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Original Research Article

Association between Pasteurized Donor Human Milk and Neonatal Complications in a Tertiary Care Centre

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Abstract

Objective: To study neonatal complications associated with Pasteurized Donor Human Milk (PDHM) in a tertiary care Centre NICU.

Material and Methods: An observational prospective case control single Centre study. All details of the newborns under study were recorded on a structured proforma designed for this study. PDHM was issued from mother milk bank on the request of doctor working in the NICU. All collected data was analyzed with standard software. Statistical analysis of the data was done with Chi-square test, Student t-test with assistance of qualified statistician. P value <0.05 was considered statistically significant.

Results: A total of 140 neonates were included in the study was divided into study group (71) and control group (69). Majority of neonates on PDHM feeding (67.8%) tolerated the feed well, 20% had abdominal distention and 11.2% had vomiting. In study group 12% babies develop NEC, whereas 5.7% babies in control group developed NEC. In the study group 19.7% babies developed clinical features of septicemia whereas in control group only 10.1%. The difference was statistically significant.

Conclusion: Babies fed on PDHM had no significant risk for developing apnea, hypoglycemia and overall complications in comparison to those fed on mothers own milk. Also there was no significant difference in terms of weight recovery time, duration of stay in the hospital and final outcome amongst babies who were fed on PDHM and who were fed on mothers own milk. Hence it is concluded that PDHM can be a safer alternative when mothers own milk is insufficient or unavailable. Also it provides the benefits of mother's milk along with eliminating the demerits of formula feed in a resource limited setting like ours. "Breastfeeding is nature's health plan."

Keywords: Human Milk Bank, Pasteurized Donor Human Milk, PDHM, Neonatal Complications

Introduction

"Bottles fill his stomach, but breastfeeding fills his soul." Breast feeding is the best method of infant feeding because human milk continues to be the only milk which

is tailor made and uniquely suited to the human infant. All mothers should be encouraged to breast feed their infants. India faces its own unique challenges, having the highest number of low birth weight babies with significant morbidity and mortality.

Because of inadequate feeding due to any cause mothers start feeding their babies over-diluted and unhygienic top milk resulting into malnutrition and infections. The benefits of human breast milk include optimum infant growth, immune functions and development at minimum cost to the family [1].

It has been shown that human breast milk fed infants in the NICU have better feed tolerance, have fewer severe infections lesser chance of NEC and a reduction in chance of colonization by pathological organism. There is a decrease length of hospital stay of babies fed on human milk. Breast fed babies have better neurodevelopmental outcomes in comparison to formula fed one [2,3].

In spite of mother's will many a times she is not able to provide adequate milk to her baby due to various maternal and neonatal conditions like maternal chronic illness , perinatal complications , LSCS delivery ,multiples births , preterm birth , separation of baby from mother due to admission in NICU ,maternal stress , drug intake by mother like anti thyroid and anti-metabolites [4,5].

In these conditions to provide benefits of mother milk to these babies concept of mother milk bank, developed over time with aiming to provide mother milk to these babies especially the VLBW and ELBW neonates [7].

Mother Milk Bank

Historical perspective: It had already been demonstrated in the early twentieth century that infants who did not receive their mother milk had increased risk of dying in the first year of life.

Pediatricians concerned to improve the prognosis of infants deprived of their own mother's milk for medical and social reasons developed a means of storing human milk for use in sick infants, and thus first milk bank was opened in Vienna in 1900. First milk bank in America was established in 1910 in Massachusetts. The first international congress on Human Milk Banking "A vision of future" was held in Brazil in 2000. [8, 9]

Mother milk bank in India: Modern human milk banking is in its infancy in India. The first milk bank in Asia under the name of SNEHA was founded by Dr. Armeda Fernandez, in Dharavi, Mumbai on Nov 27, 1989. A national consultative meet for framing guidelines was summoned by the IYCF Chapter and the ministry of Health and Family Welfare, GOV of India on 30th June 2013, with representations from various stakeholders. [9]

Aims and Objectives: The aims and objective of the study is to study the impact of Human Milk Bank on morbidity, mortality, duration of stay, and feeding characteristics of neonates in tertiary care Centre NICU.

