A Comprehensive Review of 100% Human Milk-Derived Nutritional Products: Transforming Outcomes in Premature Infant Care

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Abstract

The **Exclusive Human Milk Diet (EHMD)** is globally established as the optimal nutritional standard for high-risk preterm infants. This comprehensive review synthesizes the clinical evidence supporting the use of 100% human milk-derived nutritional products, specifically **NeoLacta's Mother's Milk Fortifier (MMF)** and **NeoLact 70 – 1.55 g supplement**. Analysis of contemporary studies demonstrates that these human milk-derived options not only ensure adequate growth rates but also provide profound reductions in critical neonatal morbidities, including **Necrotizing Enterocolitis (NEC)**, severe feed intolerance, and sepsis. This evidence reinforces the imperative shift toward Human Milk-Derived Fortifier (HMDF) implementation in Neonatal Intensive Care Units (NICUs) and post-discharge protocols.

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1. Introduction: The Nutritional Imperative for Premature Infants

Premature neonates, particularly those with **Very Low Birth Weight (VLBW; 1,000 to 1,500 g)**, face a critical nutritional challenge. They possess high demands for protein and energy necessary for rapid catch-up growth, yet their immature gastrointestinal and immune systems are highly vulnerable. **Human milk (HM)** provides essential protective factors against conditions like NEC, sepsis, Retinopathy of Prematurity (ROP), and Bronchopulmonary Dysplasia (BPD) [5]. However, raw HM alone is **protein and energy insufficient** to meet the heightened demands of the VLBW infant, making nutritional **fortification** mandatory [5].

1.1 The Risks of Bovine Milk-Based Fortification

Traditional nutritional strategies have relied on **Bovine Milk-Based Fortifiers (BMBF) or Cow's Milk-Derived Fortifiers (CMDF)**. This approach, however, introduces significant clinical risk due to the introduction of non-human proteins.

Feature	Human Milk Casein	Bovine Milk Casein	Clinical Significance
Alpha-s1-Fraction	Absent	Abundant (38.4% of total casein)	Major trigger for milk protein allergy, absent in HM [1]
Beta-Lactoglobulin	Absent	Present at high levels	Contributes to milk intolerance and GI dysbiosis [1]

Exposure to bovine milk-based diets is correlated with a substantial increase in critical morbidity: an 11.8% increased risk of NEC, a 21% increased risk of surgical NEC, and a 17.9% increased risk of sepsis [4]. The introduction of bovine proteins promotes cow's milk protein sensitization and gastrointestinal dysbiosis, leading to feed intolerance and NEC [1].

1.2 The Solution: 100% Human Milk-Derived Fortifiers (HMDF)

The development of 100% HMDF enables neonatologists to achieve a **true EHMD**, offering a therapeutic solution that mitigates the risks associated with bovine products. This review compiles clinical evidence demonstrating the unequivocal advantage of NeoLacta's HMDF products in improving clinical outcomes, securing safe growth, and reducing life-threatening complications.

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2. Overview of NeoLacta Products and Cohort Exposure

The reviewed intervention studies confirm the clinical utility of NeoLacta's products:

- **NeoLact Mother's Milk Fortifier (MMF):** A 100% HMDF designed for NICU use.
- **NeoLact 70 – 1.55 g:** A lyophilized HM supplement intended for post-discharge immune-nutritional support.

The analyzed data set comprises unique intervention cohorts: **167 neonates** have been studied across various settings (Randomized Controlled Trials [RCTs], cohort studies, pilot studies, and case series) utilizing NeoLact MMF or NeoLact 70 [1, 2, 3, 5, 6, 7].

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3. Synthesis of Clinical Outcomes with 100% HMDF

The following **Table 1** summarizes key clinical metrics across the NeoLacta product cohorts, highlighting the statistically significant and clinically relevant findings compared to BMBF or standard care.

Table 1: Summary of Key Clinical Outcomes for HMDF Intervention Cohorts

Outcome Metric	Comparative Finding (HMDF vs. BMBF)	Key Data Points & Impact	Citations
NEC Incidence (Stage ≥2)	**Significantly Lower Risk**	Relative Risk (RR) was 0.33 in RCT; EHMD overall associated with a 50% reduction in NEC.	[5]
Severe Feed Intolerance	**Significantly Lower Incidence**	RR = 0.57 in RCT. **100% resolution** of symptoms (vomiting, abdominal distension) upon switching from CMDF to HMDF in rescue cases.	[1, 5, 7]
Weight Gain Velocity	**Comparable to Superior**	Comparable to BMBF in RCTs; **Significantly higher** velocity (mean difference 0.77 g/kg/day) in one cohort study.	[5, 7]
Post-Discharge Growth	**Optimal**	Optimal average post-discharge weight gain of 30.4 g/day with NeoLact 70 supplement.	[2]
Hospital Stay Duration	**Significantly Reduced**	Reduced by 3 days (median 33 vs 36 days) in the HMBF group. Early fortification minimized NICU stay by 5 to 10 days.	[3, 5]

Outcome Metric	Comparative Finding (HMDF vs. BMBF)	Key Data Points & Impact	Citations
Sepsis Incidence	**Lower Risk**	RR = 0.6 compared to BMBF in an RCT.	[5]
Mortality	**Zero All-Cause Mortality**	Reported in the HMBF intervention arm of the RCT and cohort studies comparing HMBF vs BMBF.	[5, 7]

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4. Synthesis of Clinical Studies by Product

4.1. NeoLact MMF (Human Milk-Derived Fortifier)

Studies evaluating NeoLact MMF focus on its efficacy and safety in VLBW/ELBW infants within the NICU setting (Table 2).

