

Comparison of the effectiveness of giving breast milk (ASI) and Human Milk Fortifier (HMF) with breast milk in premature babies at H. Adam Malik general hospital Medan

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Abstract

Currently, premature baby care in neonatology units in terms of weight gain and the need for proper nutritional intake is very necessary. Human Milk Fortifier (HMF) is the method of choice for optimizing the nutritional composition of breast milk. Studies have shown that proper use of HMF can increase the growth rate of premature babies, prevent extrauterine growth restriction (EUGR) and nutritional deficiencies, and does not increase the risk of feeding intolerance (BE). Care of premature babies in the neonatology unit in terms of weight gain and the need for proper nutritional intake is very necessary, namely by providing. Human Milk Fortifier (HMF) added to breast milk. The purpose of this study was to determine the comparative analysis of effectiveness of providing breast milk and Human Milk Fortifier (HMF) with breast milk in premature infants. Analytical Study - Retrospective Cohort, a sample of all premature infants treated in the Neonatology Room of H. Adam Malik General Hospital Medan from November 2020 to April 2023. Eligible samples were divided into 2 groups, namely the breastfeeding group and HMF or only breastfeeding. Data were analyzed using SPSS Ver. 25 program with statistical tests Repeated ANOVA, post hoc, and Mann-Whitney (95% CI and significance $p < 0.05$). Infant weight was seen to show an increasing trend from the first day to the 7th day of monitoring in both groups. By using the test, Mann-Whitney showed that there was a significant difference in delta (weight gain) between the group of infants given breast milk and HMF and the group of infants given only breast milk ($p = 0.009$). D-dimer values have no association with mortality in children confirmed with Covid-19.

Keywords: Weight, Premature babies, Breast milk, HMF

Introduction

Premature babies are live births with a gestational age of < 37 weeks. Approximately 15 million premature babies are born each year, of whom 6.7% die. As highlighted World Health Organization (WHO) Preterm birth has become an important cause of death in children under 5 years. Almost all countries with available data show that the number of preterm births is increasing. Early nutritional support plays an important role in the survival, growth, metabolism, and immunity of premature babies. The final period of pregnancy is a key period for accelerating the absorption and accumulation of nutrients in the fetus. Preterm birth will cause the neonate to miss the nutrient accumulation stage, which will cause nutritional deficiencies, physical growth deficits, delayed neurological development, and affect the long-term growth and development of the newborn (World Health Organization, 2012).

WHO antenatal care guidelines include interventions that are key to help prevent preterm birth, such as counseling on healthy diet and optimal nutrition, fetal ultrasonography (USG) measurements can help

determine gestational age and detect multiple pregnancies with a minimum of 8 visits to a health professional during pregnancy to identify and reduce preterm birth (Karim et al., 2019).

The best source of nutrition for premature babies is breast milk, which plays an important role in building healthy gut nutrition and improving the baby's neurological and immune development. However, breast milk is influenced by maternal nutrition, health, mental condition, and other factors. As a single source of nutrition, breast milk cannot meet the nutritional needs of premature babies who are born with nutritional deficits and need to catch up to ensure optimal growth and development. At the same time, the condition of the baby is underdeveloped, premature babies tend to have a limited capacity to consume fluids and various nutrients, which hinders the ability of nutrition to reach the recommended intake (Roggero et al., 2020).

A number of studies have reported that adding Human Milk Fortifier (HMF) to breast milk can effectively supplement premature babies' needs for protein, calcium, iron, phosphate, and other

nutrients. Human Milk Fortifier (HMF), also known as human milk nutritional supplement, is a multivitamin additive rich in protein, energy, vitamins, iron, and minerals that is usually in liquid or powder form. In the United States, United Kingdom, and other developed countries, HMF has been used as an intervention to meet the nutritional needs of premature infants in neonatal intensive care units, neonatal care units, and after discharge (McCormick et al., 2021).

Breastfeeding is usually given 6-48 hours after birth. Human Milk Fortifier (HMF) is added later when the breast milk volume reaches 100 mL/kg/day. The use of HMF complements the nutritional deficiencies of breast milk. Human Milk Fortifier (HMF) can guarantee the nutritional needs and growth of premature babies.

