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OUTCOMES OF DONOR HUMAN MILK ON VARIOUS PARAMETERS IN PRETERM NEONATES ADMITTED TO NICU: A RETROSPECTIVE STUDY

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ABSTRACT:

Background - The best food for each infant is mother's milk for neonates. Feeding with human milk has protective effects against inflammations and infections.

Aim and Objective- to study outcomes of donor human milk on various parameters in preterm neonates.

Materials and Methods:- In this retrospective study, all premature neonates admitted to the NICU who met the inclusion criteria were recruited. The main intervention in the study was to replace formula feeds with human milk. The outcomes like the frequency of NEC,mortality rate, ROP, and SEPSIS, were compared between the two groups(pre milk bank and post milk bank).

Results: Retinopathy of prematurity (ROP) was reported in 16(10.81%) neonates in the pre-launch group and 4(2.47%) in the post-launch group (P = 0.004). In the pre-launch group, 13(8.78%) neonates and in the post-launch group, 5(3.09%) neonates had significant NEC (P = 0.048). In the present study, we also found that in the pre-launch group, 27(18.24%) neonates, and in the post-launch group, 11(6.79%) neonates had LOS which was (P = 0.003).The mortality of neonates was 28(18.92%) in the pre-launch group as compared to 18(11.11%) in the post-launch group.

Conclusion- DONOR HUMAN MILK have less chances of NEC,ROP,SEPSIS and mortality in preterm neonates.

Keywords: NEC, retanopathy of prematurity, late onset sepsis, human milk bank.

1. INTRODUCTION

When a sufficient supply of mother's milk is unavailable for neonates, other options of nutrition include donor breast milk or artificial formula. Breast milk is the preferred option for feeding newborns, especially for premature and low-birth-weight neonates, as it has been shown to have many benefits. Necrotizing enterocolitis (NEC) and late-onset neonatal sepsis (LOS) are the diseases that have a high mortality rate in premature neonates[1-4]. Breast milk can act as a preventative factor against these diseases due to several factors viz. growth factors, immune-globulins, and antioxidants[5-8].

The World Health Organization (WHO) recommends that each infant should receive their mother's milk as the best food, especially for low birth-weight neonates, as it has protective effects against inflammation and infection. In contrast, formula feeds have a high risk of morbidity and mortality especially in premature neonates[9,10,11].

Ascompared to term babies Preterms have higher rates of brain injury and consequentially reduced grey matter volumes. Adequate nutrition is crucial for their neuro-developmental outcomes. In many low-income countries, the mortality rate for babies born at 32 weeks is alarmingly high. Studies show that as many as 50% of these babies do not survive due to a lack of basic and affordable healthcare services, such as access to breastfeeding support, basic infection prevention, and respiratory care. However, there is hope for reducing these devastating statistics. One promising approach is the establishment of human milk banks, which can play a crucial role in improving neonatal and infant survival rates. By providing safe and nutrient-rich breast milk to vulnerable infants, these milk banks offer a cost-effective solution to help combat the high mortality rate among premature babies in low-income countries.[12,13,14].

Providing safe and nutritious food to hospitalized neonates is crucial to their growth and development.Fortunately, human milk banks have become increasingly popular worldwide. In Europe alone, over 210 new banks have been established, with many other being under process of opening. The Association of European Milk Banks has been instrumental in supporting this growth. Similarly, in the United States, the routine use of donor milk in ICUs has increased significantly in recent years, rising from 21.1% in 2007 to 30.8% in 2011. This upward trend in the use of human milk banks is encouraging and offers hope for improved outcomes for premature infants[15].

In a resource-poor setting implementation of a milk bank presents multiple challenges, particularly due to inadequate staffing and a lack of funds for equipment maintenance. This study aimed to conduct a retrospective observational study to analyze the impact of donor human milk on hospital stay, NEC, sepsis, and weight gain, with the hope of promoting the establishment of more milk banks in other parts of the country if the study has positive outcomes.

2. MATERIALS AND METHODS

Design:

The safety and well-being of study participants are of utmost importance and were taken into consideration during the design of the study. Before enrolling participants, approval was obtained from the institutional ethics committee. The study design involved a retrospective analysis of premature neonates who were admitted to the NICU of a government medical college in Yawatmal, India. The study was conducted over a period of 12 months, with the first 6 months being before the launch of the human milk bank (January 2020 to June 2020) and the subsequent 6 months being after the launch (July 2020 to December 2020). The inclusion criteria for the study were based on birth weight and gestational age, with neonates

weighing < 2 kg and/or having a gestational age of less than 34 weeks at birth being eligible for inclusion. Neonates with major congenital anomalies, such as gastrointestinal anomalies, genetic disorders, congenital heart diseases, hypoxic-ischemic encephalopathy, and chromosomal anomalies were excluded from the study. These measures were put in place to ensure that the study was conducted with the utmost care and safety for the participants.

