



# Role of Human Milk in the Management of Necrotizing Enterocolitis: A Review

Abdulaziz Abdulrahman A Bedaiwi<sup>1</sup>, Fiza Tariq A Alghorayed<sup>1</sup>, Wejdan Mohammed S Alshehri<sup>1</sup>, Yassmeen Hmoud S Alblowi<sup>1</sup>, Anwar Saad E Alrashidi<sup>1</sup>, Raghad Abdulrahman A Aljohani<sup>1</sup>, Rana Suliman D Alshwamin<sup>1</sup>, Salem Ahmed S Shaman<sup>2</sup>, Ibrahim Mahmoud H Ajwah<sup>3\*</sup>

<sup>1</sup> College of Medicine, University of Tabuk, Saudi Arabia.

<sup>2</sup> Department of Internal medicine, King Khalid hospital, Tabuk, Saudi Arabia.

<sup>3</sup> Department of Internal medicine, King Salman Armed Forces Hospital, Tabuk, Saudi Arabia.

## ABSTRACT

Mother milk feeding is associated with decreased risk of necrotizing enterocolitis and improves neurodevelopment among low-birth-weight infants. This is a systematic review was carried out, including PubMed, Google Scholar, and EBSCO that examining randomized controlled trials, observational, and experimental studies that study the role of human milk in the management of necrotizing enterocolitis. The study included 6 studies and concluded that; while the etiology of necrotizing enterocolitis is not well understood, studies have reported that human milk feedings reduce its' incidence significantly. Larger scale experimental studies more publications studies are needed to provide guidelines for physicians to use this approach in these cases. Also, further studies on study pasteurized donor milk role in the management of this case.

**Key Words:** management of necrotizing enterocolitis, necrotizing enterocolitis, importance of mother milk.

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## INTRODUCTION

Necrotizing enterocolitis (NEC) is a serious gastrointestinal disorder in low-birth-weight infants and it is the leading cause of gastrointestinal emergency in premature infants [1, 2]. It is one of the most frequent overwhelming diseases in infants which is difficult to prevent and manage and this has become of significance for studying [3]. The extreme inflammatory process originated in the extremely immune-reactive intestine in necrotizing enterocolitis covers the effects of the illness systemically, affecting distant organs like the brain which led to considerably increased risk for neurodevelopmental delays in these infants [4].

An infant improving from necrotizing enterocolitis have almost a chance of 25% of microcephaly and severe

neurodevelopmental deferments that go beyond concerns that concern the gastrointestinal tract [5].

Owing to the genius nature of necrotizing enterocolitis, new therapeutic methods are unlikely to produce substantial breakthroughs in reducing its related mortality and morbidity [6].

Human milk feeding has been prescribed for all pre-term infants since birth including infants at high risk for retinopathy of prematurity (ROP) due to its nutritional and immunological benefits compared to formula milk. Also, fresh, maternal milk (MM) may offer more of those advantages related to banked donor milk (DM) [7].

Previous studies point out that maternal milk feeding is linked with a reduction in the risk of NE compared with formula feeding. This finding may be due to many nutritional and immune ingredients that encourage the

**Corresponding author:** Ibrahim Mahmoud H Ajwah.

**Address:** King Salman Armed Forced Hospital PO Box 3458 Tabuk 51937, Saudi Arabia.

**E-mail:** ✉ Aj.wa@hotmail.com

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protection role of the healthy intestinal mucosa and dampen hyper-inflammatory responses to pathological bacteria [8].

