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Research Article
Effect of a Lipid-Based Nutrient Supplement on Insulin-like Growth Factor-1 Level (IGF-1) in 6-12 Month-old Children in South Central Timor of the East Nusa Tenggara Province

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Abstract

Objective: This study aimed to assess the effect of a lipid-based nutrient supplement (LNS) on the levels of insulin-like growth factor-1 (IGF-1) in 6-12 month-old children in South Central Timor, East Nusa Tenggara province. **Materials and Methods:** This study used a quasi-experimental design that was carried out in 9 districts of South Central Timor. The samples were divided into the LNS group (n = 24), the MP-ASI SUN (Breast feeding supplementary food group) (n = 24) and the control group (n = 24). Examination of IGF-1 was conducted by the ELISA method, followed by 3 months LNS intervention. **Results:** The results showed that the factors associated with the level of IGF-1 were consumption of protein (p = 0.002), zinc (p = 0.013), phosphorus (p = 0.000), family income (p = 0.023) and length of the breast feeding period (p = 0.000). The median IGF-1 level before the intervention in the LNS group was -0.004 ng mL^{-1} and the median IGF-1 level after the intervention was 3.75. Before the intervention, the median IGF-1 in the MP-ASI group was 0.005 and the median IGF-1 level was 0.21 ng mL^{-1} after the intervention. In the control group, the median IGF-1 level before the intervention was -0.005 and the median IGF-1 level after the intervention was -1.48 ng mL^{-1}. **Conclusion:** There were differences in the levels of IGF-1 after the intervention between the LNS and control groups (p = 0.000, p<0.05) and between the MP-ASI SUN group and the control group (p = 0.025, p<0.05) but there was no difference between the LNS and MP-ASI SUN groups (p = 0.066, p>0.05).

Key words: IGF-1, protein, zinc, phosphorus, lipid-based nutrient supplement, MP-ASI SUN

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Competing Interest: The author has declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

According to the World Health Organization[1], as many as 54% of the causes of infant and toddler death are influenced by nutritional factors. Each year, 150,000 children die before reaching 5 years old, especially among the poor[2]. Furthermore, undernourishment in children under 2 years old is a critical issue because it can lead to decreased immunity, increased morbidity from infectious diseases[3], the presence of developmental disorders and locomotive coordination deficits among infants and children, delays in the progress of learning and language development[4], decreased Intelligence Quotient (IQ) up to 5 points below that the mean and behavioral and cognitive disorders. These conditions may result in the loss of an asset because this age is a period of very important and critical growth processes, both physically and cognitively[5].

Riskesdas[6] found that the prevalence of malnutrition, based on the BB/U was the highest in Gorontalo (11.2%), followed by NTB (as much as 10.6%), West Kalimantan (9.5%) and West Papua (9.1%). The prevalence of malnourishment was highest in Central Kalimantan (22.3%), NTT (20.4%) and NTB (19.9%)[7]. Riset Kesehatan Dasar[8] found that the proportion of malnourished children in Nusa Tenggara Timur (NTT) were 34.6%, children who experienced stunting were 48.2% and underweight children were 15%.

Stunting is one of the largest problems in Indonesia and has not yet been fully resolved. Based on Riskesdas[6] data, the prevalence of stunting was 35.6%, where 18.5% were children under 5 years old who experienced severe stunting and 17.1% were children under five years old who experienced of stunting. The total percentage here shows that the number of stunted and severely stunted children include more than a third of the total number of children under 5 years old in Indonesia. Despite being labeled a Non-public Health Problem by the World Health Organization (WHO)[9], the incidence of stunting is 20%, one-fifth of the total number of children under 5 years old in a country. Therefore, serious treatment is necessary for this issue.

Health Office of South Central Timor[10] reported the percentage of malnourished children under 5 years old who were treated in the district. According to TTS[11], as much as 0.43% were covered for treatment, with the highest malnutrition coverage at the health center in Hoibeti that had 30 cases, Kuanfatu and Nunkolo each had 20 cases and Ayotupas and Fatumnasi each had 17 cases.

