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Original Article

Addition of human milk fortifier in breast milk on increasing body weight of premature infants

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ABSTRACT

Introduction: Human Milk Fortifier (HMF) is an additional supplement for breast milk that can meet the nutritional needs of premature. One of the efforts to support the growth of premature babies is to fulfill their nutritional intake. Objective: This study aims to determine the effectiveness of giving HMF to breast milk on increasing the weight of premature babies in Neonatal Intensive Care Unit.

Methods: The research design used a quasi-experiment design with a pre-test and post-test nonequivalent control group design. The samples are premature babies treated in the NICU in Surabaya. The sample technique used purposive sampling of 25 respondents as the treatment group (breast milk + HMF) and 20 respondents as the control group (breast milk only). The instrument uses a questionnaire and observation sheet. Data were analyzed using the repeated measures ANOVA test and the independent sample t-test. The repeated measures ANOVA test results indicate a statistically significant difference in weight gain over time (*P*-value <0.05), demonstrating that HMF supplementation contributes more effectively to weight gain compared to breast milk alone.

Results: The study demonstrated a significant increase in body weight over time in both the treatment group and the control group, as measured by the Fenton chart (weight on days 7, 14, 21, and 28) with a *P*-value = 0.000. Notably, the treatment group (HMF+breast milk) exhibited a more pronounced weight gain by day 28 compared with control group (breast milk only), with a *P*-value = 0.015, indicating the superior efficacy of breast milk+HMF in promoting weight gain.

Conclusion: Adding human milk fortifier to breast milk effectively increases weight in premature infants due to its high-calorie content. It is particularly beneficial for infants requiring fluid restrictions.

Keywords: fenton chart, human milk fortifier, premature baby's weight, quasi-experiment non-equivalent control group design

INTRODUCTION

Marriage is the completion of half of religious obligations Weight gain is a critical concern in the care of premature infants. Typically, newborns rely on breast milk to fulfill their nutritional requirements. However, for premature infants, the protein and fat content in breast milk may not be sufficient to compensate for their growth delays. To address this, human milk fortifier (HMF) supplementation can be added to breast milk. HMF provides higher levels of calcium, phosphorus, carbohydrates, and protein, which are essential for premature infants' growth and development. It is important to note that HMF is only used under medical guidance (Koletzko & Osterrieder, 2009).

In 2020, approximately 13.4 million babies were born preterm, representing about 1 in 10 live births worldwide, or 10% of all births (Ohuma et al., 2023). In East Java, data from the Central Statistics Agency reveal that 3.75% were premature babies. Additionally, between January 2021 and December 2022, 46.25% of premature infants treated in the NICU were either born in the hospital or referred from other facilities.

Premature infants, defined as those born before 37 weeks of gestation, face numerous health challenges. These include limited nutritional reserves, immature metabolic systems, incomplete absorption pathways, and underdeveloped oromotor functions, all of which increase the risk of weight loss. Premature and very low birth weight infants have nutritional requirements distinct from full-term infants. HMF administration can begin when enteral nutrition intake reaches 100 ml/kg/day (Zhang et al., 2022).

Several studies have demonstrated improved growth outcomes in low birth weight infants who received HMF. HMF administration can begin when enteral nutrition intake reaches 50-100 ml/kg/day (Koletzko & Osterrieder, 2009). Without adequate energy and protein, extrauterine growth can be compromised. Aggressive nutritional interventions, including protein and fat as non-protein energy sources, along with early enteral feeding, are critical to stimulate intestinal villi growth. Therefore, HMF supplementation is a key strategy for ensuring adequate nutrition in premature infants. Human milk fortifiers provide additional calories, protein, and essential vitamins that promote bone growth and development. Increasing the intake of carbohydrates, proteins, vitamins, and minerals can significantly enhance the growth rate of premature infants (Harding, 2017). This study aims to investigate the impact of HMF supplementation on weight gain in premature infants.

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METHODS

Study Design

This quasi-experimental study employed a pre-test and post-test nonequivalent control group design. The experimental group (breastfeeding + human milk fortifier) and the control group (breastfeeding only) were not randomly selected. Both groups underwent initial testing.