Material and Method:

Study type: An observational prospective case control single Centre study.

Study population: Newborns admitted in NICU at Department of Pediatrics.

Study group: Low birth weight and very low birth weight newborns (weight ≥1000g - <2500g) who were supplemented or completely on PDHM due to insufficient mother's milk. After counseling consent was taken preferably from mother or other family member if mother was unavailable to give consent. When mother milk became adequately available PDHM feeding was stopped.

Control group: Newborns who had similar weight and gestational age and were fed on mother's own milk.

Inclusion Criteria

Study group- Low birth weight and very low birth weight (weight ≥1000g - <2500g) newborns who were supplemented or completely on PDHM.

Control group- Low birth weight and very low birth weight (weight ≥1000g - <2500g) newborns who were fed on their own mother's milk.

Exclusion Criteria

- Babies who had any illness
- Parents who did not give consent
- Those babies who had any risk factor for sepsis

All details of the newborns were recorded on a structured proforma. Indication of admission, hour of life when enteral feeding was started, the indication of feeding the baby on PDHM ,hours of life when PDHM was started, amount of feed required per day, amount of PDHM given per day, percentage of daily feed requirement fulfilled by PDHM, percentage of PDHM issued out of PDHM demanded, duration of PDHM feeding, total volume of PDHM fed by the baby, tolerance of feed, weight changes on each day of stay , day of life on which daily feed requirement was fulfilled by enteral feed, motivation of mother to breastfed their baby, day of life on which transition from PDHM to own mother's milk occur, complication during stay in terms of NEC, probable sepsis, jaundice requiring phototherapy, hypoglycemia, apnea, length of stay in the hospital and final outcome was recorded on Performa.

A nutritional support protocol was used to ensure that milk advancement and use of parenteral nutrition was consistent for all study infants. Infants who weighed <1500g or gestational age <34 weeks were initially fed by tube feeding. The recommended volume goal for feedings was 140-160 ml/kg/day. Babies who weighed >1500g or >34 weeks were mostly fed on breast. PDHM was issued from mother milk bank on the request of doctor working in the NICU during the working hour in sealed glass bottles of 30ml each. Most of the feedings were given by patient mothers or care giver. Weight of the newborn was measured at the same time each day.

All the collected data was analysed with standard software of Biostatics. Statistical analysis of the data was done with Chi-square test (for quantitative analysis), Student t-test (for continuous data) with assistance of qualified statistician. P value <0.05 was considered statistically significant.

Result

Present study was observational prospective case control single centre study conducted in tertiary care centre NICU. This work was carried out to study the impact of human milk bank on the outcome of neonates in terms of complications. This study was conducted on LBW and VLBW neonates (weight ≥ 1 kg - < 2.5 kg) as they are the major beneficiaries of human milk bank with exclusion of neonates who had any illness at the time of recruitment for the study.

A total of 140 neonates were included in the study. These 140 neonates were divided into study group (71) and control group (69). Study group includes those neonates who were supplemented or completely on Pasteurized Donor Human Milk (PDHM), while the control group includes those neonates who were fed on their own mother's milk.

Table 1: Tolerance of Feed in Study and Control Group.

Tolerance of Feed	Study Group(n=71)	Control Group(n=69)
Abdominal distention	15(21%)	8(11.5%)
Vomiting	8(11.2%)	4(5.7%)
Well tolerated	48(67.8%)	57(82.8%)

Majority of the neonates on PDHM feeding 48(67.8%) tolerated the feed well. 15(21%) had abdominal distention and 8(11.2%) had vomiting. While in control group 57(82.8%) neonates tolerated the feed well, 8(11.5%) had abdominal distention and 4(5.7%) had vomiting. These feeding problems are not significantly more as compared to control group (p-0.121).