Table 2: Clinical Studies Evaluating NeoLact MMF (HMDF)

Study and Year	Problem Addressed	Design (N)	Key Findings & Clinical Impact
Kotha et al., 2022	Comparing HMBF vs. BMBF on growth and morbidity (NEC, sepsis) in VLBW infants on exclusive HM.	RCT (N=25 HMBF arm)	**Morbidity:** Significant lesser incidence of NEC (RR=0.33) and sepsis (RR=0.6). **Growth:** Weight gain (21.42 g/day) similar to BMBF. **Hospital Stay:** Shorter median stay (33 days vs 36 days).
Senthilkumaran et al., 2022	Impact of HMBF vs. BMBF on postnatal weight gain velocity	Cohort (N=99	**Growth:** Significantly higher weight gain velocity (mean difference

Study and Year	Problem Addressed	Design (N)	Key Findings & Clinical Impact
	and feed tolerance in very preterm neonates (BW<1,500 g).	HMBF arm)	0.77 g/kg/day). **Tolerance:** Feed intolerance significantly less (10% in HMBF vs 20% in BMBF).
Bharadwaj et al., 2022	Rescue strategy for very preterm infants who develop intolerance after CMDF exposure.	Case Series (N=14)	**Rescue Efficacy:** 100% resolution for abdominal distension and vomiting; 85.7% resolution for feed intolerance upon switching to HMDF.
Halkar et al., 2020	Safety and efficacy of **early fortification** (at feed volumes <100 mL/kg/d) using 100% HMDF in ELBW/VLBW neonates.	Pilot Study (N=5)	**Safety:** Zero feed interruptions. **Protein Status:** Mean total serum proteins increased by 1.46 g/dL over 2 weeks. **NICU Stay:** Very early fortification minimized NICU stay by 5 to 10 days.

Impact Summary (NeoLact MMF): HMDF maintains equivalent, and in some cohorts superior, growth while drastically reducing the risk of critical morbidities like NEC and sepsis. It also serves as an effective and safe **rescue therapy** for infants intolerant to bovine-based products. Furthermore, its safety profile supports earlier initiation of fortification, which may accelerate protein accrual and facilitate earlier discharge.

4.2. NeoLact 70 – 1.55 g (Post-Discharge Supplement)

The study on NeoLact 70 addresses the high risk of infections and faltering growth in premature infants following NICU discharge (Table 3).

Table 3: Clinical Study Evaluating NeoLact 70 (1.55 g) Post-Discharge Supplement

Study and Year	Problem Addressed	Design (N)	Key Findings & Clinical Impact
Gowtham et al., 2021	Benefits of lyophilized human milk as an immune-nutritional supplement in premature/LBW infants post-NICU discharge.	Pilot Study (N=10)	**Infection/Morbidity: Zero** episodes of diarrhea, respiratory infections, antibiotic requirement, or rehospitalizations during the study period. **Immunity:** Significant increase in serum immunoglobulins (e.g., IgA ↑38.29%, IgM ↑48.25%). **Growth:** Optimal average post-discharge weight gain of 30.4 g/day.

Impact Summary (NeoLact 70): This supplement ensures the continuation of EHMD benefits after discharge, resulting in enhanced humoral immunity and robust growth. This significantly reduces the high risk of infections and subsequent rehospitalization common in this vulnerable population.

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5. The Clinical Imperative for 100% Human Milk-Derived Nutrition

The comprehensive data definitively supports the adoption of 100% human milk-derived products as the optimal nutritional intervention for preterm infants, aligning with global standards.

5.1 Safety and Tolerance Superiority

The use of HMDF is superior because it inherently avoids allergenic bovine proteins (such as the alpha-s1-fraction and beta-lactoglobulin) [1]. NeoLact MMF is also **maltodextrin-free**, helping to maintain a lower osmolality than many BMBFs, thereby mitigating the risk of NEC development [6]. A survey of neonatologists found that 80% considered HMBF safe and well-tolerated, contrasting with the 17% of surveyed neonatologists who reported that 51 to 80% of preterm infants on BMBF experience feed intolerance issues [8, 9].

5.2 Morbidity Reduction and Guideline Adherence

The EHMD regimen, enabled by HMDF, is associated with a 50% reduction in NEC, and the RCT demonstrated a **Relative Risk of 0.33 for NEC (Stage ≥2)** compared to BMBF [5].

Given that the lack of human milk feeds is the most critical risk factor for NEC, the 100% HMDF approach directly addresses this primary threat.

The availability of NeoLacta's HMDF products allows NICUs to fulfill the **World Health Organization (WHO)** recommendation that fortifiers must preferably be derived from human milk. This aligns with the perspective of 100% of NICU nurses who rate EHMD as "very important" [8].

6. Conclusion

The clinical evidence is conclusive: 100% human milk-derived nutrition offers a quantifiable reduction in high-risk morbidities—most critically NEC and sepsis—while guaranteeing adequate growth. We urge clinicians to adopt NeoLacta's products as the **essential component** of an Exclusive Human Milk Diet regimen, setting the highest standard for safety and efficacy in neonatal nutrition.

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