



ORIGINAL ARTICLE

Comparison of the frequency of necrotizing enterocolitis in preterm infants with formula feed versus breast feed.

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ABSTRACT... Objective: To find out the frequency of necrotizing enterocolitis (NEC) in preterm infants and to compare the frequency of NEC in preterm infants with formula feed versus breast feed. **Study Design:** Cross-sectional study. **Setting:** Department of Pediatric Medicine, Ghazi Khan Medical College, Dera Ghazi Khan, Pakistan. **Period:** January 2022 to June 2022. **Material & Methods:** A total of 174 preterm infants were enrolled. The NEC was diagnosed as abdominal distention or intolerance to nasogastric feed with pneumatosis intestinalis / portal venous gas or free intraperitoneal air which was confirmed by abdomen X-ray. At the time of enrollment, gestational age and weight were recorded. All preterm neonates were called for follow up every week for 4 weeks to diagnose NEC. **Results:** Of these 174 study cases, 101 (58.0 %) were male patients while 73 (42.0 %) were female patients. Mean gestational age of our study cases was 30.48 ± 3.24 weeks. Of these 174 study cases, 102 (58.6%) mothers were illiterate. Breastfeeding was noted in 74 (42.5%) infants while formula feeding was recorded among 100 (57.5%) infants. The NEC was reported among 61 (35.1%) cases whereas NEC in breastfeeding cases was found in 14 (18.9%) and 47 (47.0%) infants with formula feeding. **Conclusion:** High frequency of NEC was observed among preterm infants given formula feeding in comparison to breastfed preterm infants. Significant linkage of NEC was noted with gender, maternal literacy, birth weight and pattern of feeding.

Key words: Breast Feed, Preterm, Nasogastric Feed, Necrotizing Enterocolitis.

INTRODUCTION

Necrotizing enterocolitis (NEC) is considered to be a frequent gastrointestinal emergency reported in neonatal intensive care units (ICUs) globally.^{1,2} Literature reports the incidence of NEC ranging between 1-3/1000 live-births while around 90% of NEC cases are preterm infants.³ Among the premature infants having birth weight as low as 1500gm, 4-11% infants present NEC.⁴ An important factor which leads towards NEC in a lot of infants is prematurity but the actual etiopathogenesis of NEC is still not clear.⁵ Gut mucosal injury, inadequate barrier functioning as well as bacterial translocation are known to be important pathophysiological factors behind NEC.⁶

Although 90-95% NEC cases are thought to have some kind of enteral feedings but NEC can also

be evident among neonates who never received any feeding.⁷ In comparison to breastfeeding, formula feeding is a major risk factor observed in NEC cases as there is lack of cellular and soluble immunoprotective factors in formula feedings such as IgA and various other natural antimicrobials that alters the normal postnatal bacterial colonization having proclivity to that.⁸ Data in newborn animals, formula feeding has been found to induce inflammatory changes in the gut mucosa.⁹ Experimental and clinical studies indicate human milk feeds have more protective effect than formula feedings in NEC.¹⁰ Even pasteurized, banked donor milk has a protective effect against NEC.¹¹ Sullivan et al recently presented that human milk-based diet is more protective than mother's milk feeding which contains bovine-milk derived human milk fortifier and preterm formula feeding to treat NEC

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and surgical NEC.¹² A study showed that 39% of preterm infants on formula feeding presented with NEC in comparison to 13% on breast feeding.¹³

Healthcare facilities of our region provide medical care for a wide variety of diseases but no local data exists in our local population of Southern Punjab analyzing frequency of NEC in preterm infants on formula feed versus breast feed. This study was thought to pave the way for clinicians regarding improvement in maternal counseling about better feeding practices in neonates to avoid incidence of NEC. Our aim was to determine the frequency of NEC in preterm infants and to compare the frequency of NEC in preterm infants with formula feed versus breast feed.

MATERIAL & METHODS

This cross-sectional study was conducted at “The Department of Pediatric Medicine, Ghazi Khan Medical College, Dera Ghazi Khan”, Pakistan from January 2022 to June 2022. Approval was taken from ethical committee of the institute (letter number: 8860/DGKMC), patients were included from indoor department of the study institute. Informed and written consent was acquired. Sample size was calculated to be 174 considering $p = 13\%$ ¹³ (frequency of NEC in breastfed preterms) and $d = 5\%$ (margin of error) with 95% confidence level.