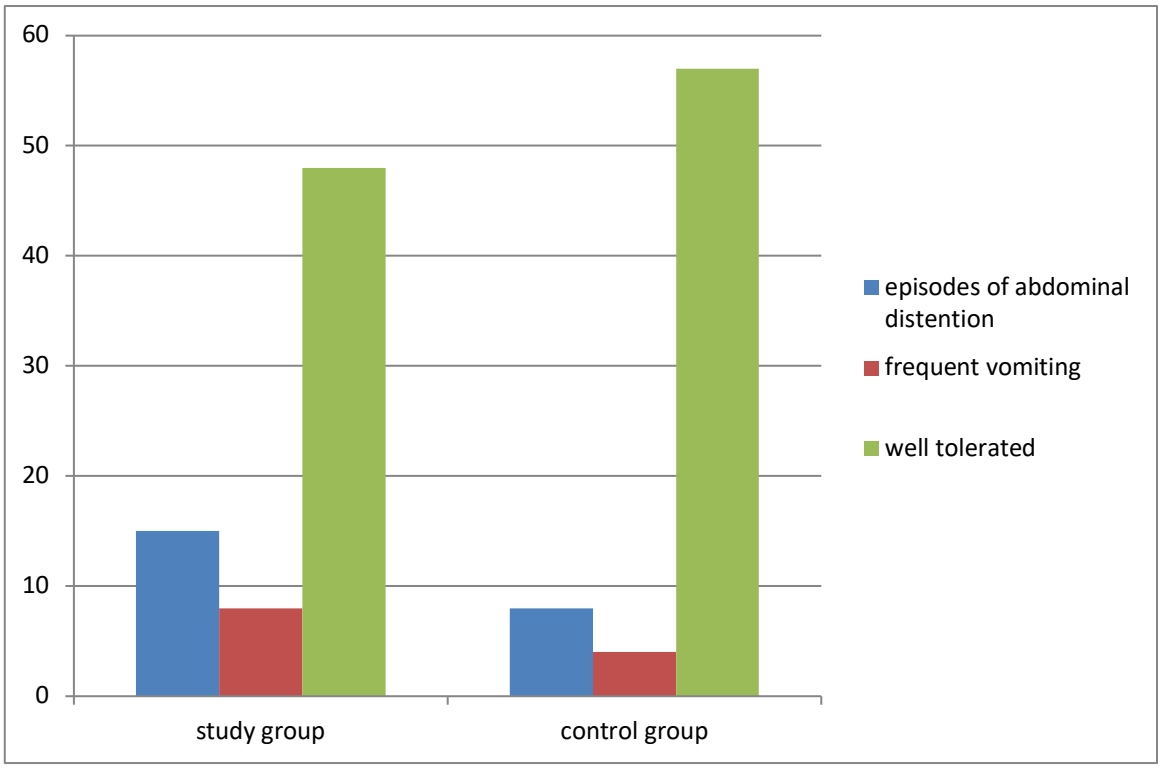

Figure 1: Distribution of Neonates Based on Tolerance of Feed

Table 2: Neonatal Complications in Study and Control Group

Complication	Study Group(n=71)	Control Group(n=69)
Necrotising Enterocolitis	9(12%)	4(5.7%)
Clinical sepsis	16(19.7%)	7(10.1%)
hypoglycemia	15(21.1%)	12(17.3%)
apnea	2(2.8%)	0(0%)
Jaundice requiring phototherapy	28(39.4%)	21(30.43%)

Nine babies (12%) developed NEC in study group whereas 4(5.7%) babies developed NEC in control group. The difference between two groups is statistically non-significant (p-0.160). Sixteen (19.7%) babies in study group and 7(10.1%) in control group developed clinical features of septicemia along with supportive evidence. The difference was statistically significant (p-0.047) Fifteen (21.1%) babies in study group had episodes of hypoglycemia as compared to 12(17.3%) in control group. The difference was statistically non-significant (p-0.575). Two (2.8%) babies in study group developed apnea whereas none babies developed apnea in control group. The difference was statistically non-significant (p-0.16). Twenty eight (39.4%) babies in study group developed jaundice requiring phototherapy whereas 21(30.43%) babies in control group developed jaundice requiring phototherapy. The difference was statistically non-significant (p-0.264).