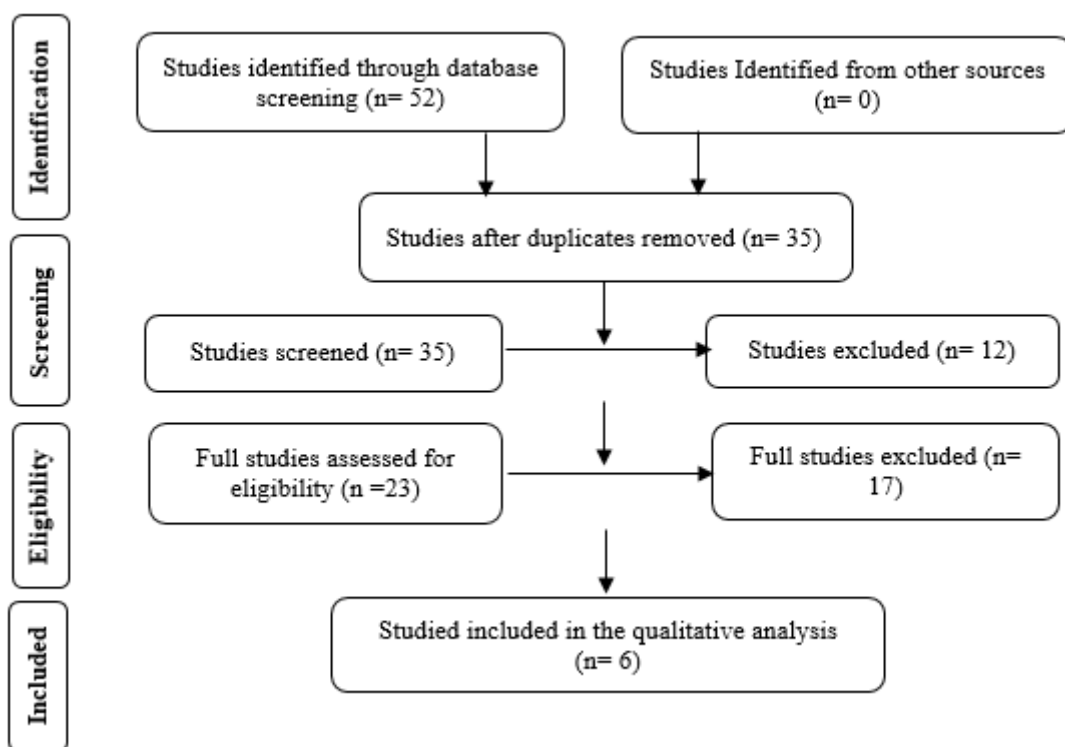
**METHODOLOGY:**

A systematic review was carried out, including PubMed, Google Scholar, and EBSCO using the following terms in different combinations: management of necrotizing enterocolitis, necrotizing enterocolitis, importance of mother milk. We included all full texts [randomized controlled trials, observational, and experimental studies]. The authors extracted the data (as shown in figure 1), and

then the author's names, year and region of publication, the study type, period of study, and the result were reported (Table 1).

**Statistical Analysis:**

The data was extracted based on a specific form that contains (Author's name, publication year, country, methodology, and results). These data were reviewed by the group members to determine the initial findings and the modalities of performing the surgical procedure. Double revision of each member's outcomes was applied to ensure the validity and minimize the mistakes.



**Figure 1: Flow chart illustrating the precess of data extraction**

**RESULTS:**

The search of the mentioned databases returned a total of 52 studies that were included for title screening. 35 of them were included for abstract screening, which leads to the

exclusion of 12 articles. The remaining 23 publications full-texts were reviewed. The full-text revision led to the exclusion of 17 studies, and 6 were enrolled for final data extraction (Table 1).

**Table 1: Author, year of publication, study type, and study outcome:**

Author Study Region Year of publication	Study type	Sample size	Outcome
Schanler, Richard J et al. [9] USA 2005	randomized, blinded trial	243 infants	DM offers a short-term benefit over PF for feeding premature infants. Advantages of an exclusive diet of MM were observed in terms of fewer infection-related events and shorter hospital stays.
Altobelli, E et al. [10] Italy 2013	A Systematic Review and Meta-Analysis	Six randomized controlled trials (RCTs) and 26 observational studies (OS).	Breastfeeding has great benefits as well as donated milk if mother milk is absent. There's a relationship between feeding and development of NEC

Nolan, L.S. et al. [11] USA 2020	A Narrative Review	---	Human milk contains a variety of bioactive components required by premature infants for adequate growth as well as intestinal and immune maturation.
Sisk et al. [12] USA 2016	A retrospective study	551 infants	MM and PDHM feedings, specified till 34 weeks postmenstrual age, remained accompanying with lesser rates of NEC in very low birth weight newborns without inquisitive with growth.
Corpeleijn W. E. et al. [13] Netherlands 2016	A multi-center, double-blind randomized clinical trial	930 infants	Pasteurized donor milk and preterm formula milk as supplementary nursing through the first 10 days of life produced alike short-term consequences in very-low-birth-weight infants concerning safety and effectiveness when their own mother's milk convenience was deficient.
Updegrove, Kim. Et al. [14] USA 2004	Review Article	---	Human milk, whether mother's own or donor, delivers substantial defense against numerous of the recognized risk influences of NEC as well as therapeutic defense for the infant improving from NEC.

