

Perbedaan Gizi pada Bayi: Membandingkan Profil Karbohidrat dan Lipid antara Bayi dengan Status Gizi Normal dan Obesitas

Nutritional Difference in Infants: Contrasting Carbohydrate and Lipid Profiles between Normal and Obese States

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Article Info

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Submitted: 30-08-2023

Accepted: 02-09-2024

Published: 12-12-2024

Citation:

Puspitasari, R., Widjaja, N. R., Ardianah, E., & Fitriari, T. R. (2024). Nutritional Difference in Infants: Contrasting Carbohydrate and Lipid Profiles between Normal and Obese States. *Media Gizi Kesmas*, 13(2), 763–772.

<https://doi.org/10.20473/mgk.v13i2.2024.763-772>

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ABSTRAK

Latar Belakang: Air Susu Ibu (ASI) merupakan sumber gizi terbaik bagi bayi untuk menunjang pertumbuhannya selama 6 bulan. Bayi yang diberi ASI, lebih kurus dibandingkan dengan bayi yang diberi susu formula, namun beberapa bayi yang diberi ASI mengalami kelebihan berat badan/obesitas.

Tujuan: Untuk membandingkan kandungan makronutrien ASI pada bayi normal dan bayi kelebihan berat badan/obesitas usia <12 bulan.

Metode: Desain penelitian case-control, dilakukan kepada 20 ibu menyusui (residen dan pekerja) di bagian pediatri di Rumah Sakit Umum Daerah (RSUD) Dr. Soetomo Surabaya pada bulan Maret–April 2018. ASI yang diberikan pada bayi dengan berat badan berlebih dimasukkan ke dalam kelompok Overnutrition (ON), Sedangkan ASI yang diberikan pada bayi dengan status gizi normal dimasukkan ke dalam kelompok Normal (N). Untuk mendapat sampel ASI, peneliti merekrut ibu menyusui yang berpartisipasi secara sukarela serta menyusui bayi mereka secara eksklusif dengan usia bayi berkisar antara 1-12 bulan. Makronutrien ASI diukur menggunakan Human Milk Analyzer (HMA) (MIRIS®, Uppsala, Swedia). Analisis statistik yang dilakukan adalah tes normalitas Shapiro Wilk dan tes homogenitas lalu uji Mann Whitney U dan uji Fisher exact dengan level signifikansi <0.05.

Hasil: Sebanyak 20 sampel HM diperoleh dari 20 ibu menyusui, di mana 10 bayi dinyatakan kelebihan gizi (2 dikategorikan kelebihan berat badan dan 8 obesitas) dan dikelompokkan dalam kelompok ON, sedangkan 10 bayi normal dan dikelompokkan dalam kelompok N. Diperoleh bahwa kelompok ON memiliki kandungan lipid yang lebih tinggi dibandingkan kelompok N (4,33 [2,0-6,8] vs 2,40 [1,2-3,9] g, $p=0,019$). Kandungan protein hampir sama pada kedua kelompok ($p=0,853$), Kelompok ON memiliki kandungan karbohidrat yang lebih rendah (2,42 [1,5-3,7] g) dibandingkan kelompok N (3,42 [2,1-4] g), $p=0,004$. Kelompok ON memiliki kandungan energi yang lebih tinggi (53.85 [31.20-76.20] kkal/ml) dibandingkan kelompok N (39.90 [26.40-51.90] kkal/ml, $p=0.065$).

Kesimpulan: Lipid yang terkandung dalam ASI mempunyai pengaruh yang lebih besar terhadap bayi ON dibandingkan dengan zat gizi makro lainnya. Kandungan karbohidrat secara signifikan rendah pada bayi ON.

Kata kunci: ASI, Gizi Lebih, Kandungan Makronutrien, Status Gizi

ABSTRACT

Background: For supporting the infant's growth and development, Human Milk (HM) is the most suitable nutritional source, especially during 6 months. Growth study showed different growth between breastfed infants and formula-fed infants, in which they are thinner compared to formula-fed infants, but some breastfed infants are overnutrition (overweight and obese).

Objective: to investigate the macronutrient content of HM in exclusive breastfeeding infants aged under 12 months old.