Sample and Setting

The sample comprised 40 premature infants hospitalized in the NICU in Surabaya from March 2022 to December 2022. Inclusion criteria included gestational age <37 weeks, enteral nutritional intake of 80-100 ml/day, and feeding via orogastric tube. Exclusion criteria included oral or bottle feeding, severe asphyxia, digestive tract disorders, and neonatal sepsis.

Variable, Instrument, and Data Collection

Data collection involved a demographic questionnaire and observational sheets. Demographic data included gender, birth weight, gestational age, chronological age, corrected age, complications, diet type, drinking frequency and amount in 24 hours, and feeding method. The independent variable (breast milk with HMF) was measured using an observation sheet detailing sampling code, type of enteral nutrition (one sachet of Enfamil HMF mixed with 25 ml of breast milk), and the amount given (25 ml every three hours, eight times daily). The dependent variable (weight gain) was measured using an observation sheet with sampling code, pre-test weight, and weights on days 7, 14, 21, and 28, converted to Fenton chart percentiles. The research was conducted starting with the preparation of a proposal, data collection and preparation of a report in March 2022-March 2023.

Data Analysis

Bivariate analysis was conducted using the repeated measures ANOVA test to assess the effect of breast milk+HMF on weight gain over five measurement points (pre-test, days 7, 14, 21, and 28). Normality was confirmed using the Shapiro-Wilk test, with significance *P*-value >0.05 indicating normally distributed data.

Ethical Consideration

This research was approved by the ethics committee of Premier International Hospital, Indonesia vide reference number 07/RSPS/ KERS/XI/2022.

RESULTS

The results presented below offer a detailed comparison of weight gain between the treatment group and the control group over time.

Demographic Data

Table 1 reveals that the demographic characteristics of both groups are comparable in terms of gender distribution, gestational age, and birth weight, all of which are critical factors that may influence weight gain outcomes. Notably, the treatment group had a higher proportion of infants with birth weights between 1500-1999 grams (56%) compared to the control group (25%). Additionally, the frequency and volume of feeding were notably higher in the control group, with 70% of infants receiving more than 200 ml/day.

Body Weight in Treatment and Control Group

In the treatment group, a steady and significant increase in weight was observed over the 28-day period, as shown in Table 2. The results of the study showed an increase in body weight every week in the treatment group that received breast milk and HMF. By day 28, 96% of infants in the treatment group achieved "Good" weight gain according to the Fenton chart, demonstrating a significant improvement from baseline. A repeated measures ANOVA revealed a statistically significant increase in weight gain over time (*P*-value <0.05), indicating that HMF supplementation had a pronounced impact on weight gain.

The research results based on the Table 3 show an increase in body weight every week in the control group that only received breast milk. At day 28, only 60% of infants in the control group achieved "Good" weight gain, with 30% attaining "Sufficient" weight gain. A small proportion (10%) continued to exhibit "Low" weight gain. The repeated measures ANOVA also showed a significant difference in weight gain over time (*P*-value <0.05), although the results were less pronounced than in the treatment group.

Differences in Weight Gain in the Treatment and Control Group

Table 4 showed that in both groups there was a significant increase in body weight every week from day 1 to day 28. However, when comparing the two groups, the weight gain achieved by the two groups each week did not differ significantly on days 7, 14, or 21. The difference in weight gain in the two groups was significant on day 28. By day 28, infants in the treatment group had gained significantly more weight, with a mean increase of 937.4 grams compared to 672.5 grams in the control group. The difference in average weight gain was statistically significant (*P*-value = 0.015), highlighting the efficacy of HMF in promoting weight gain compared to breast milk alone.

DISCUSSION

Weight Gain of Premature Babies Before and After Giving Breast Milk + HMF in the Intervention Group

Table 2 shows that from 25 babies in the treatment group (breast milk + HMF) there was a significant increase in the weight of premature babies. This study showed an increase in weight than before giving breast milk + HMF, weight on days 7, 14, 21 and 28. From each weight measurement based on the Fenton percentile chart, there were babies who achieved a "Good" weight gain starting with 19 babies increasing to 21 babies on day 7. Then it decreased to 20 babies on day 14 and increased to 24 babies on days 21 and 28.