Insulin-like growth factor-1 (IGF-1) is a polypeptide with a sequence that is very similar to insulin. The IGF-1 is part of a complex system that is used by cells to communicate with their physiological environment. The IGF-1 circulating in the blood is synthesized in the liver. The synthesis of IGF-1 is regulated by several factors. *In vivo*, the synthesis of IGF-1 is stimulated by growth hormone and nutrient intake. Growth Hormone (GH) stimulates the synthesis and secretion of hepatic IGF-1. In contrast, IGF-1 regulates secretion of GH from the pituitary through a negative feedback mechanism. In addition to GH, IGF-1 synthesis is stimulated by insulin. The absence of insulin, as seen in people with type 1 diabetes is characterized by a decrease in insulin and IGF-1 levels despite increased GH secretion[12]. Previous studies that have been conducted at Wahidin Hospital by Sunarto[13] stated that there is a correlation between insulin-like growth factor-1 (IGF-1) and fetal biometry in the third trimester of pregnancy.

Ready to Use Food (RUF) that is appropriate for the prevention and treatment of malnourishment have the potential to improve nutritional status with dramatic results in children[14]. For a few years, there have been a number of concerns over the suitability and density of energy in cereal/legume blends used as sufficient food for children aged 6-24 months. However, there are limitations to improving the nutritional quality and energy density of the cereal without technological advances[15,16]. Despite all its success, the food system is full of challenges. Food insecurity and hunger are still major problems throughout the world and for countries that have easy access to food, many choose products high in salt, fat and added sugar[17].

A lipid-based nutrient supplement (LNS) is one type of RUF in the form of an oil-based paste that has a texture similar to peanut butter. An energy-dense food, it has minerals and is enriched with vitamins that can be consumed directly from the pack without cooking. Because it can be consumed directly and does not need to be cooked or diluted with water and because these supplements contain the needed quantity of macro and micronutrients, the requirement for alternative sources of energy fuel will be reduced[18].

An LNS is a nutritional supplement that can be used in an emergency response. An LNS can provide several advantages compared with food-based interventions, such as meeting the micronutrient needs of vulnerable groups, namely children under 2 years old. The LNS also contains macronutrients (fat, protein and carbohydrates) that can provide important advantages. For example, Essential Fatty Acids (EFA) added to an LNS have been associated with growth and brain development in children[19]. When added to other foods they eat, the fat content of the LNS can increase the energy density of the food and can increase the absorption of soluble vitamins, such as vitamin A and iron and provide some energy from fat[20].

Table 1: Characteristics of respondents in the treatment groups and the control group

Variables	LNS (ng mL^{-1}) n = 24	MP-ASI SUN (ng mL^{-1}) n = 24	Control (Person) n = 24	Total (Person) n = 72	p-value
Sex					
Male	16 (66.7)	12 (50.0)	9 (37.5)	37 (51.4)	0.128
Female	8 (33.3)	12 (50.0)	15 (62.5)	35 (46.6)	
Age (Month)	13.9±4.3	12.5±3.9	13.9±4.6	13.4±4.3	0.398
6-11 months (n(%))	7 (29.2)	13 (54.2)	8 (33.3)	28 (38.9)	0.163
12-24 months (n(%))	17 (70.8)	11 (45.8)	16 (66.7)	44 (61.1)	
History of disease					
Fever	11 (78.6)	11 (78.6)	8 (88.9)	30 (76.9)	0.509
Cough	11 (78.6)	11 (78.6)	6 (66.7)	28 (71.8)	0.776
Diarrhea	4 (33.3)	4 (25.0)	0 (0.0)	8 (21.6)	0.680
Snotty nose	9 (75.0)	11 (78.6)	4 (44.4)	24 (64.9)	0.318
Asphyxia	2 (16.7)	1 (6.2)	1 (11.1)	4 (10.8)	0.680
Nutritional status (%)					
Stunting	3 (12.25)	1 (7.2)	1 (4.2)	5 (6.9)	0.458
Wasting	7 (29.2)	4 (16.7)	8 (33.3)	19 (26.4)	0.228
Underweight	7 (29.2)	4 (16.7)	9 (37.5)	20 (27.8)	0.172