Methods: The study's design was a case-control, conducted on 20 lactating mothers (residents and employee) in the pediatric departemen at Regional General Hospital Dr. Soetomo Surabaya in March–April 2018. HM of the infant with overnutrition was included in the Overnutrition (ON) group, and HM of the infant with normal nutrition was included in the Normal (N) group. To obtain the HM samples, the researchers recruited lactating mothers who participated in this study voluntarily. The lactating mothers must breastfeed their infants predominantly, and their infant's age must be less than 12 months old. The macronutrients content in HM were measured using a Human Milk Analyzer (HMA) (MIRIS®, Uppsala, Sweden). Statistical analysis conducted was test of normality (Shapiro Wilk) and test of homogeneity followed by Mann Whitney U test and Fisher exact test with the level of significance <0.05.

Results: We got 20 samples of HM from 20 lactating mothers, in which ten infants were determined as overnutrition (2 were categorized as overweight and 8 were obese) and grouped in ON, while 10 infants were normal and were grouped in the N group. It was found that the ON group had higher lipid content than the N group (4.33[2.0-6.8] vs. 2.40 [1.2-3.9] g, $p=0.019$). Protein content was almost similar in both groups ($p=0.853$), The ON group had lower carbohydrate content than (2.42 [1.5-3.7] g) than the N group (3.42 [2.1-4] g), $p=0.004$. The ON group had higher energy content (53.85 [31.20-76.20] kcal/ml) than the N group (39.90 [26.40-51.90] kcal/ml, $p=0.065$).

Conclusion: The incidence of overnutrition during infancy is likely affected by high lipids content in HM than other macronutrients. The carbohydrate content was significantly low in overnutrition infants.

Keywords: Human milk, Macronutrient, Nutritional status, Overnutrition

INTRODUCTION

For ensuring the optimum growth and development of the infants, Human Milk (HM) is the most suitable source, especially during 6 months of life. HM always changed to respond to the needs of the infant, and never had the specific nutrient contents, in both macro- and micronutrient. HM is influenced by many factors, such as lactation stage (Duale, Singh and Al Khodor, 2022), maternal diets (Aumeistere *et al.*, 2019), maternal body composition (Bzikowska-Jura *et al.*, 2018; Lima *et al.*, 2019), infant's mode of delivery (Gedefaw *et al.*, 2020), maternal age (Gila-Díaz *et al.*, 2020), etc.

There was a different pattern of infant's growth between breast-fed and formula-fed infants. Infants receiving HM exclusively have different growth compared with infants with formula milk, in which formula-fed infants had a rapid weight gain, especially during the first 6-month-old (Singh *et al.*, 2017) and 6-12 months of age (Appleton *et al.*, 2018). Meanwhile, the breastfed infant has relatively slow weight gain (Singhal, 2017; Lindholm *et al.*, 2020), starting at the age of 6-8 months. That is why infants with HM intake were thinner than an infant with formula milk.

Human Milk (HM) contains leptin which is controlling fat accumulation in infants with HM intake during early life (Palou, Picó and Palou, 2018). In some cases, breast-fed infants under 12

months of age are overweight and obese while others are normal, especially during the exclusive breastfeeding period. It was stated that high levels of Insulin-like Growth Factor 1 (IGF-1) are associated with overweight/obese infants (Uwaezuoke, Eneh and Ndu, 2017; Galante *et al.*, 2020) while ghrelin was high during the age of 1-4-month-old (de Fluiter *et al.*, 2021). But there is limited evidence that investigates the nutrient contents in human milk, especially macronutrients that correlate with the incidence of overnutrition in infants. Leptin in HM was correlated with the rapid growth (weight gain) and Body Mass Index (BMI) of infants (Soori, *et al.*, 2020), but not with the macronutrient contents, infant's BMI had a negative correlation with the fat content of HM, while protein and carbohydrate were found no correlation (Abdelhamid *et al.*, 2020). Pediatric residents and employee complains that their baby was overweight/obesity while the only intake was human milk, several started to have complementary feeding, so the researchers had initiative to examine the human milk to investigate the macronutrients content as the researchers suspected that the macronutrients content within human milk of overweight/obese baby exceeding the normal baby.