HMF content includes protein, calcium, phosphorus and other nutrients that can increase the nutrition of premature babies to catch up on the growth of premature babies (Gu et al., 2021). Based on Cochrane Reviews, it was found that multicomponent fortification of breast milk can increase nitrogen retention, improve growth, and bone mineral content. Fortification begins if drinking tolerance is >100ml/kgBW/day (Zhang et al., 2022). The findings of the current study demonstrate a clear advantage in using HMF to promote

Table 1. Demographic data of premature babies in the NICU Room of the Hospital in Surabaya (Treatment = 25 babies, Control = 20 babies)

Demographic Data of Respondent	Treatment Group		Control Group	
	n	%	n	%
Gender				
Baby boy	13	52.0	12	60.0
Baby girl	12	48.0	8	40.0
Birth Weight				
<1000 gram	2	8.0	0	0.0
1000-1499 gram	6	24.0	7	35.0
1500-1990 gram	14	56.0	5	25.0
>2000 gram	3	12.0	8	40.0
Gestational Age				
24-30 week	10	40.0	6	30.0
31-36 week	15	60.0	14	70.0
37-38 week	0	0.0	0	0.0
Age				
1-9 days	14	56.0	14	70.0
10-20 days	9	36.0	4	20.0
21-30 days	0	0.0	2	10.0
>30 days	2	8.0	0	0.0
Correction Age				
29-34 week	13	73.3	17	85.0
35-37 week	12	26.7	3	15.0
Disease Complication				
Asphyxia	3	12.0	3	15.0
PDA	8	32.0	5	25.0
ASD	11	44.0	9	45.0
Sepsis	2	8.0	2	10.0
Persistent Pulmonary Hypertension of Newborn	1	4.0	1	5.0
Nutrition Type				
Breastmilk	0	0	20	100
Breastmilk + HMF	25	100	0	0.0
Feeding Frequency				
4x/day	3	12.0	3	15.0
8x/day	22	88.0	17	85.0
Amount of Nutrition				
100-200 ml	24	96.0	6	30.0
> 200 ml	1	4.0	14	70.0
Feeding Method				
Oral/ bottle	0	0.0	0	0
OGT/NGT	25	100	20	100

Note: HMF (Human Milk Fortifier)

Table 2. Increasing body weight in the treatment group (breastmilk + HMF)

Increasing Body Weight	Body Weight									
	Pre-test		Post day 7		Post day 14		Post day 21		Post day 28	
	n	%	n	%	n	%	n	%	n	%
Low	2	8.0	2	8.0	1	4.0	1	4.0	1	4.0
Sufficient	3	12.0	1	4.0	3	12.0	0	0.0	0	0.0
Good	19	76.0	21	84.0	20	80.0	24	96.0	24	96.0
Over	1	4.0	1	4.0	1	4.0	0	0.0	0	0.0
Total	**25**	**100**	**25**	**100**	**25**	**100**	**25**	**100**	**25**	**100**

Statistic test - Repeated Measures Anova *P*-value =0.000; α=0.005

Table 3. Increasing body weight in the control group

Increasing Body Weight	Body Weight									
	Pre-test		Post day 7		Post day 14		Post day 21		Post day 28	
	n	%	n	%	n	%	n	%	n	%
Low	2	10.0	2	10.0	2	10.0	1	5.0	2	10.0
Sufficient	1	5.0	3	15.0	4	20.0	6	30.0	6	30.0
Good	17	85.0	15	75.0	14	70.0	13	65.0	12	60.0
Over	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Total	**20**	**100**	**20**	**100**	**20**	**100**	**20**	**100**	**20**	**100**