LNS: Lipid-based nutrient supplement

Results from study on the benefits of an LNS to the increased production of IGF-1 are still very limited, which stimulated the researchers to conduct the present study. The purpose of this study was to analyzed the effect of the consumption of an LNS on the levels of IGF-1 in children 6-24 months old.

MATERIALS AND METHODS

This study used a quasi-experimental design. Treatment (intervention) was completed by providing an LNS or a complementary food-based (MP-ASI SUN = breast feeding supplementary food) product and a control group was monitored. This study used ethical clearance issued by the Ethics Committee of the Medical Faculty of Hasanuddin University, No. UH14050270.

This study was conducted in South Central Timor of the East Nusa Tenggara province. The determination of location was conducted randomly and 3 sub-districts were chosen for the provision of the LNS; Kuatnana, Batu Putih and South Molo. Three additional sub-districts were chosen for the provision of MP-ASI SUN; Soe, West Amanuban and Kuanfatu. Three sub-districts were also chosen as control group; East Amanuban, Polen and Kualin. Data collection before and after the intervention was conducted on samples from those 9 districts.

The study was conducted across 5 months in 2014 from January-May. The first month of preparations included collecting baseline data, followed by 3 months for providing the intervention, then one month for collecting post-intervention data, data analysis and finally report preparation. Total 72 samples were required, which was amounted to 24 samples for each treatment. Data processing was performed using a computer program, Nutrisurvey, from the diet recall to obtain a description of nutrient intake.

Statistical analysis: Data were analyzed using statistical tests, both descriptive and analytic, such as univariate analysis, Mann-Whitney tests, Wilcoxon tests, ANOVA and chi-square tests.

RESULTS AND DISCUSSION

Table 1 shows that there were no differences in sex, age, morbidity history or nutritional status of respondents between treatment groups and the control group.

Table 1 shows that the results of the homogeneity tests of respondents by sex, age and history of morbidity. The results of this study indicated that the values between the treatment groups and the control group were on average, equal/homogenous in all variables tested including the sex distribution ($p = 0.128$), the mean age ($p = 0.398$), those suffering from fever ($p = 0.509$), those with a cough ($p = 0.776$), those suffering from diarrhea ($p = 0.680$), those suffering from a snotty nose ($p = 0.318$), those suffering from asphyxia ($p = 0.680$) and the means of stunting ($p = 0.458$), wasting ($p = 0.228$) and being underweight ($p = 0.172$).

Table 2 shows that the analysis of the socio-economic characteristics of the respondents.

Table 2 shows that the results of homogeneity tests of respondents' families by maternal age, paternal age, total family members, maternal education, paternal education, maternal occupation and paternal occupation of the respondent. The results of this study indicated that the

Table 2: Analysis of socio-economic characteristics of the respondents in the treatment and control groups

Variables	LNS (ng mL^{-1}) n = 24	MP-ASI SUN (ng mL^{-1}) n = 24	Control (Person) n = 24	Total (Person) n = 72	p-value
Age of mother (years)	32.65±8.1	34.5±12.3	35.2±12.1	34.1±10.9	0.593
Age of father (years)	41.13±9.9	40.9±15.9	39.7±9.4	40.6±12.1	0.797
Total family members	4.29±7.1	2.7±2.8	3.1±4.1	4.3±6.9	0.276
Maternal education					
Basic education (n(%))	15 (62.5)	16. (66.7)	20 (83.3)	51 (70.8)	0.244
Paternal education (n(%))					
Basic education	20 (83.3)	22 (91.7)	19 (79.2)	61 (84.7)	0.472
Maternal occupation (household)	21 (87.5)	16 (66.7)	20 (83.3)	57 (79.2)	0.221
Paternal occupation (farmer)	9 (39.1)	11 (47.8)	15 (62.5)	35 (50.5)	0.421
Family income (less)	12 (50.0)	6 (25.0)	19 (79.2)	37 (51.4)	0.001