METHODS

Materials

Study design

The study design was a case-control, conducted at Regional General Hospital Dr. Soetomo, Surabaya, Indonesia from March to April 2018. The researchers obtain the HM samples from lactating mothers who are willing to participate in this study voluntarily. After the infant's nutritional status determination, the researchers found two infants were overweight, and eight infants were obese, and those with overweight and obese were grouped in Overnutrition (ON), while HM of the infant with normal nutritional status was included in the Normal (N) group. The nutritional status of the infant has already been established by a paediatrician staff in outpatient installation in the Hospital.

Samples

Population in this study was lactating mothers of healthy baby with normal, overweight and obese nutritional status whom their parents, especially mothers, working or studying on Pediatric Department. The sample was human milk of mothers with normal, overweight or obese babies in Pediatric Department. The samples were very limited, as the infants were physically healthy, and not every mother was available for this study due to inclusion criteria restriction. Most of the healthy babies receive formula milk predominantly as their nutritional sources, so the samples were determined using total sampling. In final recruitment process, we recruited 20 lactating mothers who were willing to participate in the study, consisting of mothers who had overweight babies (2 subjects) and obese babies (8 subjects). These 10 samples were placed in the ON group. Then 10 mothers who had normal weight babies formed the N group. To obtain the HM samples, researchers recruited lactating mothers who participated in this study voluntarily.

The lactating mothers must breast feed predominantly, and the infant's age was less than 12 months. The nutritional status was determined using WHO child growth standard in which normal infants had BMI-for-age z-score between >-2 SD until $<+2$ SD, overweight had $>+2$ SD, and obese had $>+3$ SD. Inclusion criteria for the lactating mothers were: healthy and not under medication. The lactating mother who participates in this study must be healthy and not in medication treatment such as steroids or hormones. The lactating mother participating in this study were mostly the employee (nurses, dieticians, and residents) of the Paediatrics department with overweight or obese complaints about their young child, and good nutrition, confirmed by physical examination and nutritional status measurement performed by nutrition and metabolic diseases staff, and a small part of patients from the outpatient

installation of Nutrition and Metabolic disease with the main complaints of overweight or obesity. Before we took the HM, we explained the aim of this study, the procedures of HM measurement, and the outcomes for the mother. Macronutrient contents of HM which have been measured will be reported back to the mother.

Most of the young children who come to outpatient installation for Nutrition and Metabolic disease have feeding problems (feeding difficulties) or growth disturbances (stunted, wasted, underweight), or mothers who have just given birth with medical complaints such as low birth weight, asphyxia, and so on. Therefore, they couldn't fulfill the inclusion criteria of the study.

Human milk analysis

After obtaining Human Milk (HM) from selected mothers, it was collected in milk bags and then stored in a cooler box. To determine the macronutrient content of the HM, a Human Milk Analyser (HMA) from MIRIS® in Uppsala, Sweden, was used. The device's accuracy was reported to be less than 0.1 g/100 ml. The analysis took place in the Neonatal Division's nursery room within the Child Health Department. Before utilizing the HMA for measuring HM, it underwent calibration to ensure accurate measurements. Cleaning and calibration procedures were repeated after analysing 10 HM samples. If the variability exceeded 10%, the sample was rejected. Each sample underwent two separate analyses. To obtain valid results, the two measurements for each sample were added together and then divided by two to calculate the average value.

The HM samples were collected using a sterile syringe, with an amount of up to 1.5 ml. Afterward, only 1 ml of the sample was promptly injected into the cell for HMA analysis, and the process was initiated by clicking the "start" button. These devices operate based on the absorption of the infrared spectrum. Specific wavelengths are absorbed by fats, proteins, and carbohydrates. Therefore, when the light intensity is accurately transmitted at these wavelengths, their concentrations in the compounds are assessed.

Ethical Clearance

This research ethics was submitted to the Health Research Ethics Committee of our hospital and obtained approval with the issuance of a Code of Ethical Feasibility Number 0234/KEPK/IV/2018 and registered on International Standard Randomized Controlled Trial (ISRCTN) ISRCTN18118021 (<https://doi.org/10.1186/ISRCTN18118021>). Before the lactating mothers participated in this study, they signed information for consent and participant agreement without any coercion and they have been

informed of the aim, importance, procedures, and the benefit of this study.

Data Analysis

Statistical analysis including test of normality (Shapiro Wilk) and Mann Whitney U Test. For participants' characteristics was analysed using Fisher exact Test (gestational age, infant's gender). Nutritional status was analysed using Pearson's chi-square. The significance value was $p < 0.05$.