Setting:

This study was conducted at the NICU of a government medical college in Yawatmal, India. The main intervention in the study was to replace formula feeds with human milk in the NICU, aimed at meeting the nutritional needs of premature neonates. The study aimed to evaluate the short-term impact of the human milk bank on hospitalized premature neonates. The primary outcome measure was the incidence of necrotizing enterocolitis (NEC),retinopathy of prematurity (ROP), mortality rate during hospitalization, and sepsis. These outcomes were compared between the group of premature neonates who received milk from the human milk bank and the group that did not.

Sample population

This study involved premature neonates who were admitted to the NICU of a government medical college in Yawatmal, India and met the inclusion criteria. During the pre-launch period, the feeding of the neonates was primarily based on their mother's milk (MM) or infant formula. After the establishment of the human milk bank, the neonates received both mother's milk and pasteurized donor milk.

Data collection:

In this study, various maternal and neonatal characteristics were recorded and analyzed to assess their impact on the outcomes of hospitalized premature neonates. Maternal information in terms of Demography, antenatal medical risk factors, prenatal steroids usage were noted. Along with routine neonatal data we also recorded days of hospital stay, need for oxygen and type of respiratory support. Data regarding the type of milk used for feeding the neonates were collectedand information related to ROP(retinopathy of prematurity), NEC(necrotizing enterocolitis), LOS (late onset sepsis), mortality, and other related factors were gathered during hospitalization.

Data Analysis:

In this study, descriptive statistics were utilized to provide a comprehensive overview of the data collected. The frequency and mean (SD) were used to describe the data, and the Kolmogorov-Smirnov test, normal probability plot, and measures of dispersionwere used to evaluate the normal distribution of the data. To compare maternal-neonatal features, Fisher's exact tests and chi-square were used for qualitative variables, and for quantitative variables Independent t-test was used. P value < 0.05 was considered statistically significant.

3. RESULTS

Table 1. Comparison of basal characteristics of the patients

Characteristic		**Before Milk Bank (N = 148) (100%)**	**After Milk Bank (N = 162) (100%)**	**P-Value**
Gestational Age(Weeks)	<28	24(16.22%)	27(16.66%)	0.88
	28-30	40(27.02%)	47(29.1%)	
	30-34	84(56.76%)	88(54.32%)	
Birth Weight (G)(Mean)		1.45	1.42	0.9
Gender	Male	84(56.76%)	90(55.55%)	0.9

	Female	64(43.24%)	72(44.44%)	
Intrauterine Growth Restriction (Iugr)		15(10.14%)	20(12.35%)	0.598
Small For Gestational Age (Sga)		20(13.51%)	18(11.11%)	0.60
Maternal Age (Y), Mean		28.3	28.7	0.62
Mode Of Delivery	Vaginal	100(67.57%)	112(69.14%)	0.8
	Caesarean	48(32.43%)	50(30.86%)	
Hypertension		30(20.27%)	45(27.78%)	0.25
Preeclampsia		7(4.73%)	13(8.02%)	0.36
Gestational Diabetes Mellitus		16(10.81%)	10(6.17%)	0.22
Neonatal Feeding At Least During The First 28 Days Of Life	Mother Milk	43(29.05%)	58(35.80%)	<0.001
	Mother Milk + Donar Milk	0(0%)	38(23.46%)	
	Donar Milk	0(0%)	68(41.98%)	
	Mother Milk + Formula Feed	69(46.62%)	0(0%)	
	Formula Feed	36(24.32%)	0(0%)	

This study had enrolled 158 preterm neonates before the launch of human milk bank alongwith 168 neonates after launch. Out of 158 neonates in the pre-launch group,total 10 were excluded due tocauses like congenital abnormalities,early death etc. In the post-launch group, total 6 neonates were excluded due similar causes. In total, 310 neonates were included in the study, with 148 in the pre-launch group and 162 in the post-launch group.

The mean maternal age was comparable in both the pre-launch and post-launch groups, and both groups had similar demographic and maternal features. The gestational age, gender, and weight of neonates did not differ significantly between the two groups. (Table 1).

Descriptive statistics were used to report the feeding practices of neonates in both the pre-launch and post-launch groups. In the pre-launch group, 36 neonates (24.32%) received only artificial formula, and 69 neonates (46.62%) received both mother's milk and artificial formula. In the post-launch group, 58 neonates (35.80%) were exclusively fed mother's milk, 38 neonates (23.46%) were fed with a combination of mother's milk and donor milk, and 68 neonates (41.98%) were exclusively fed donor milk.(Table 1).

Table 2. Growth parameters of patients Comparison of clinical outcomes

Parameter	**Before Milk Bank (n = 148)**	**After Milk Bank (n = 162)**	**p-value**
Average hospital stay	19.4	17.2	0.19
Average Days on oxygen	10.3	7	0.03
Average Days on non-invasive respiratory support	8.4	6.7	0.73

Average Days on mechanical ventilation	6.5	4.8	0.24
Necrotizing enterocolitis	13(8.78%)	5(3.09%)	0.048
Late-onset sepsis	27(18.24%)	11(6.79%)	0.003
Retinopathy of prematurity (any stage)	16(10.81%)	4(2.47%)	0.004
Death	28(18.92%)	18(11.11%)	0.038

The incidence of Retinopathy of Prematurity was compared between the pre-launch and post-launch groups. 16(10.81%) neonates in the pre-launch group and 4(2.47%) neonates in the post-launch group were reported to have ROP. The statistical difference was statistically significant, with a P-value of 0.004. (Table 2).

