk of intraventricular hemorrhage (IVH) in preterm neonates.

All preterm neonates (gestational age <32 weeks) admitted to the NICU during the study period were included. Babies with major congenital anomalies, chromosomal abnormalities, or incomplete medical or nutritional records were excluded.

Data Collection

Clinical data were extracted from electronic medical records (Alshifa 3+) using a structured data collection sheet. Variables collected included: Gestational age (GA), birth weight (BW), sex and Timing to reach full enteral feeds (defined as 150 ml/kg/day).

The timing of transition to full enteral feeds was grouped into:

- Early Nutrition Group: reached full enteral feeds (150 ml/kg/day) within ≤7 days of life
- Delayed Nutrition Group: more than 7 days to reach full enteral feeds

All babies included in this study started 3.5 grams of 10% amino acid within 6 hours after birth with Dextrose 10% at a rate of 80 ml/kg/day. Electrolytes were added after 24 hours. The increment rate of total fluid intake was 20 ml/kg/day until reaching 150 ml/kg/day. This protocol aligns with current evidence-based recommendations for nutritional support strategies in preterm infants when TPN is unavailable.[9,10]

IVH status was defined as the presence of an intraventricular hemorrhage diagnosed via cranial ultrasound performed routinely within the first week of life and repeated after one month of age unless

indicated earlier as per unit protocol. IVH was graded using Papile classification[20]; for this analysis, IVH was categorized as present or absent.

Clinical risk factors included Invasive Mechanical ventilation (total days), non-invasive ventilation (NIV days), use of surfactant, inotropes, presence of proven sepsis (culture-positive), patent ductus arteriosus (PDA) requiring treatment, use of postnatal steroids, and presence of necrotizing enterocolitis (NEC).

Primary Outcome

The primary outcome was the occurrence of intraventricular hemorrhage (IVH), defined as any grade of IVH detected on cranial ultrasound.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Ver 26.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. The Chi-square test was used for categorical variables. Binary logistic regression was performed to identify independent predictors of intraventricular hemorrhage (IVH). A p-value <0.05 was considered statistically significant.

Results

A total of 88 preterm infants were included in the analysis. The mean gestational age was 28.4 ± 2.1 weeks (range: 23–31 weeks), and the mean birth weight was 1.15 ± 0.32 kg. The median time to achieve full enteral feeds (defined as 150 mL/kg/day) was 9 days.

The overall incidence of intraventricular hemorrhage (IVH) was 23.9% (21/88) with 17.0% of infants experiencing Grade II or higher, with most cases occurring among infants with lower gestational age. The rate of IVH was 100% at 23 weeks, 66.7% at 24 weeks, and progressively declined to 0% at ≥31 weeks (Figure 1).

Infants were categorized according to time required to reach full enteral feeds: early feeding (≤7 days; n = 16) and delayed feeding (>7 days; n = 72). IVH occurred in 3 of 16 infants in the early feeding group (18.8%) compared to 18 of 72 (25.0%) in the delayed feeding group (Figure 2).

Binary logistic regression showed that a longer time to reach full feeds was significantly associated with increased odds of developing intraventricular hemorrhage (IVH). Each additional day to full enteral feeds increased the odds of IVH by 13% (OR = 1.13, 95% CI: 1.01–1.26, p = 0.030).

Binary logistic regression analysis was performed to assess the association between early feeding and the risk of intraventricular hemorrhage (IVH), adjusting for gestational age, birth weight, mechanical ventilation, proven sepsis, necrotizing enterocolitis (NEC), postnatal steroid use, and inotropic support. Among all variables, gestational age was the only factor that demonstrated a borderline statistically significant association with IVH, with each additional week of gestation associated with decreased odds (OR = 0.56; 95% CI: 0.32–1.00; p = 0.050). No other covariates showed statistically significant associations in the adjusted model.

Discussion

In this retrospective cohort study of 88 preterm infants, we investigated the association between early achievement of full enteral nutrition and the incidence of intraventricular hemorrhage (IVH) in a resource-limited neonatal intensive care unit (NICU) where TPN is not available. The overall incidence of IVH was 23.9%, with 17.0% of infants developing Grade II or higher IVH, consistent with recent contemporary data.[11,12]

The inverse relationship between gestational maturity and IVH risk aligns with the established pathophysiology of IVH, which is predominantly related to germinal matrix fragility and impaired autoregulation in the most immature infants.[1]

Although early achievement of full enteral feeds (≤7 days) was associated with a lower IVH incidence (18.8%) compared to delayed feeding (>7 days, 25.0%), Multivariable logistic regression confirmed that early feeding was not a significant independent protective factor. In the model, gestational age was the only statistically significant predictor, while necrotizing enterocolitis (NEC) showed a borderline significant association.

Our study highlights a clinically relevant and actionable finding: in the absence of TPN, prioritizing early advancement of enteral feeds may be protective against IVH. Several pathophysiologic mechanisms may underlie this effect. Early feeding has been linked to improved gut integrity, reduced inflammatory signaling, and more stable systemic hemodynamics, all factors that may mitigate cerebral blood flow fluctuations, a major contributor to IVH in fragile preterm neonates.[13,14] Additionally, better nutritional status early in life may support vascular maturation and resilience in the germinal matrix.

Our results complement recent randomized trials and meta-analyses supporting early feeding strategies. A comprehensive 2022 systematic review and meta-analysis demonstrated that early initiation of enteral feeding within 72 hours likely reduces mortality and may reduce sepsis risk in preterm infants.[15] A 2013 Cochrane review showed that early initiation of enteral nutrition did not increase NEC risk and was associated with shorter hospital stays and improved weight gain.[16] However, our study is one of the few that examines this relationship in the context of no total parenteral nutrition access, offering novel insights for neonatal care in low-resource environments.

Recent evidence supports the effectiveness of neonatal care bundles in reducing IVH incidence, with quality improvement initiatives showing significant reductions in severe IVH rates through systematic implementation of evidence-based practices.[17] The implementation of standardized early feeding protocols represents a feasible quality improvement intervention that could be adapted across resource-limited settings by providing partial parenteral nutrition, particularly in settings where TPN is unavailable.

The primary strength of our study is its focus on a critical neonatal care practice (early feeding) in a real-world, resource-constrained NICU setting where TPN is not available. Though IVH was not the primary outcome in most trials, some observational data have similarly shown trends toward reduced IVH and improved

neurologic outcomes with early feeding.[18,19]

However, several limitations must be acknowledged. The sample size was modest (n=88), and the number of IVH cases was relatively small (n=21), which limits the statistical power and precision of effect estimates. Additionally, residual confounding is possible despite multivariable adjustment. We were unable to include variables such as delivery room management, fluid boluses, or specific feeding volumes, which may influence outcomes.

Conclusion

The observation that early full enteral feeding reduces the incidence of intraventricular hemorrhage (IVH), highlights a critical area for further research. We recommend a multicenter study to achieve a larger sample size and include a proper control group. Comparing NICUs that utilize partial parenteral nutrition with those that have full access to TPN would allow for a more definitive conclusion on the role of early nutrition in preventing IVH, a particularly important question for low-resource environments.

Compliance with Ethical Standards

Funding: None

Conflict of Interest: None

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