RESULTS AND DISCUSSION

This study included 20 lactating mothers. Among them, 2 infants were overweight, and 8 were obese. These 10 samples constituted the ON group, 10 mothers had infants with normal weight, forming the N group. The characteristics of the participants,

such as maternal age, delivery time, infant age, infant sex, and infant body weight, were found to be normally distributed Shapiro Wilk, $p > 0.05$) and exhibited homogeneity (t-test for equality of means $p > 0.05$) between both the ON and N groups, as outlined in Table 1.

The average age of the infants was 5.6 ± 1.85 months, and their average weight was 7.775 ± 2.17 grams. Regarding nutritional status, 10% of infants were classified as obese (2 out of 20), 40% as overweight (8 out of 20), and 50% as normal weight (10 out of 20). The number of male was 9 and female was 11; with 3 males and 7 females in the ON group, and 6 males and the remaining females in the N group. Among the infants in the ON group, 6 were born as term infants, and 4 were preterm, while in the N group, 8 were term infants, and the rest were preterm.

Table 1. Characteristic of subjects of the ON Group and N Group

Characteristic of subjects	All Mean (min-maks)	ON Mean (min-maks)	N Mean (min-maks)	p-value
Average of Maternal's Age (years)	27.25 (17-41)	27.40 (17-40)	27.1 (18-41)	0.971 ^a
Maternal Body Height (cm)	155.95 (143-165)	157.90 (145-165)	154 (143-162)	0.165 ^a
Maternal Body Weight (kg)	63.70 (43-116)	72.30 (50-116)	55.10 (43-70)	0.019 ^{a*}
Maternal Arm Circumference (cm)	27.40 (20-45)	30.40 (24-45)	24.40 (20-32)	0.023 ^{a*}
Nutritional status				0.000 ^{b*}
- Normal	10	0	10 (100)	
- Overweight	2	2 (20)	0	
- Obesity	8	8 (80)	0	
Prematurity, (n[%])				0.314 ^b
• Term infants	14 (70)	6 (60)	8 (80)	
• Preterm infants	6 (30)	4 (40)	2 (20)	
Infant's sex (n[%])				0.185 ^a
• Male	9 (45)	3 (30)	6 (60)	
• Female	11 (55)	7 (70)	4 (40)	
Average of Infant's Age (month)	5.60 (2.0-8.0)	5.8 (3.0-8.0)	5.4 (2.0-8.9)	0.684 ^b
Average of Infant's Body Weight (month)	7.78 (4.0-11.8)	9.47 (6.5-11.8)	6.08 (4.0-7.2)	0.000 ^{a*}

^aMann Whitney U Tesr; ^bFisher's Exact Test, *Significance of $P < 0.05$

Abbreviations: ON, overnutrition; N, normal nutrition

Table 2. Human Milk Macronutrient Content between ON Group and N Group

Variable	ON Grup Mean (min-maks)	N Grup Mean (min-maks)	p-value
Lipid (g/ml)	4.33 (2.0-6.8)	2.40 (1.2-3.9)	0.019 ^{a*}
Protein (g/ml)	1.3 (0.5-2.10)	1.33 (0.8-2.10)	0.853 ^a
Carbohydrate (g/ml)	2.42 (1.5-3.7)	3.42 (2.1-4)	0.004 ^{a*}

Energy (kcal/ml)	53.85 (31.20-76.20)	39.90 (26.40-51.90)	0.065 ^{a*}
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^aMann Whitney U Test; ^{*}Significance of P<0.05