In its use, it is necessary to exclude conditions in babies who are allergic to milk protein, congenital malformations and premature babies who have undergone surgery after birth. Compared with babies who are breastfed with additional HMF derived from cow's milk, babies who are breastfed with HMF derived from breast milk have a higher level of necrotizing enterocolitis (NEC) and better feeding tolerance (Hopperton et al., 2019).

Human Milk Fortifier (HMF) is the preferred method for optimizing the nutritional composition of breast milk. Studies have shown that proper use of HMF can increase the rate of early weight gain in premature infants, prevent extrauterine growth restriction (EUGR) and nutritional deficiencies, do not increase the risk feeding intolerance (FI) and NEC in newborns (Ji et al., 2020).

Currently, premature baby care in neonatology units in terms of increasing body weight and the need for proper nutritional intake is very necessary. So based on the review above, this study was conducted to see the comparison of the effectiveness of providing breast milk and HMF with breast milk for premature babies at H. Adam Malik General Hospital, Medan.

Research Methods

The research design used was (Analytical - Retrospective Cohort) to determine the comparison of the Effectiveness of Giving Breast Milk and HMF

with Breast Milk in premature babies at H. Adam Malik General Hospital, Medan. This study was conducted in the Neonatology ward of H. Adam Malik General Hospital, Medan during the research period from October 2022 to May 2023. The population of this study was all premature babies treated in the Neonatology Room at H. Adam Malik General Hospital, Medan. The sample in this study is the entire population that meets the inclusion and exclusion criteria as follows:

Inclusion criteria:

All premature babies treated in the Neonatal Room of H. Adam Malik General Hospital Medan from November 2020 to April 2023.

Exclusion criteria:

- Babies with incomplete physical examination data
- Babies who have congenital abnormalities or congenital diseases

So the minimum sample size for each group in this study was 21 babies (the group of premature babies given breast milk and HMF was 21 babies, and the group of premature babies given breast milk was 21 babies).

All infants treated in the neonatology room with data collection from neonatology medical records at H. Adam Malik General Hospital. Data collection started from November 2020 to April 2023.

In this study, the data obtained will be analyzed statistically and presented in the form of a frequency distribution table and find the most influential variables. This statistical analysis will be carried out with the help of computerized statistical applications. The data analysis techniques used are univariate and bivariate.

Results and Discussion

Results

Demographic characteristics

This study included 36 infants who received breast milk and HMF and 111 children who received breast

milk in the Neonatology ward of H. Adam Malik General Hospital, Medan from November 2020 to April 2023. All infants involved in this study met the

inclusion criteria. Complete demographic characteristics are presented in the following table.

Table 1. Demographic characteristics Breast milk and HMF

Demographic Characteristics	Breast milk and HMF n = 36	BUT n = 111	p
Gender			
Man	19 (52,8)	61 (55)	0,820 ^a
Woman	17 (47,2)	50 (45)	
Age, days			
Mean (SD)	33,61 (21,68)	12,12 (16,99)	<0,001 ^b
Median (Min – Mak)	26 (5-85)	5 (0 – 77)	
Gestational Age, n (%)			
< 28 weeks	9 (25)	13 (11,7)	0,034 ^a
28 - < 32 weeks	18 (50)	46 (41,4)	
32 - < 38 weeks	9 (25)	52 (46,8)	
Body Weight, grams			
< 1000 gram	7 (19,4)	4 (3,6)	<0,001 ^a
1000 - < 1500 gram	22 (61,1)	44 (39,8)	
1500 - 2000 gram	7 (19,4)	63 (56,8)	

^aWho Square, ^bMann-Whitney

Male infants dominated both groups, namely 52.8% (19 people) in the breast milk and HMF group and 55% (61 people) in the breast milk group. The age range of infants in the breast milk and HMF group was 2–85 days, while the breast milk group was 0–77 days. The majority of gestational ages in the breast milk and HMF groups were in the range of 28–<32 weeks (50%), while in the breast milk group, the largest gestational age was 32–<38 weeks (46.8%). The highest birth weight in the breast milk and HMF

groups was 1000–<1500 grams (61.1%), while in the breast milk group it was dominated by infants with a birth weight of 1500–<2500 grams (56.8%).

Weight changes in the breast milk and HMF groups

The following table shows changes in infant weight in the breast milk and HMF groups.