LNS: Lipid-based nutrient supplement, significant difference among groups (p<0.05)

Table 3: Factors associated with the level of IGF-1 in the treatment and control groups

Variables	(Mean±SD)	p-value
Consumption of protein (g)	10.17±7.74	0.002
Consumption of zinc (g)	1.65±1.29	0.013
Consumption of phosphorus (g)	163.75±10.7.09	0.000
Family income (Rupiah)	913.722±818.1	0.023
Length of breastfeeding period (h)	8.13±5.614	0.000

treatment groups and control group were equal/homogenous in variables including mean maternal age (p = 0.953), mean paternal age (p = 0.797), mean maternal education (p = 0.244), mean paternal education (p = 0.472), mean number of family members (p = 0.276), maternal occupation (p = 0.221) and mean paternal education (p = 0.421). However, a difference was seen in family income (p = 0.001), such that family income in the treatment group was not homogeneous with family income in the control group.

Factors associated with the levels of IGF-1 were consumption of protein, phosphorus, zinc, economic status and the duration of time spent breastfeeding. Mean consumption of protein was 10.17±7.74 g. Statistical analysis with a correlation test revealed that there was a relationship between the consumption of proteins and the levels of IGF-1 (p = 0.002, p<0.05). Furthermore, mean consumption of zinc was 1.65±1.29 mg. Statistical analysis with a correlation test revealed that there was a relationship between the consumption of zinc and the levels of IGF-1 (p = 0.013, p<0.05). The mean consumption of phosphorus was 163.75±107.09 mg. Statistical analysis with correlation tests revealed that there was a relationship between the consumption of phosphorus and the levels of IGF-1 (p = 0.000, p<0.05). Mean family income obtained was Rp. 913.722±818.174, which is still under the minimum wage for South Central Timor (Rp. 1.100.000 per month). Statistical analysis with correlation tests revealed a relationship between family income and levels of IGF-1(p = 0.023, p<0.05). Breastfeeding duration was on average, 8.13±5.614 months and correlation tests revealed a relationship between breastfeeding duration and levels of IGF-1(p = 0.000, p<0.05) (Table 3).

Table 4: Multivariate analysis of factors associated with IGF-I in the treatment and control groups

Variables	(Mean±SD) (ng mL^{-1})	p-value
Consumption of protein	0.359	0.221
Consumption of zinc	0.058	0.001
Consumption of phosphorus	-1.545	0.381

Correlation tests: After collecting the data variables, some variables were included in the multivariate analysis (Table 3). In this analysis, the most influential variable on the level of IGF-1 was consumption of zinc (B = -1.492) (Table 4).

Linear regression test: Table 5 shows that whether there was a difference in the levels of IGF-I before and after intervention between the treatment groups and the control group.

Table 5 shows that the median IGF-1level in the LNS group before the intervention was -0.004 ng mL^{-1} and the median IGF-1 level after the intervention was 3.751 ng mL^{-1}. The results of the Wilcoxon test showed differences in the IGF-1 levels before and after the intervention were significant with p = 0.028. In the MP-ASI SUN group, the median IGF-1level was -0.005 ng mL^{-1} before the intervention and the median IGF-1 level after the intervention was 0.215 ng mL^{-1}. The results of the Wilcoxon test showed that there were no significant difference in the IGF-1 levels before and after the intervention in the MP-ASI SUN group (p = 0.458). For the control group, the median IGF-1 level was -0.005 ng mL^{-1} before the intervention and the median IGF-1 level after the intervention was -1.48 ng mL^{-1}. The results of the Wilcoxon test showed that there was not a difference in the IGF-1 levels