## DISCUSSION:

Necrotizing enterocolitis (NEC) is a very common and overwhelming intestinal condition in preterm babies. It was expected that 52.9% of premature infants take place in Asia, 25% in sub-Saharan Africa, 7.7% in Latin America, 5.7% in Europe, 4.1 % in North Africa, 3.1 in North America, and 0.5% in Oceania [15]. In the USA and Canada, the pooled incidence of NEC in young children with bodyweight at birth around 500 - 1,500 g is approximately 7%, nonetheless may be far higher indefinite neonatal intensive care units (NICUs) [16]. In an exertion to avoid NEC, pasteurized donor human milk (PDHM) is progressively being used as a substitute to formula when Mother Milk amount is inadequate despite restricted confirmation for this practice [17].

Certain studies recommend that mother's milk is defensive in contradiction of sepsis since it comprehends bioactive ingredients that possess bactericidal and immunomodulating actions [10]. An existing deterrence challenge of necrotizing enterocolitis is to offer enteral feedings of little quantities of the mother's expressed breast milk; this method seems talented. A new study recommended that the exclusive use of mother's milk in addition to human milk-derivative fortifier might lead to a lesser incidence of necrotizing enterocolitis [18].

Giver milk pasteurization reduces or abolishes some of the valuable possessions of human milk and this has resulted in uncertainty on its capability to improve the health consequences for preterm infants [19]. Colaizy et al and Hair et al established that satisfactory growth can be accomplished using PDHM with fortification beyond 24 calories/oz and supplementary protein supplementation.

Research on the hazards and benefits of neither feeding pasteurized donor milk as an alternative to preterm formula (PF) milk to very low birth weight infants is scarce. A meta-analysis that comprised 1070 young children established that formula milk feeding augmented the hazard of NEC [20]. Schanler et al reported no influence of donor milk on late-onset sepsis or NEC occurrence. Though, they simply comprised sepsis or NEC cases that arisen after a substantial quantity of enteral nourishment was accepted, in their situation after 16 to 18 days, when a considerable number of proceedings should previously have arisen [21].

Cristofalo et al stated that premature infants nourished donor milk supplemented with a human milk-based fortifier required not as much time on parenteral nourishment (primary outcome) in comparison with infants' nourished preterm formula. Secondary consequences comprised NEC, which was reduced in suggestion with a whole human milk-based diet [22].

## CONCLUSION:

While the etiology of necrotizing enterocolitis is not well understood, studies have reported that human milk feedings reduce its' incidence significantly. Larger scale experimental studies more publications studies are needed to provide guidelines for physicians to use this approach in these cases. Also, further studies on study pasteurized donor milk role in the management of this case.

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### List of abbreviation:

ROP: Retinopathy of prematurity  
MM: Maternal milk  
NEC: Necrotizing enterocolitis  
EBSCO: Elton B. Stephens Company  
PDHM: Pasteurized donor human milk  
DM: Donor milk  
PF: Preterm formula  
NICUs: Neonatal Intensive Care Units