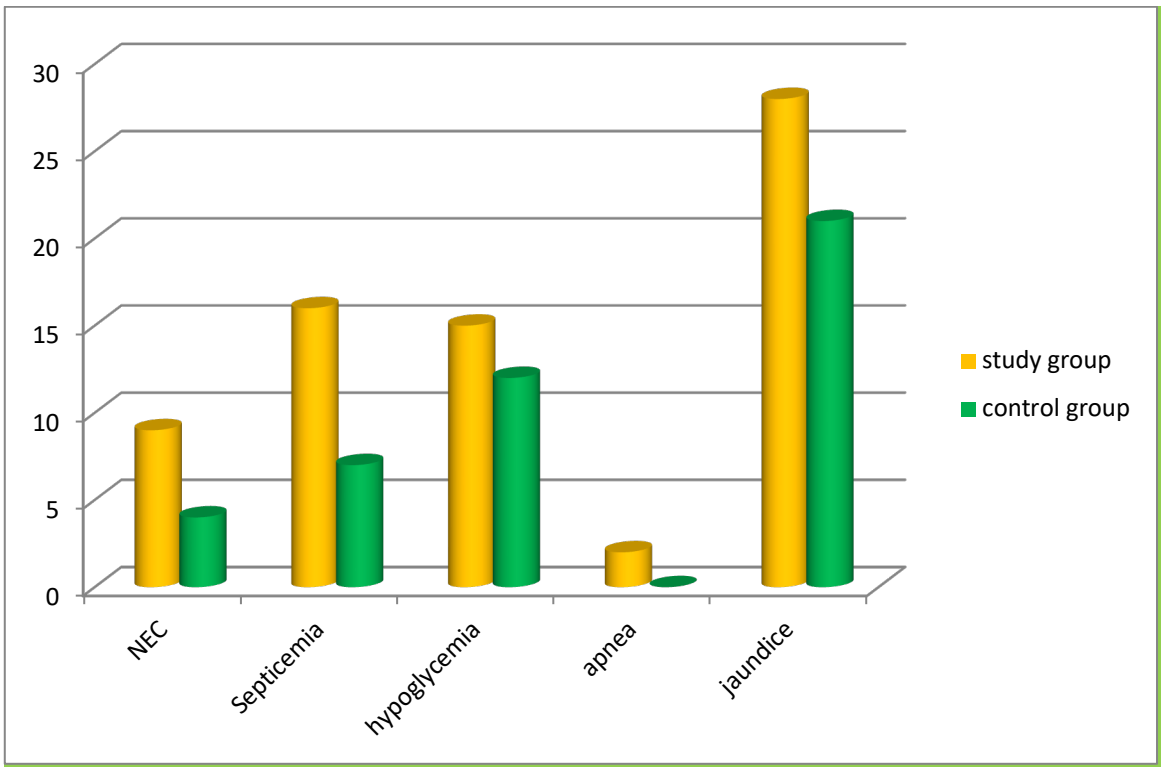

Figure 2: Prevalence of Neonatal Complications in Study and Control Group

Table 3: Neonates developing septicemia on the basis of number of days PDHM was supplemented in study group

Number of Days	Neonates developing Septicemia	Total Number of Neonates (n=71)
0-3	6(14.63%)	41
4-6	5(27.7%)	18
7-9	2(50%)	4
10-12	1(33%)	3
>12	2(40%)	5

Out of 41 neonates who were fed on PDHM up to three days 6(14.63%) developed septicemia, 5(27.7%) neonates out of 18 neonates who were fed on PDHM for the duration of 4-6 days developed septicemia. Two out of four neonates (50%) neonates who were fed on PDHM for 7-9 days developed septicemia. 1 out of 3 (33%) neonates who were fed on PDHM for 10-12 days developed septicemia. Two out of five (40%) neonates who were fed on PDHM for >12 days developed septicemia.

Table 4: Complication in Study Group and Control Group

Complication	Study Group(N=71)	Control Group(N=69)
Yes	23(32.4%)	15(21.7%)
No	48(67.6%)	54(78.2%)

Out of 71 neonates in study group, 23(32.39%) developed complications during their stay in the NICU, whereas 15(21.7%) neonates in control group developed complications during their stay in the NICU. The difference was statistically non-significant (p value-0.156).