Abbreviations: ON, overnutrition; N, normal nutrition

The measurement of HM macronutrient composition is crucial, as HM is the primary and most beneficial source of nutrition to ensure infants receive the necessary nutrients for optimal growth (Léké *et al.*, 2019). This study found that the lipid content ranged from 2.0 to 6.8 grams (with mean value of 4.33 grams) in the ON group, whereas in the N group, it was lower, ranging from 1.2 to 3.9 grams (with mean value of 2.4 grams). There was a significant difference between the ON group and the N group in terms of lipid content ($p=0.019$). A study of HM macronutrient content reveals fat content was similar to the ON group (Abdelhamid *et al.*, 2020). Most of those studies had higher lipid and carbohydrate contents, due to the duration of breastfeeding at the age of 1 month old or under 6 months old. HM macronutrients are affected by several factors, including maternal HMI (every increment of 1 kg/m², will increase 0.56 g/L of HM lipid) (Berger *et al.*, 2020). Maternal obesity reduces the carbohydrate contents by 30%, especially oligosaccharides (Berger *et al.*, 2020) and Fatty Acid (FA) composition, in which higher Short-chain Fatty Acids (SFAs) and higher ratio n-6 to n-3 FA (De la Garza Puentes *et al.*, 2019). It has been hypothesized that an imbalance of PUFA (Polyunsaturated Fatty Acid) metabolism, in favor of n-6 than n-3 PUFA could increase the prevalence of overweight and adiposity in children and adults, which was proved in rodent models (Guesnet *et al.*, 2019). This finding and hypothesis supported this study, in which, lipid content in the ON group was higher compared to normal infants. However, we did not calculate the maternal HMI.

Lipids play a crucial role in enhancing taste and influencing the texture, flavour, and aroma of food (Affordable Learning Solution, 2019). They contribute approximately 9 kcal per gram, whereas carbohydrates and proteins provide only 4 kcal per gram of energy (Lestari and Purwayantie, 2018; Fenton and Elmrayed, 2021). The recommended daily average intake of lipids is approximately 21.4 grams during the first 0-6 months of life, accounting for 20%-35% of the total energy requirement (EFSA, 2017). In the mother's enterocyte, lipids from diets are packaged into chylomicrons, and then secreted into the bloodstream via lymphatics, and further to the mammary gland (Linderborg *et al.*, 2020).

Several factors were affecting lipid content in HM such as the period of lactation (George *et al.*, 2021), higher at the age of 6 and 12 months old of lactation (Siziba *et al.*, 2019). Maternal diets also have strong lipid content in HM and are described as the long-term consumption of maternal fatty acids (Chen *et al.*, 2017). During lactation, dietary LC

(long-chain)-PUFA and PUFA precursors are transferred into HM lipids. PUFA on HM is also derived from maternal adipose tissue before and during pregnancy (Guesnet *et al.*, 2019). Excessive cooking oil, seafood, and soybean product consumption in the maternal diet leads to a high proportion of linoleic acids (n-6) in HM (Wu *et al.*, 2021). High-fat diet during lactation alters not only macronutrient milk composition in mice, but also its bioactivity (Chen *et al.*, 2017), and was proved in human study that high fat and sugar diet increases HM triglycerides, cholesterol, and lactose, but decrease the protein contents in short term diets (Ward *et al.*, 2021), which affecting the weight pup on in vitro study (Chen *et al.*, 2017). This finding is in line with this study, and it seems to be related to the rapid weight gain during the first 12 months of life, which was stated in another study, an infant's intake of lipids was related to infant growths and development (George *et al.*, 2021).

Lipids and carbohydrates exhibited a positive correlation with weight gain, Human Milk Intake (HMI), and adiposity in infants aged 3-12 months. In human milk, lipids play a critical role as the primary energy source for infants (Linderborg *et al.*, 2020), half of the energy requirement was supplied by lipid in the form of neutral lipids (triacylglycerols, diacylglycerols, and monoacylglycerols) (Vergilio Visentainer *et al.*, 2018). However, in the ON group, the intake of lipids was nearly double that of the normal weight group (4.3 grams/ml sample of human milk versus 2.4 g/ml). This translates to the ON group having approximately 1.9 times more energy intake, equivalent to approximately 17.1 kcal/ml of excess energy compared to the N group.

The protein content was quite similar in both groups, ranging from 0.5 to 2.10 g (with mean value of 1.3 g) in the ON group and 0.8 to 2.1 g (with mean value of 1.33) in the N group. However, there was no significant difference in protein content between the ON group and the N group ($p=0.853$). On the other hand, carbohydrates, primarily in the form of lactose, were lower in the ON group, ranging from 1.5 to 3.7 grams (with mean value of 2.42 grams), compared to the N group where they ranged from 2.1 to 4 grams (with mean value of 3.42 grams). There was a significant difference in carbohydrate content between the two groups ($p=0.004$) (Table 2.). The protein content was similar in both groups and confirmed in line with other studies, while carbohydrate content was lower than in this study (Basir *et al.*, 2019; Lubis and Amelin, 2019; Huang and Hu, 2020).