Statistic test - Repeated Measures Anova *P*-value =0.000; α= 0.05

Table 4. The differences in weight gain in the treatment group and control group

Time	Treatment group			Control group			*P*-value
	Mean	St. Deviation	n	Mean	St. Deviation	n	
Pre-test	1638.60	227.411	25	1769.00	258.012	20	0.079
Day 7	1871.60	208.770	25	1914.00	258.928	20	0.546
Day 14	2110.00	168.90	25	2080.00	252.982	20	0.637
Day 21	2337.20	131.673	25	2252.50	229.456	20	0.127
Day 28	2576.00	135.370	25	2441.50	199.058	20	0.015

Statistic test - Repeated Measures Anova *P*-value =0.000; α= 0.05

weight gain in premature infants. The significant weight gain observed in the treatment group, especially by day 28, aligns with previous studies highlighting the benefits of nutrient fortification in breast milk for preterm infants.

In this study, breast milk fortification was given after enteral administration of 80-100ml/kg/day when the stomach tolerates increased osmolarity and to catch up on growth if given earlier. By adding HMF to breast milk, it can increase and improve the calorie content or quality of breast milk so that the nutritional needs of premature babies can be met as indicated by an increase in body weight every day. In providing HMF in breast milk, it is adjusted to the enteral nutritional needs of each premature baby, which vary according to the instructions and recommendations of the pediatrician.

However, there was one baby with poor criteria in the pre-test until day 28. Based on demographic data, the one baby had a history of patent ductus arteriosus (PDA). Heart disorders or congenital heart disease (CHD) that are often found in premature babies are PDA which persists until the baby is three days old, especially in babies with hyaline membrane disease (Alyousif et al., 2021). Nutrition is important to ensure adequate energy for basal metabolism, growth, and physical activity especially for a premature baby (Hossain et al., 2021). PDA is associated with mild to severe gastrointestinal complications such as feeding intolerance, gastrointestinal perforation, and necrotizing enterocolitis, which are major challenges in nutritional management in premature infants (Lembo et al., 2023). The study's findings also underscore the importance of managing comorbid conditions, such as PDA, which were present in some infants. The results suggest that while HMF contributes to significant weight gain, comorbidities may still impede growth in some cases, which should be factored into nutritional interventions.

Weight Gain of Premature Babies in Control Group (Breast Milk Only)

Table 3 shows that from 20 respondents in the control group there was also a significant increase in premature infant weight in the pre-test (day 0), days 7, 14, 21 and 28. 85% of infants on day 0 had achieved a "Good" weight gain but decreased from day 7 to 75% of infants, on day 14 to 70% of infants, day 21 to 65% and on day 28 there were 65% of infants achieving good condition. There were two infants who had a weight with the "Bad" criteria on the Fenton chart from pre-test to day 28. This is because the two babies had a history of ASD complications. A history of congenital heart disease complications is a factor that causes premature infants to have difficulty gaining weight.

Birth weight was statistically related to weight gain according to the Fenton graph in LBW. One of the causes of increased weight in premature babies is the obstruction of early enteral nutrition and the lack of adequate parenteral nutrition, which will result in more than normal weight loss in early life (Yitayew et al., 2021). Infants with congenital heart disease have a high metabolic rate and are at risk of experiencing energy deficiency and have a significant risk of energy imbalance due to increased energy expenditure and inadequate nutrient intake so that optimal nutritional support is needed (Alyousif et al., 2021). Protein is more strongly correlated with growth than other macronutrients and protein intake in the second week is most strongly correlated with head circumference growth. Protein intake can decrease significantly in the second week after birth during the transition from intravenous to enteral feeding, if breast milk is not fortified (Yitayew et al., 2021). Unfortified breast milk at 150 mL/kgBW/day only supplies 2g/kgBW/day of protein, in contrast to fortified breast milk which can provide 3.5 to 4.1 grams/kgBW/day. Preterm infants often experience drinking intolerance, which is the inability to digest enteral nutrition characterized by increased gastric residue, abdominal distension and/or vomiting. Most cases of feeding intolerance are caused by immaturity of the digestive tract in preterm infants. Preterm infants also have immaturity of mechanical functions, such as sucking-swallowing coordination, gastroesophageal sphincter tone, gastric emptying and intestinal motility (Kim et al., 2015). As a result of feeding intolerance, the achievement of full feeding in preterm infants can be hampered, which can cause nutritional disorders.