Table 2. Changes in body weight in the ASI and HMF groups

Monitoring	Mean (SD)	Median (Min –Max)	p
Day 1	1484,17 (269,45)	1545 (800-1980)	<0,001
Day 2	1505,31 (265,82)	1552,5 (825-1995)	
Day 3	1531,64 (260,96)	1595 (835-2010)	
Day 4	1565,97 (302,62)	1575 (850-2570)	
Day 5	1591,81 (302,83)	1625 (850-2570)	
Day 6	1610,11 (310,08)	1640 (850-2640)	
Day 7	1636,86 (307,22)	1678,5 (915-2640)	

*Repeated ANOVA

The baby's weight appeared to show a trend that continued to increase since monitoring on the first day until the 7th day. The average baby's weight on the first day was 1484.17 grams and reached the highest value on the 7th day with an average of 1636.86 grams. The results of the analysis using the Repeated ANOVA test showed that there was a

difference in weight between the first day and the 7th day.

Weight changes in the breastfed group

The table below shows changes in infant weight in the breastfed group.

Table 3. Changes in body weight in the breast milk group

Monitoring	Mean (SD)	Median (Min - Max)	p
Day 1	1579,53 (376,13)	1580 (720-2715)	<0,001
Day 2	1602,57 (378,05)	1625 (720-2775)	
Day 3	1611,71 (380,34)	1620 (720-2780)	
Day 4	1629,68 (384,08)	1650 (720-2850)	
Day 5	1650,63 (380,68)	1670 (740-2820)	
Day 6	1664,64 (380,46)	1670 (720-2765)	
Day 7	1680 (376,48)	1675 (720-2770)	

*Repeated Anova

The weight of infants in the breastfed group also showed a trend that continued to increase since monitoring on the first day to the 7th day. The average weight of infants on the first day was 1579.53 grams and reached the highest value on the 7th day with an average of 1680 grams. The results of the analysis using the Repeated Anova test showed that there was a difference in weight between the first day and the 7th day in the group of infants who were only given breast milk.

Difference in body weight during monitoring from day 1 to day 7 in the breast milk and HMF group and the breast milk group

The following table shows the differences in infant weight between groups at each monitoring time.

Milk and HMF group and the breast milk group

Table 4. Differences in body weight during monitoring from the first day to the 7th day in the Breast Milk and HMF Group and the Breast Milk Group

Monitoring	Breast milk and HMF, Mean (SD)	BUT, Mean (SD)	p*
Day 1	1484,17 (269,45)	1579,53 (376,13)	0,100
Day 2	1505,31 (265,82)	1602,57 (378,05)	0,092
Day 3	1531,64 (260,96)	1611,71 (380,34)	0,160
Day 4	1565,97 (302,62)	1629,68 (384,08)	0,366
Day 5	1591,81 (302,83)	1650,63 (380,68)	0,400
Day 6	1610,11 (310,08)	1664,64 (380,46)	0,437
Day 7	1648,84 (311,56)	1680 (376,48)	0,529

In the two study groups, both in the group of infants who received breast milk and HMF and the group of infants who only received breast milk, all data were presented in the form of mean and SD because all data were normally distributed. The results of the analysis using the Independent T test showed that there was no significant difference in body weight between each observation time, ($p>0.05$)

Differences in weight change between the breast milk and HMF groups and the breast milk group

The table below shows the differences in changes in infant weight between the first day and the 7th day in the breast milk and HMF groups and the breast milk group.

Table 5. Differences in weight changes between the breast milk and HMF groups and the breast milk group.

Group	Weight Change, grams		p
	Mean (SD)	Median (Min - Max)	
Breast milk and HMF	152,69 (133,65)	140 (0 - 840)	0,018*
BUT	101,01 (130,45)	85 (-180 - 490)	

*Mann Whitney

Delta (weight change) between the first and 7th day in the breast milk and HMF group appeared much higher with a median of 140 grams (0 - 840 grams) compared to the breast milk group which only

showed an increase of 85 grams (-180 – 490 grams). Using the Mann Whitney test showed that there was a significant difference in delta (weight gain) between the group of infants given breast milk and HMF and the group of infants given only breast milk ($p = 0.018$).