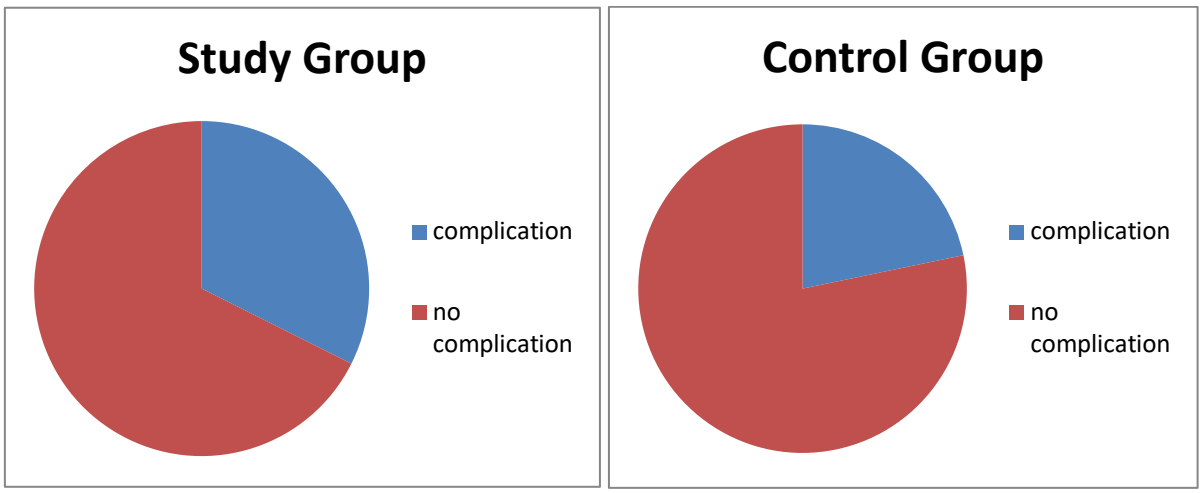

Figure 3: Comparison between Study Group and Control Group on Basis of Complications

Discussion

Majority of the neonates on PDHM feeding 48(67.8%) tolerated the feed well. 15(21%) had abdominal distention and 8(11.2%) had vomiting. While in control group 57(82.8%) neonates tolerated the feed well, 8(11.5%) had abdominal distention and 4(5.7%) had vomiting. These feeding problems are not significantly more in study group as compared to control group (p-0.121). [Table 1] Assad M *et al* observed that implementing an exclusive human milk diet in very low birth weight infants decreases the incidence of feeding intolerance. Vohr D R *et al* in a study on ELBW infants also observed that clinical feeding tolerance is improved by a diet of human milk. In our study both the groups were fed on breast milk either own mothers milk or PDHM, hence tolerance is similar in both study and control group. [10] Another study by Coutsoudis *et al* shows feeding intolerance is relatively less in neonates on PDHM (11.1%) in comparison to those on formula milk (22.7%). The difference was statistically non-significant [11].

The immunological and biologically active substance present in human milk modify the GI flora and imparts better feed tolerance feature in comparison with formula milk. Out of 71 neonates fed on PDHM only 9(12%) babies developed NEC in study group whereas 4(5.7%) babies developed NEC in control group. The difference between two groups was statistically non-significant (p-0.160) (table no 10). Schanler*et al* found a 6% incidence of NEC in the group of neonates fed with donor human milk, 11% in the group of preterm formula whereas 6% in the own mother milk group. The difference was statistically non-significant (p-0.39) [12]. Aprile M D M *et al* in a similar study observed that 10% neonates were supplemented with donor human milk developed suspect light NEC whereas none neonates who were fed on their mother's milk developed NEC. The difference was statistically non-significant (p-0.5597). Several other studies also confirmed that neonates fed on formula milk had relatively higher chances of developing NEC in comparison to those fed on donor human milk [13].

Several studies show that donor human milk, typically the breast milk of mothers who delivered at term has a lower content of protein and host defence protein then the breast milk of a mother who delivered a preterm infant. The process of pasteurization significantly affects the immunological and biologically active components present in human milk. These immunologically and biologically active components modulate the gut flora and provide protection against NEC [14].