Frequency of necrotizing enterocolitis was evaluated in both groups, and the results showed a significant difference(P-value of 0.048). In the pre-launch group, 13 (8.78%) neonates had significant NEC, while in the post-launch group, only 5 (3.09%) neonates had NEC.(Table 2).

The incidence of late onset sepsis in the post-launch group showed a significant reduction with 11 cases (6.79%) compared to 27 cases (18.24%) in the pre-launch group. The presence of the human milk bank had a notable impact with a 70.3% reduction in the risk of LOS among premature neonates (P-value = 0.003).(Table 2).

After launching the human milk bank, there was a significant decrease in neonatal mortality, with 28 (18.92%) deaths in the pre-launch group compared to 18 (11.11%) in the post-launch group(P = 0.038) (Table 2).

The post-launch group had a shorter average hospital stay, fewer days on non-invasive respiratory support, and fewer days on invasive respiratory support compared to the pre-launch group. However, these differences did not reach statistical significance.(Table 2).

The study indicates that creating a human milk bank can result in substantial advancements in neonatal outcomes such as decreasing ROP, NEC, LOS, and mortality.

4. DISCUSSION

Feeding preterm neonates with donor milk has been shown to be beneficial in reducing mortality and morbidity in cases where a mother's own milk is unavailable or insufficient. However, there have been concerns regarding the nutritional adequacy of donor milk compared to artificial formula, which is enriched with more nutrients, resulting in greater weight gain and linear growth. Preterm formulas are designed to provide higher energy and mineral content, as well as varying levels of protein, when compared to mature human milk. Additionally, pasteurization of donor milk may further compromise its nutrient content.[16,17,18]

In this study, the feeding practices of preterm babies were compared between the pre-launch and post-launch periods of milk bank. Before its launch, most preterm infants received both artificial formula and mother's milk (75.68%). However, after the launch, the majority of infants received both mother's milk and pasteurized donor milk, with the use of artificial formula being eliminated. The results showed a significant decrease in rates of NEC, LOS , mortality, and ROP in the post-launch group compared to the pre-launch group. Additionally, a reduction in the average hospital stay and the need for supportive care was observed in the post-launch group, although these differences were not statistically significant.

Numerous studies have reported similar findings, highlighting the potential benefits of pasteurized donor human milk (PDHM) in reducing the incidence of necrotizing enterocolitis

(NEC) in low-birth-weight (LBW) infants. For example, studies conducted by Chowning et al.[19] and O'Connor et al.[20] found significantly lower rates of NEC in the PDHM group compared to formula-fed groups. Cristofalo et al.[21] reported that infants receiving PDHM had significantly lower rates of surgical NEC compared to those fed with formula. Similarly, Quitadamo et al.[15] confirmed the protective effect of nutrition with mother's milk or donor milk against NEC in LBW infants. However, a Cochrane Systematic Review[18] showed that while formula-fed preterm infants experience rapid growth, they also have a nearly doubled risk of NEC progression, as observed by Larena et al.[22].In several studies, pasteurized donor human milk (PDHM) has been associated with a decrease in the incidence of retinopathy of prematurity (ROP). Kreissl et al.[23] reported a significant decrease in ROP from 13% to 4% in premature infants using DM ($P < 0.01$). However, Miller et al[10] found inconclusive evidence for the impact of any human milk versus preterm infant formula on either ROP or severe ROP in a systematic review and meta-analysis. In Korea, Kim et al.[24] showed a significant decrease in the rate of late-onset sepsis (LOS) in the donor group, and Cortez et al.[25] found that fewer infants fed own mother's milk suffered from LOS compared to the group fed formula. There is evidence to suggest a relationship between infection and nutrition among premature and low-weight infants, and the American Academy of Pediatrics recommends the use of donor milk in LBW infants when own mother's milk is unavailable, as it significantly decreases infections compared to formula[26]. Although a double-blind RCT by Willemijn E et al.[27] found no significant effect of PDHM during the first 10 days of life for preventing all-cause mortality in premature neonates, E. Narayanan et al.[28] observed a reduction in mortality after starting a human milk bank, which is consistent with the findings of this study.

5. CONCLUSION

Use donor milk instead of formula feed have less chances of developing NEC,ROP, SEPSIS and mortality in preterm neonates. Also any of the above complication occurs, it has better chances of early improvement if neonate fed with mother milk or donor milk.

Limitations-
The study's limitations must be considered while interpreting the findings. Firstly, the long-term effects of donor milk on the neurodevelopment of premature infants were not investigated. Secondly, as a retrospective study, the association observed between the study variables does not necessarily imply a causal relationship. Therefore, additional research is needed to explore the long-term effects of donor milk.
Conflicts of interest. None.

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