Inclusion criteria were preterm infants of either gender born between 25+0 to 31+6 weeks of gestation till 4 weeks following birth. Exclusion criteria were neonates reporting with reasonably less chances of survival (as per clinical and laboratory findings), congenital heart disease or existence of major congenital anomalies (as clinical examination and medical history/record). Necrotizing enterocolitis was diagnosed as abdominal distention or intolerance to nasogastric feed with pneumatosis intestinalis / portal venous gas or free intraperitoneal air which was confirmed by abdomen X-ray (cross table view).

Formula feed was used in shape of infant formula (same brand to all newborns to whom breast feeding will not be available). Infant formula was advised to be given as one ml bolus feeds two to

six hourly (as extra fluid) through nasogastric or orogastric tube and was increased as tolerated until one ml two hourly. The quantity was further increased by one ml, every eight to twenty four hours to a maximum quantity of 20–35 ml/kg per day. Exclusive breast milk (EBM) was used by nasogastric tube and was given at same schedule as for formula feed. Literacy status was labeled as literate for those who could read and write or illiterate if otherwise. All cases were called for a weekly follow-up for a total study duration of 4 weeks and diagnose of NEC was labeled by the end of 4 weeks.

Data was analyzed with “Statistical Package for Social Sciences (SPSS)”, version 26.0. Frequency and percentage was computed for qualitative variables like age groups, gender, residential status, monthly family income, pattern of feeding (breastfeeding/formula feeding) maternal education and NEC. Mean \pm SD was presented for quantitative variables like gestational age and birth-weight. Frequency of NEC was compared for study variables in both groups (formula fed versus breastfeeding) by applying chi-square considering $p < 0.05$ as significant.

RESULTS

Out of a total of 174 infants, 101 (58.0%) were male. The mean gestational age was 30.5 ± 3.2 weeks (ranging 25-36 weeks). There were 94 (54.0%) cases who had residential status as rural. There were 102 (58.6%) mothers who were illiterate. Breastfeeding was observed among 74 (42.5%) infants whereas formula feed was noted in 100 (57.5%). Table-1 shows characteristics of study cases.

The frequency of NEC was recorded in 61 (35.1%) infants as shown in figure-1. Furthermore, NEC among infants who were breastfeeding was observed in 14 (18.9%) and 47 (47.0%) who were formula fed. The NEC was stratified with respect to study variables and shown in Table-II.

Characteristics		Frequency (%)
Gender	Male	101 (58.0%)
	Female	73 (42.0%)
Gestational Age	Up to 30 weeks	100 (57.5%)
	More than 30 weeks	74 (42.5%)
Residence	Rural	94 (54.0%)
	Urban	80 (46.0%)
Family Income (Pakistani Rupees)	<30000	81 (46.6%)
	≥30000	93 (53.4%)
Maternal Literacy	Illiterate	102 (58.6%)
	Literate	72 (41.4%)
Birth Weight	Up to 2 kg	133 (76.4%)
	More than 2 Kg	41 (23.6%)
Feeding	Breastfeeding	74 (42.5%)
	Formula feeding	100 (57.5%)

Table-I. Demographical characteristics (n=174)

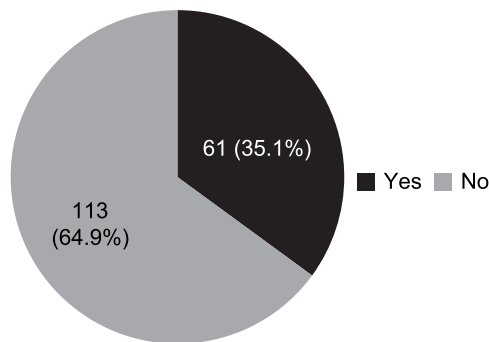


Figure-1. Frequency of necrotizing enterocolitis (n=174)

DISCUSSION

Human milk is known to result in reduction in the occurrence of NEC, however there is no comparison available between bovine-based artificial milk and mother’s own milk (MOM) in any randomized controlled study.¹⁴ From the premature infant’s diet, bovine milk products which include bovine-based milk fortifiers have been completely eliminated not long ago, which could be explained in the reduction NEC. In some of the retrospective studies, human milk has shown a dose-dependent reduction in the risk of NEC.¹⁵ But the aim of those studies was not to actually evaluate exclusive human milk diet as a baseline risk factor for the development NEC.