Protein contents on HM were influenced by maternal protein intake (meat, cereals, and eggs). Protein intake is related to the HMI of infants aged 12 months old through hind milk at the age of 4-8 weeks and does not affect adiposity (Eriksen *et al.*, 2018). A study investigated the effect of protein in infant formula on the risk of obesity due to higher protein content and its association with greater weight gain (Tang, 2018). Every 1 g increase in protein intake at the age of 9 months will increase 0.016-HMI z-score, and increase 0.034-HMI z-score at the age of 5 years old (Zheng *et al.*, 2021). Research conducted on children between the ages of 2 and 6 years, using infant formula, demonstrated that high-protein formula led to an increase in fat mass. In contrast, formula with lower protein content (specifically, 1.65 grams per 100 kilocalories) encouraged the development of a more balanced and proportional body composition (Singh *et al.*, 2017). However, HM protein content at 4-8 weeks (hindmilk) was correlated with infant HMI at the age of 12 months old, but not associated with infant length or adiposity. Free Amino Acids (FAA) are suggested to regulate appetite, especially glutamic acid, and glutamine, which was found at high concentration in HM, and was associated with infant length at the age of 4 months old (Eriksen *et al.*, 2018).

Lactose content in HM is the main sugar and carbohydrate in milk (Kalyanasundaram, Narayanan and Krishnamurthy, 2021). There was evidence that carbohydrates on HM affected infant's growth, the increment of oligosaccharide was associated with 0.40 to 1.11 kg lower infant weight and lower infant fat mass accumulation during the first six-months-old (Berger *et al.*, 2020). Disaccharides on HM mostly increase the infant's weight, such as fructose, the increment of 1 μ /ml HM fructose content, affecting 257-g increase in weight, followed by 170 g increase in lean mass, 131 g increase in fat mass, and 5 g increase in bone mineral contents (Goran *et al.*, 2017). Lactose was positively correlated with the infant's anthropometry, lean body mass, and adiposity (Aumeistere *et al.*, 2017), which is in line with this study, which showed higher lactose content in the N group compared to the ON group, it was stated that carbohydrate affecting infant's appetite, breastfeeding patterns, and body composition. Higher carbohydrate concentrations were associated with the increment in infant length, weight, and decreased fat mass (Gridneva *et al.*, 2019). In the N group, the carbohydrate content of human milk (in the form of lactose) was significantly higher than that in the ON group. It's worth noting that a study has indicated that carbohydrate intake is influenced by the increase in infant length and weight. However, it appears to have the opposite effect on fat mass during the first 12 months of age, with the aim of promoting the development of a more balanced and proportional body composition

(Gridneva *et al.*, 2019). Lactose is a low glycaemic index disaccharide with metabolically advantageous, and has a role to shape the intestinal microbiota, supporting immune function, and facilitating mineral absorption (Cianciosi, Simal-Gándara and Forbes-Hernández, 2019).

However, macronutrient contents in both groups are still in the normal range, energy, protein, and lipid composition ranged from 51-72 kcal/dl, 0.8-3.3 g/dl, 2.1-9.8 g/dl respectively, but the carbohydrate content was lower in this study, ranged from 5.8-7.5g/dl (Adhikari *et al.*, 2021). The adding sugar to the maternal diet is suspected as the cause which is the influence of HM carbohydrate content, especially lactose, glucose, and fructose (Berger *et al.*, 2020).

The energy content of human milk (HM) in the ON group was notably higher, ranging from 31.20-76.20 kcal/ml (with mean value of 53.85 kcal/ml), compared to the N group where it ranged from 26.40-51.90 kcal/ml (with mean value of 39.90 kcal/ml). There was no significant difference in the energy content between these two treatment groups ($=0.065$). The energy content in this study was similar to the study conducted in Malay, between 49.6-59.2 kcal/100 ml during exclusive breastfeeding (Basir *et al.*, 2019), but lower than others, ranging between 60 kcal/ml to 72,97 kcal/ml (Czosnykowska-Łukacka, Królak-Olejniak and Orczyk-Pawilowicz, 2018; Léké *et al.*, 2019; Murty *et al.*, 2019). Obesity is caused by excess energy, which leads to excess body weight, especially body fat (Maślak *et al.*, 2020). The difference in energy consumption between the OW and N groups was 0.645 kcal/ml of sample and statistically significant. The caloric requirement for the infant during the 12 months of life is about 536 - 868 kcal/kg/day. The energy consumption difference between the OW and N groups amounted to 0.645 kcal/ml of the sample, and this difference was statistically significant. It's important to note that the caloric requirement for infants during the first 12 months of life typically falls within the range of approximately 536 to 868 kcal/kg/day (Stan *et al.*, 2021), over that reference could lead to obesity. Here we did not measure the volume of human milk when pumping and did not recall the diet consumed in 24 hours, including the history of complementary feeding.