Discussion

This study involved 147 infants treated in the Neonatology Unit of H. Adam Malik General Hospital Medan, consisting of 36 infants who received breast milk and HMF and 111 infants who received breast milk alone, according to the inclusion and exclusion criteria. Most of the subjects were male infants, namely 52.8% (19 infants) in the breast milk and HMF group and 55% (61 infants) in the breast milk group. The age range of infants in the breast milk and HMF group was 2–85 days, while in the breast milk group it was 0–77 days. The majority of gestational ages in the breast milk and HMF groups were 28–<32 weeks (50%), while in the breast milk group the largest gestational age was 32–<38 weeks (46.8%). The highest birth weight in the breast milk and HMF group was in the range of 1000–<1500 grams (61.1%), while in the breast milk group it was in the range of 1500–<2500 grams (56.8%).

The neonatal period, from its beginning to its end, is the phase with the highest mortality rate compared to other age intervals. Perinatal mortality, which includes fetal deaths from 20 weeks of gestation to 28 days after birth, is expressed as the number of deaths per 1,000 live births, with intrauterine fetal death accounting for 40–50% of total perinatal deaths (Ong et al., 2015). Research shows that neurodevelopment in very low birth weight (VLBW) infants is highly dependent on early acquisition of fat-free body mass and rapid linear growth (Victora et al., 2016). Inadequate nutrition during the care of premature infants in the NICU is often associated with decreased neurocognitive function and poor short- and long-term developmental outcomes. Therefore, breast milk, with its unique nutritional and functional content, is considered the best form of nutrition and is recommended as the primary source for all infants, including full-term and preterm infants (Ramel et al., 2016).

Breast milk fortification has been implemented since the 1980s and has become a standard practice for

nutritional supplementation in most NICUs worldwide (Jochum et al., 2019). A meta-analysis showed that preterm infants fed preterm formula (PF) experienced higher weight gain, linear growth, and head circumference during hospitalization, but also showed a higher risk of necrotizing enterocolitis (NEC) and feeding intolerance (Chinnappan et al., 2021). Over time, fortification methods have improved in quality, with individualized fortification that can be specifically tailored considered more optimal than standard methods. The main goal of fortification is to optimize the concentration of nutrients in a limited volume of food to meet the nutritional needs of preterm infants. Previously, EBM (expressed breast milk) was fortified using commercial PF powder, but since November 2018, fortification has been carried out using Human Milk Fortifier (HMF), replacing the previous method (Arslanoglu et al., 2010).

In this study, infant weight appeared to show an increasing trend since monitoring on the first day to the 7th day. The average infant weight on the first day was 1484.17 grams and reached the highest value on the 7th day with an average of 1636.86 grams. The results of the analysis using the Repeated Anova test showed that there was a difference in weight between the first day and the 7th day. To determine the difference in average weight from day to day, a posthoc test was carried out, based on the results of the analysis using the Tukey test, it appeared that there was a difference in weight between the first day and all monitoring days. However, there was no significant difference in weight between the 2nd and 4th days, between the 3rd and 4th days, and between the 3rd and 5th days.

Postnatal growth of preterm infants is essential for long-term development, and breast milk is the best food choice to support optimal growth at this stage. However, breast milk alone is not sufficient to meet the nutritional needs of preterm infants born before 32 weeks of gestation because its composition varies depending on gestational age and days postpartum (WHO, 2018). To meet the nutritional recommendations of ESPGHAN and prevent growth and developmental failure, the addition of Human Milk Fortifier (HMF) and/or nutritional supplements (NS) to breast milk is required (Brown et al., 2016). However, the addition of HMF and NS increases the osmolality of breast milk, which has been associated

with the risk of gastroesophageal reflux, impaired gastrointestinal tolerance, and NEC. The American Academy of Pediatrics (AAP) recommends that the osmolality of enteral nutrition should not exceed 450 mOsm/kg (400 mOsm/L) (Barness et al., 1976), while pure breast milk has an osmolality of around 300 ± 6 mOsm/kg. Recent studies have shown many HMF products exceed this limit, and manufacturers recommend that HMF be added just before feeding because osmolality will increase over time due to carbohydrate hydrolysis (Donovan et al., 2017).

In this study, the weight of infants in the breast milk group also showed a trend that continued to increase since monitoring on the first day to the 7th day. The average weight of infants on the first day was 1579.53 grams and reached the highest value on the 7th day with an average of 1680 grams. The results of the analysis using the repeated ANOVA test showed that there was a difference in weight between the first day and the 7th day in the group of infants who were only given breast milk. To determine the difference in average weight from day to day, a post hoc test was carried out. Based on the results of the analysis using the Tukey test, it appears that there is no significant difference in weight between the first day and the second day ($p = 0.101$), but the second to seventh days showed a significant difference in average weight ($p < 0.05$). Between the second and third days also did not show a significant difference in average weight ($p = 0.484$).