In this study, 58.0% neonates were male. Male predominance among premature neonates has already been reported by Rashid et al.¹⁶ Male gender percentage in preterm in our study is same as reported by Parveen from Abbottabad.¹⁷ Khan et al reporting 57% preterm neonates to be male are in accordance with our study results.¹⁸

In this study, mean gestational age was 30.48±3.24 weeks while 57.5% neonates had gestational age below 30 weeks. Mean gestational age reported by Khan et al among preterm neonates was 33±2.4 weeks which is little more than what we reported.¹⁸ Rashid et al found mean age of preterm neonates admitted to NICU to be 32.4±1.8 weeks.¹⁶

Study Variables		Necrotizing Enterocolitis		P-Value
		Yes (n=61)	No (n=113)	
Gender	Male	20 (32.8%)	81 (71.7%)	<0.001
	Female	41 (67.2%)	32 (28.3%)	
Gestational Age	≤30 weeks	34 (55.7%)	66 (58.4%)	0.750
	>30 weeks	27 (44.3%)	47 (41.6%)	
Residence	Rural	28 (45.9%)	66 (58.4%)	0.151
	Urban	33 (54.1%)	47 (41.6%)	
Monthly family income (Pakistani Rupees)	≤Rs. 30000	34 (55.7%)	47 (41.6%)	0.082
	>Rs. 30000	27 (44.3%)	66 (58.4%)	
Literacy	Illiterate	50 (82.0%)	52 (46.0%)	<0.001
	Literate	11 (18.0%)	61 (54.0%)	
Birth Weight	≤2 Kg	54 (88.5%)	79 (69.9%)	0.005
	>2 Kg	07 (11.5%)	34 (30.1%)	
Feeding	Breastfeeding	14 (23.0%)	60 (53.1%)	<0.001
	Formula feeding	47 (77.0%)	53 (46.9%)	

Table-II. Stratification of necrotizing enterocolitis with regards to study variables (n = 174)

Venkataraman and colleagues revealed mean age of preterm neonates presenting to NICU to be 28.8 ± 2.0 weeks which is close to what we observed.¹⁹

Mean birth weight of our study cases was 1832.52 ± 624.47 grams while 76.4% cases were aged below 2000 grams. Khan et al shared mean birth weight of preterm neonates to be 1.88 ± 0.5 kg which is very close to our findings.¹⁸ Rashid et al noted mean birth weight of preterm neonates admitted in NICU to be 1.6 ± 1.1 kg.¹⁶ Venkataraman et al found mean birth weight of their study cases to be 1129 ± 219 grams but mean gestational age of their study cases was also less than what we noted.¹⁹

In this study, 42.5% neonates were on breast feeding while 57.5% neonates were using formula feed. Prevalence of NEC was found to be 35.1% among preterm neonates. Among NEC cases, 18.9% were on breastfeeding in comparison to 47.0% on formula feeding. In another study 39% of preterm infants showed NEC on formula feed as compare to 13% on breast feed.¹³ These findings are in compliance with our study results. Some other researchers have also shown that evidence is convincing that human milk feeding results in reduction in the incidence of NEC in comparison to formula feed among premature infants.^{20,21}

CONCLUSION

High frequency of NEC was observed among preterm infants given formula feeding in comparison to breastfed preterm infants. Significant linkage of NEC was noted with gender, maternal literacy, birth weight and pattern of feeding. There is a dire need of awareness campaign at national level for the awareness regarding benefits of breastfeeding.






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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
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2	Shakeel Ahmad	Drafting supervision.	
3	Irum Jabeen	Study idea, Design.	
4	Sonia Ilyas	Data analysis, Discussion.	
5	Zohaib Hassan	Data collection, Literature review.	
6	Kiran Kanwal	Data collection, Data interpretation.	