Table 5: Significant difference for increased IGF-1 and between treatment and control groups

Groups (n = 24)	Level of IGF-1 (ng mL^{-1}) Before (Median)	After (Median)	*p-value	Delta	**p-value
LNS	-0.004	3.751	0.028	3.754	0.066
MP-ASI SUN	-0.005	0.215			
MP-ASI SUN	-0.005	0.215	0.251	0.22	0.025
Control	-0.005	-1.48			
Control	-0.005	-1.480	0.458	-1.473	0.000
LNS	-0.004	3.751			

*Wilcoxon test **Mann-Whitney test, LNS: Lipid-based nutrient supplement

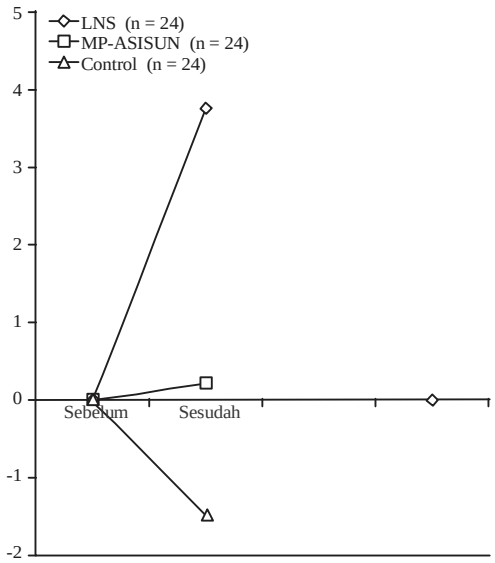

Fig. 1: Differences in IGF-1 level in the treatment and control groups
Source: Rantesalu[41]

before and after the intervention (p = 0.253). The delta value for the LNS group was 3.754, the delta value for the MP-ASI SUN group was 0.22 and the delta value for the control group was -1.473.

Comparisons between the LNS group and the MP-ASI SUN group showed no statistical difference in IGF-1 levels (p = 0.066, p>0.05). Comparison of the level of IGF-1 between the LNS and control groups before and after treatment showed a significant difference (p = 0.000, p<0.05). The comparison of IGF-1 between the MP-ASI SUN and control groups before and after treatment showed a difference in IGF-1 levels (p = 0.025, p<0.05).

Figure 1 shows that the increase in IGF-1 in the LNS group was larger than in the MP-ASI SUN group and IGF-1 levels decreased in the control group.

DISCUSSION

Based on the test results of the characteristics of the respondents' family, there were no differences among the treatment and control groups. The mean maternal age (p = 0.953), the mean paternal age (p = 0.797), the mean number of family members (p = 0.276), the mean maternal education (p = 0.244), the mean paternal education (p = 0.472), the mean value for maternal occupation (p = 0.221) and the mean value for paternal occupation (p = 0.421) did not different among groups.

The LNS group still had 62.5% of mothers and 83.3% of fathers with a value below the mean for basic education, the MP-ASI SUN group had 66.7% of mothers and 91.7% of fathers with a value below the mean for basic education and the control group had 83.3% of mothers and 79.2% of fathers with a value below the mean for basic education. The level of education for parents, especially for mothers were very influential in child care, as argued by Wang *et al.*[16] and parental education and experience in child care will affect their readiness to carry out the parenting role.

Maternal occupation was typically as a housewife for the LNS group (87.5%), the MP-ASI SUN group (66.7%) and the control group (83.3%). Paternal occupation was typically as a farmer for the LNS group (39.1%), the MP-ASI SUN group (47.8%) and the control group (62.5%). The total number of family members averaged was 4.3±6.9 (p = 0.276). Typically, the respondent's mother was a house wife or did not have an additional occupation to support the family income, which typically came from farming. Adequate income will provide greater opportunities to the family/mother to support the needs of the children and to facilitate the development of the child. The total number of family members also influences family spending and economic revenue. The larger the family, the greater the family's needs and the greater the needed economic revenue[21].