Sixteen (19.7%) babies in study group as compared to 7(10.1%) in control group developed clinical features of septicemia along with supportive evidence. The difference was statistically significant (p-0.047). [Table 2] Though the gold standard for diagnosing septicemia is culture of blood or any other body fluid, because of the low yield of blood culture(40% and 41.1%) in the previous studies in our own NICU and 32% – 48% in data published by National neonatal perinatal database report 2002-2003 we did not send culture of all babies with suspected sepsis.

Aprile M D M *et al* found that 33.3% neonates who were fed on their own mothers milk developed septicemia whereas 23.3% neonates who were fed on donor human developed sepsis. The difference was statistically non-significant (p-0.6893). Schanler *et al* found that late onset sepsis incidence was 29% in the group of neonates fed with donor milk, 23% in the maternal milk group and 30% in group using formula milk. The difference was statistically significant (p-0.022) [15].

Biologically and immunologically active substance present in human milk may provide protection against infection. These components are less in donor human milk due to their loss during pasteurization. It is also important to know that these biologically active anti-infective agents are more in preterm as compared to term breast milk. In the PDHM there is a pool of preterm and term milk, hence the higher concentration of anti-infective agent in preterm milk are further diluted when it is pooled with term mother milk. When the availability of PDHM is inadequate, mainly due to limited working hour of milk bank (9 am to 5 pm) and the mothers own milk is also deficient to compensate to fulfil the need of the baby. Fifteen (21.1%) babies in study group had episodes of hypoglycemia as compared to 12(17.3%) in control group.

The availability of donor Pasteurized human milk is limited 9 am to 5 pm, which expose babies dependent on PDHM to the risk of inadequate feeding during the evening and night time which may lead to hypoglycemia also De Moraes *et al* in their study "caloric profile of pasteurized milk in the human milk bank at a university hospital" observed that a large volume of collected milk is hypochloric. Despite this the difference was statistically non-significant (p-0.575). [Table 2]

Two (2.8%) babies in study group developed apnea whereas no baby developed apnea in control group. Despite the higher incidence of apnea in study group which may be due to higher incidence of complications the difference was statistically non-significant (p-0.16). Earlier no similar study has been done to see the incidence of apnea. Twenty eight (39.4%) babies in study group developed jaundice requiring phototherapy whereas 21(30.43%) babies in control group developed jaundice requiring phototherapy. The difference was statistically non-significant (p-0.264). [Table 2]

Coutsoudis *et al* in their study "feasibility and setting up a donor breast milk bank in a neonatal unit in a resource limiting setting : A longitudinal observational cohort study in preterm babies" observed that 81.8% neonates fed on formula milk and 83.3% neonates fed on breast milk developed jaundice [16]. The result was statistically non-significant. Higher proportion of neonates who were fed on PDHM for more number of days developed septicemia in comparison to those fed on PDHM for lesser number of days. This is probably due to more dependency on PDHM which is immunologically and biologically poorer than mothers own milk. No other study has been done regarding the duration of PDHM feeding and its relation with development of septicemia. [Table 3]

Out of 71 neonates in study group, 23(32.39%) developed complications during their stay in the NICU, whereas 15(21.7%) neonates in control group

developed complications during. There was no statistically significant difference (p-0.156) in the clinical complication between the study and control group. Aprile M D also found statistically non-significant result in clinical complications when comparing preterm neonates fed on donor human milk to those fed on mother's own milk. [Table 4]

Conclusion

Babies fed on PDHM had no significant risk for developing NEC, apnea, hypoglycemia, jaundice and overall complications in comparison to those fed on mothers own milk. Also there was no significant difference in terms of weight recovery time, duration of stay in the hospital and final outcome amongst babies who were fed on PDHM and who were fed on mothers own milk. But babies fed on PDHM had significantly higher risk of developing clinical features of septicemia and PDHM feeding also had significant negative impact on motivation of mother to breast feed. Hence it is concluded that PDHM can be a safer alternative when mothers own milk is insufficient or unavailable. Also it provides the benefits of mother's milk along with eliminating the demerits of formula feed in a resource limited setting like ours.

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