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### REFERENCES

- [1] Ismaeel Gholam A, Aied Alosaimi F, Dham Aldhafeeri M, Saad Alahmari A, Hussein A Bohassan R, *et al.* Gastroenteritis Diagnosis and Management in Children: A simple Literature Review. *Arch. Pharma. Pract.* 2019;10(3):43-6.
- [2] Alsimail MW, Alnaim AA, Alramadhan FS, Sagga BK, Alnomari LF, Almeashi NA, *et al.* Role of Gastrografin Challenge in Diagnosis of Small Intestinal Obstruction. *Arch. Pharma. Pract.* 2019;10(4):21-5.
- [3] Obladen M. Necrotizing enterocolitis — 150 years of fruitless search for the cause. *Neonatology.* 2009;96:203–10.
- [4] Hintz SR, Kendrick DE, Stoll BJ, Vohr BR, Fanaroff AA, Donovan EF, *et al.* Neurodevelopmental and growth outcomes of extremely low birth weight infants after necrotizing enterocolitis. *Pediatrics.* 2005;115(3):696-703.
- [5] Bedrick AD. Necrotizing enterocolitis: neurodevelopmental “risky business” *J Perinatol.* 2004;24:531–3.
- [6] Neu J, Walker WA. Necrotizing enterocolitis. *N Engl J Med.* 2011;364(3):255-64. doi:10.1056/NEJMra1005408.
- [7] Manzoni P, Stolfi I, Pedicino R, Vagnarelli F, Mosca F, Pagni L, *et al.* Human milk feeding prevents retinopathy of prematurity (ROP) in preterm VLBW neonates. *Early Hum. Dev.* 2013;89:S64-8.
- [8] Lucas A, Cole TJ. Breast milk and neonatal necrotizing enterocolitis. *Lancet* 1990;336(8730):1519–23.
- [9] Schanler RJ, Lau C, Hurst NM, Smith EO. Randomized trial of donor human milk versus preterm formula as substitutes for mothers' own milk in the feeding of extremely premature infants. *Pediatrics.* 2005;116(2):400-6.
- [10] Altobelli E, Angeletti PM, Verrotti A, Petrocelli R. The Impact of Human Milk on Necrotizing Enterocolitis: A Systematic Review and Meta-Analysis. *Nutrients* 2020, 12, 1322.
- [11] Nolan LS, Rimer JM, Good M. The Role of Human Milk Oligosaccharides and Probiotics on the Neonatal Microbiome and Risk of Necrotizing Enterocolitis: A Narrative Review. *Nutrients* 2020, 12, 3052.
- [12] Sisk PM, Lambeth TM, Rojas MA, Lightbourne T, Barahona M, Anthony E, *et al.* Necrotizing Enterocolitis and Growth in Preterm Infants Fed Predominantly Maternal Milk, Pasteurized Donor Milk, or Preterm Formula: A Retrospective Study. *Am. J. Perinatol.* 2017;34(7):676-83.
- [13] Corpeleijn WE, De Waard M, Christmann V, van Goudoever JB, Jansen-van der Weide MC, Kooi EM, *et al.* Effect of donor milk on severe infections and mortality in very low-birth-weight infants: the early nutrition study randomized clinical trial. *JAMA pediatrics.* 2016;170(7):654-61.
- [14] Updegrave K. Necrotizing enterocolitis: the evidence for use of human milk in prevention and treatment. *J. Hum. Lact.* 2004;20(3):335-9.
- [15] Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, *et al.* Global, regional, and national estimates of levels of preterm birth in 2014: A systematic review and modeling analysis. *Lancet Glob. Health.* 2019, 7, e37–e46.
- [16] Holman RC, Stoll BJ, Curns AT, Yorita KL, Steiner CA, Schonberger LB. Necrotizing enterocolitis hospitalizations among neonates in the United States. *Paediatr. Perinat. Epidemiol.* 2006;20:498–506.
- [17] Perrine CG, Scanlon KS. Prevalence of use of human milk in US advanced care neonatal units. *Pediatrics.* 2013;131(6):1066–71.
- [18] Sullivan S, Schanler RJ, Kim JH, Patel AL, Trawöger R, Kiechl-Kohlendorfer U, *et al.* An exclusively human milk-based diet is associated with a lower rate of necrotizing enterocolitis than a diet of human milk and bovine milk-based products. *J. Pediatr.* 2010;156(4):562-7.
- [19] Ewaschuk JB, Unger S, Harvey S, O'Connor DL, Field CJ. Effect of pasteurization on immune components of milk: implications for feeding preterm infants. *Appl. Physiol. Nutr. Metab.* 2011;36(2):175-82
- [20] Quigley M, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane. Database Syst. Rev.* 2014;4:CD002971.
- [21] Schanler RJ, Lau C, Hurst NM, Smith EO. Randomized trial of donor human milk versus preterm

formula as substitutes for mothers' own milk in the feeding of extremely premature infants. *Pediatrics*. 2005;116(2):400-6.

[22] Cristofalo EA, Schanler RJ, Blanco CL, Sullivan S, Trawoeger R, Kiechl-Kohlendorfer U, *et al.*

Randomized trial of exclusive human milk versus preterm formula diets in extremely premature infants. *J. Pediatr*. 2013;163(6):1592-5.