Several factors that were associated with the levels of IGF-1 included the consumption of protein, zinc, phosphorus and family income. All these factors were correlated statistically at p<0.05. Correlation tests revealed a relationship between the consumption of proteins and IGF-1 levels (p = 0.002, p<0.05). Protein is very important in the formation of IGF-1. The results of previous studies providing meals high in protein showed increased levels of IGF-1 in

infants[22]. Furthermore, present study also clarified that the provision of an additional 5% protein in mice can increase the levels of IGF-1 as a growth hormone[23]. Likewise, another study found that IGF-1 was correlated with child's weight. Foods high in protein can reduce the need for insulin and insulin resistance is accompanied by increased levels of IGF-1, which is produced from the synthesis of IGF-1 and protein binding, leading to increased levels of IGF-1 in plasma[24].

Studies in animals have indicated that the intake of protein can cause post-receptor changes responsible for the decreased transcription of IGF-1 mRNA, which can cause a decrease in the production of IGF-1[25] and increase affinity for IGF-1 to bind IGFB-3 proteins that lack of protein and disappear from the serum. Protein plays a role in modulating circulating concentrations of IGF-1 related to less protein intake. The results of a study conducted by Yakar *et al.*[26] showed that high protein intake may promote increased levels of IGF-1, whereas low protein intake reduces the activity of IGF-1.

Consumption of zinc was also found to be significantly correlated with IGF-1 levels ($p = 0.013$, $p<0.05$). Zinc is also involved in the regulation of bioactivity of IGF-1 and affects concentrations of circulating IGF-1 levels in humans. Low zinc status is associated with low circulating levels of IGF-1 despite adequate caloric intake[27].

Zinc is needed by the body as zinc has an influence on the synthesis of DNA during the IGF-1 stimulation phase of the cell cycle. Total zinc concentrations of 3T3 cells treated with DTPA for 16 h did not differ from untreated cells. Only a small groups of the cells were affected by MacDonald *et al.*[28]. Other studies have provided strong evidence that the presence of zinc deficiency contributes to stunted growth in children. It can be concluded that the production and presence of IGF-1 was also determined by the concentration of zinc in serum, enough such that adequate protein intake must be followed by sufficient intake of zinc to produce IGF-1.

Consumption of phosphorus was also significantly correlated with IGF-1 levels ($p = 0.000$, $p<0.05$). These results are consistent with other study suggesting the intake of phosphorus is the most powerful factor related to the levels of IGF-1 ($p<0.0001$). Studies by Norat et. al.[29] and Hurks *et al.*[30] reported that the serum levels of IGF-1 were significantly, positively correlated with phosphorus levels. Gerschman and Marenzi[31] and Rivera *et al.*[32] found changes in blood inorganic phosphorus levels of 4.25-7.88 mg as a result of injections of pituitary extracts[18].

Family income was significantly correlated with IGF-1 levels ($p = 0.023$, $p<0.05$). Other studies have explained that there is a large influence of economic status on the formation of IGF-1 and IGF binding protein-3. Economic status (family income) is critical to the ability to purchase food that provides the essential elements needed by the body, such as proteins, zinc and phosphorus, which are important in the formation of IGF-1 in children.

Similar results were found in studies conducted in Senegal of breastfeeding for up to 2 years. A longitudinal study of 133 Afro-Colombian infants aged 5-7 months who were followed until the age of 18 months also stated a positive effect of breastfeeding on weight gain and body length. Study conducted in the Republic of Belarus observed the results of exclusive breastfeeding and breastfeeding for longer triggers weight gain and body length increase in the first months yet showed no deficit in weight or height at 12 months[33].