Providing fortification to premature babies after adequate breastfeeding has been provided can result in suboptimal weight gain initially, but overall, better neurological development is said to occur. "apparent breastfeeding paradox". To record the growth of premature infants from birth to discharge from NICU care, providing input on the nutritional practices followed and their impact on longitudinal growth patterns (Roze' et al., 2012). An observational cohort study with preterm infants weighing less than 1250 g compared growth with historical growth standards and a previously breastfed cohort, achieving targeted preterm growth with low EUGR levels (Hair et al., 2013). In this study, In two study groups both in the group of infants who received breast milk and HMF and the group of infants who only received breast milk, all data were presented in the form of mean and SD because all data were normally distributed. The results of the analysis using the Independent T test

showed that there was no significant difference in body weight between each observation time, ($p > 0.05$).

In this study, a Delta test was conducted using the method Mann Whitney to show the difference in changes in infant weight between the first day and the 7th day in the breast milk and HMF group and the breast milk group with the Delta results (change in weight) between the first and 7th day in the breast milk and HMF group appeared much higher with a median of 140 grams (0 - 840 grams) compared to the breast milk group which only showed an increase of 85 grams (-180 - 490 grams). Using the Mann-Whitney test showed that there was a significant difference in delta (weight gain) between the group of infants given breast milk and HMF and the group of infants given only breast milk ($p = 0.018$).

The nutritional content of breast milk varies widely and may not be adequate as the sole source of nutrition for VLBW infants. For mothers who are unwilling or unable to provide sufficient expressed breast milk, donor breast milk (DBM) is generally given to VLBW babies. Donor breast milk (DBM) is given to maintain the immunological benefits of maternal breast milk (MBM), but is less nutrient-dense than MBM. Thus, the benefits of breast milk fortification for premature infants have mainly been reported with the use of breast milk fortifier powders. However, the product's liquid human milk fortifier (LHMF) which is more recent has become a recommendation the U.S. Centers for Disease Control and Prevention and U.S. Food and Drug Administration to avoid powdered products in the NICU.

Conclusion

The main cause of poor postnatal growth and weight gain in premature, VLBW infants, especially the process of weight gain, usually occurs during the third trimester of pregnancy. Inadequate nutrition during the critical period of brain and lung development and growth in size and weight can lead to irreversible negative outcomes. Postnatal growth of premature babies is key to long-term evolution and breast milk is the best food choice to allow optimal growth at this stage. Fortified breast milk is indicative to increase and optimizing nutrient concentration, meeting the nutritional needs of premature infants at

the proposed feeding volume. There was no significant difference in the average age of babies in the group of babies who received breast milk and HMF with babies who received breast milk alone, namely 0 up to 85 days.

Based on demographic characteristics, it was found that most of the research subjects were male babies, where in the group of babies who received breast milk and HMF there were 19 babies (52.8%) and in the group of babies who received breast milk alone there were 61 babies (55%). Most of the gestational ages in the breast milk and HMF group were 28 - <32 weeks as many as 18 people (50%) while in the breast milk group there were 52 people (46.8%) with a gestational age of 32 - <38 weeks. The highest body weight in the breast milk and HMF group was between 1000 - <1500 grams as many as 22 people (61.1%) while in the breast milk group the highest birth weight was 1500 - <2500 grams as many as 63 people (56.8%). On the baby's weight appeared to show a trend that continued to increase since monitoring on the first day until the 7th day. The average baby's weight on the first day was 1484.17 grams and reached its highest value on the 7th day with an average of 1636.86 grams. The results of the analysis using the test Repeated Anova show that there is a difference in body weight between the first day and the 7th day. The difference in changes in infant weight between the first day and the 7th day in the breast milk and HMF groups and the breast milk group with Delta results (changes in weight) between the first and 7th day in the breast milk and HMF groups appeared much higher with a median of 140 grams (0 - 840 grams) compared to the breast milk group which only showed an increase of 85 grams (-180 - 490 grams). By using the test Mann Whitney showed that there was a significant difference in delta (weight gain) between the group of infants given breast milk and HMF and the group of infants given only breast milk ($p=0.018$).

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