Heart disorders that often occur in premature infants are ventricular septal defects which are often experienced by premature infants weighing less than 2500 grams and gestational age less than 34 weeks. Most are treated with fluid restriction. Fluid restrictions on the intake of premature babies will also affect the increase in body weight each day. Providing enteral nutrition such as breast milk is indeed very good, but it must still be considered that balanced and adequate nutritional needs are needed in premature babies which need a lot of calories to be able to catch up on their growth. The faster the nutritional needs are met, the faster the growth and weight gain of premature babies will be. Therefore, premature babies really need energy for basal metabolism, activity, cold stress, specific dynamic activities, for defecation and for growth.

Impact of HMF in Body Weight of Premature Baby

The average weight on day 0 in the treatment group with the control group had an average difference of 130.4 grams higher in the control group. Although both groups experienced an increase in average weight starting from day 7, 14, 21 and 28, the average weight gain in the treatment group tended to be higher than the control group. The treatment group showed a weight gain in the range of 227.2 - 238.8, while the control group was in the range of 145-189 grams. The average difference in weight gain of the two groups was 42,400 grams. The study found a statistically significant difference in weight gain between the treatment and control groups by day 28, supporting the hypothesis that HMF provides enhanced nutritional benefits over breast milk alone. The p-value of 0.015 indicates clinical significance in this weight gain, especially considering the accelerated growth trajectory in the treatment group.

Factors that influence weight gain on post-day 7 are respondents with complications or a history of diseases such as sepsis, asphyxia and persistent pulmonary hypertension of newborn (PPHN). On the other hand, organs of premature babies are not yet mature. Thus, giving HMF to premature babies helps achieve optimal nutrition. Breast milk fortification contains bovine whey-predominant protein or hydrolysate, carbohydrates that specifically consist of glucose/maltodextrin polymers, contains sodium, calcium and phosphorus and vitamins that can help meet the nutrition of premature babies optimally.

The difference in the average weight gain of the two groups is 30.00 grams. Body weight of premature babies without complications will grow faster when compared to premature babies with complications. With the presence of immature organs, fluid restrictions must be imposed due to complications which will affect the nutritional intake obtained. Complications experienced by infants can affect weight in various ways. In addition to affecting the tolerance of the amount of fluid intake, complications and accompanying diseases can also affect metabolism in neonates. catabolism becomes higher, thus affecting weight gain. On the other hand, unstable hemodynamics can increase glucose uptake in the heart, thus affecting the baby's metabolism and weight.

However, in giving HMF fortification, several things need to be considered, including the age of the baby, the baby's weight, the ability of the baby's digestive system function and paying attention to the dose given according to the recommendations of the pediatrician. In previous studies, there was a difference in weight gain and body length of babies between breast milk with HMF compared non-HMF. Standard fortification can provide the recommended energy, but does not provide adequate protein for premature infants (Arslanoglu et al., 2019).

The results of this study were influenced by several factors. As mentioned earlier, complications and comorbidities varied, which made it challenging to gain weight in both groups. Consequently, the provision of HMF to the treatment group in this study led to weight gain that may not have been optimal due to these complications. In the control group, there was also a natural increase in weight, which further highlights the benefits of breast milk in providing essential nutrients for infants. However, in clinical settings, there are often situations where immediate weight gain is considered necessary to improve the baby's condition, making HMF a recommended option. Additionally, the sample size in this study was limited, given the strict clinical criteria for administering either HMF or breast milk alone.

CONCLUSION

HMF administration has been proven to increase the weight of premature neonates with LBW. Significant impact occurred mainly on the 28th day of HMF and breast milk administration in the treatment group compared to the control group that only received breast milk. This study recommends HMF administration especially in neonates with clinical considerations that require weight gain that must be achieved immediatelys.

Declaration of Interest

There are no conflicts of interest.

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Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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