The building block for obesity development started during the first year of life due to rapid weight gain (Arisaka *et al.*, 2020). Obesity during the early first years of life is influenced by several factors: high free sugar consumption (Jardí *et al.*, 2019), higher milk intake and energy intake (Wells *et al.*, 2021), infant breastfeeding practices (Rito *et al.*, 2019), early introduction of complementary feeding (Laving, Hussain and Atieno, 2018), sleep duration less than 12 - 24 hours during the first years of life that leads to rapid weight gain (Yu *et al.*, 2021), etc. The mechanism by which HM causes rapid weight

gain during infancy remains unclear and complex, but overweight/obese infants increase the risk of childhood overweight/obesity. The mechanism through which Human Milk (HM) contributes to rapid weight gain in infancy remains unclear and complex. However, it's worth noting that overweight or obese infants have an increased risk of developing childhood overweight or obesity (Yu *et al.*, 2021). Regarding HM, a recent study found that maternal obesity influences free Branch-Chain Amino Acids (BCAA) and tyrosine levels in HM, and they might be contributing to the obesity risk of infants (Eriksen *et al.*, 2018). There was a suspicion that Branched-Chain Amino Acids (BCAA) might stimulate pancreatic insulin secretion, milk production, adipogenesis, and enhance immune function. This potential effect was believed to be mediated by the mammalian Target Of the Tapamycin (mTOR) signalling pathway (Siddik and Shin, 2019). Moreover, ghrelin levels were found to have a positive correlation with infant growth ($r=0.163$) (Soori, Mohammadi, Taghi Goodarzi, *et al.*, 2020). The lipid profile of HM also took part in the incidence of overweight/obesity during infancy, high levels of linoleic acids/LA (n-6) in HM compared to alpha-linolenic acid /ALA (n-3) have been suspected to play a role in the pathology of obesity due to excessive weight gain on adults (Torres-Castillo *et al.*, 2018), as stated above, the present of high ratio of n-6 to n-3 has been detected on human milk based on maternal diet and HMI (Chamorro *et al.*, 2022), in which n-6 fatty acids had pro-inflammatory properties compared to n-3 (D'Angelo, Motti and Meccariello, 2020), which exert anti-obesity effect (Albracht-Schulte *et al.*, 2018). The imbalance of maternal diet on n-6 and n-3 trigger overeating in offspring in mice due to upregulating of dopaminergic systems in the midbrain (Sakayori *et al.*, 2020).

However, the study needs further study with other overweight/obesity biomarkers including other parameters such as leptin, ghrelin, or other lipid adipokines and cytokines such as adiponectin level on overweight/obese infants to investigate the effect of infants overweight on adipokines profile and the effect on metabolic syndrome. Further information is needed to explore the lipid profile of HM, with a bigger sample size of infants with overweight/obesity, and measured human milk consumed by the infant and recall diet. With the short time of the study, we had some difficulties searching for the subjects who can meet the inclusion criteria, so the samples were taken in total sampling from the mother with complaints of being overweight or obese for their young child, or good nutritional status.

CONCLUSION

The incidence of overnutrition during infancy is likely affected by high lipids content in HM than other macronutrients. The carbohydrate content was significantly low in overnutrition infants.

Acknowledgement

The authors thank to the lactating mothers involving this study.

Conflict of Interest dan Funding Disclosure

None.

Author Contributions

NAW: conceptualization, investigation, methodology, supervision, writing–review and editing; TRF: methodology, writing–original draft; RP: methodology; formal analysis, writing–original draft; EA: formal analysis, resources.

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