In the MP-ASI SUN group, the median level of IGF-1 before the intervention was -0.005 ng mL^{-1} and the median level of IGF-1 after the intervention was 0.22 ng mL^{-1}. The results of the Wilcoxon test observed no significant difference in the levels of IGF-1 before and after the intervention ($p = 0.458$). The control group had a median level of IGF-1 of -0.005 ng mL^{-1} before the intervention and a median level of IGF-1 of 1.48 ng mL^{-1} after the intervention. The results of the Wilcoxon test observed that there was no significant difference in the levels of IGF-1 before and after the intervention ($p = 0.253$).

Based on Mann-Whitney tests, there was no statistical difference in the levels of IGF-1 between the LNS and MP-ASI SUN groups ($p = 0.066$, $p>0.05$) but there were differences in the average increase in IGF-1 between the LNS and control groups ($p = 0.000$, $p<0.05$) and between the MP-ASI SUN with control groups ($p = 0.025$, $p<0.05$).

This study provided evidence that the administration of LNS is better for increasing IGF-1 levels than MP-ASI SUN and better than no intervention. The results of this study are supported by another study[32] that used controlled experiments to complete community-based interventions that included animal food sources, either together with micronutrient supplements or other food sources and showed positive growth among children. Three trials that used animal food sources alone (skim milk powder) also produced a positive growth response. However, the geographical scope of the last three trials was limited and it is unclear to what extent additional animal food sources and the type of animal food sources can be used to enhance the growth of at-risk children[32, 34-36].

The LNS fulfills nutritional needs for about half of the dietary allowances. The level of IGF-1 will increase after subjects reach an adequate nutritional status. The decrease in

free IGF-1 appears to be the result of the increase in IGFBP-1, which occurs due to a decrease in insulin. It is speculated that the reduced levels of IGF-1, driven by an increase in IGFBP-1, serves to protect against insulin-like activity from nutritional deficiencies[37]. Similarly, restricted nutrients can modulate the insulin signal in response to the intake of energy through the suppression of growth hormone IGF-1. A study in Germany, Belgium, Italy and Spain on the intake of protein from milk found that endocrine metabolic response and growth in infancy and IGF-1 was higher in the group with high protein intake compared to the group with low protein intake[38-40].

CONCLUSION AND RECOMMENDATIONS

This study can be concluded that factors associated with the levels of IGF-1 are the consumption of protein ($p = 0.002$), zinc ($p = 0.013$), phosphorus ($p = 0.000$), family income ($p = 0.023$) and breastfeeding duration ($p = 0.000$). Multivariate analysis observed that the consumption of zinc ($B = -1.492$) was the most significant factor. The median value of the level of IGF-1 in the LNS group before intervention was -0.004 ng mL^{-1} and the median IGF-1 level after the intervention was 3.751 ng mL^{-1}, which the Wilcoxon test results indicated a significant difference with ($p = 0.028$). The MP-ASI SUN group had a median IGF-1 level of -0.005 ng mL^{-1} before the intervention and a median IGF-1 level of 0.21 ng mL^{-1} after the intervention, which Wilcoxon test results showed a non-significant difference with ($p = 0.458$). The control group had a median IGF-1 level of -0.005 ng mL^{-1} before the intervention and a median IGF-1 level of -1.480 ng mL^{-1} after the intervention. The results of the Wilcoxon test found that the difference was not significant ($p = 0.253$). The delta value for the LNS group was 3.754, the delta value for the MP-ASI SUN group was 0.22 and the delta value for the control group was -1.473. There were differences in the concentration of IGF-1 between the LNS and control groups ($p = 0.000$) as well as between the MP-ASI SUN and control groups ($p = 0.025$). The LNS intervention was better at increasing the levels of IGF-1 compared to MP-ASI SUN.

The recommendation for the government, especially the Health Office of TTS is to create a policy to implement an LNS program, as it has been shown to increase the levels of IGF-1, which is an important element in the growth of children under 2 years old. For scientific advancement, further study is needed on the efficacy of LNS on IGF-1 levels by developing other variables and variations in the research methods and instruments that can be used to study components of the LNS program.

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