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Research Article

THE EFFECT OF GIVING MORINGA-HONEY ON LEUCOCYTE AND TOTAL LYMPHOCYTE COUNT IN PREGNANT WOMEN IN MAROS DISTRICT

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Abstract: Nutrition is one of the basic human needs required for energy, cell regeneration, and wound healing. This study aimed to assess the effect of Moringa-Honey on leukocyte and Total Lymphocyte Count in Turikale and Lau Health Centers. It was a Randomized Controlled Trial with Pre and Post Double-Blind, examined the leukocyte and Total Lymphocyte Count conducted in the working area of the Turikale Public Health Center and Lau Public Health Center, Maros District, from February 3 to April 30, 2020. Based on purposive sampling, about 46 pregnant women were involved (24 respondents obtained 5 ml/day of Moringa-Honey (MK) plus Fe Tablets; 22 respondents obtained 15 ml/day of Regular-Honey (MB) plus Fe Tablets) and intervention was every morning during 8 weeks. Data were analyzed using Paired T-Test and Independent Sample T-Test using SPSS version 26. There was a significant decrease in Leukocyte levels after the intervention in the Moringa-Honey and Regular-Honey groups, with the difference of 1225/µL and 1154/µL, respectively. The p-value of both groups was 0.252 (α= 0.05), which indicated no significant difference between the two groups. However, the total lymphocyte count (TLC) in the two groups showed no changes occurred. The significant reduction in leukocyte levels in both groups and a greater slope was developed after consuming Moringa-Honey. There was no change in the total lymphocyte count in either the Moringa-Honey or Regular Honey groups.

Keywords: Moringa Honey, Leukocyte, Total Lymphocyte Count, Pregnant Women.

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1. Introduction

Pregnancy is a susceptible period in a woman's life, which is vulnerable to physical and mental disorders (Ashraf-Ganjoei, Mirzaei, & Anari-Dokht, 2011). Nutrition is one of the basic human needs required to conserve energy, regenerate cells, and play a role in the wound healing process (Harjodisastro, Syam, & Sukrisman, 2006)(Sudoyo, Setiyohadi, Alwi, Simadibrata, & Setiati, 2006)(Braunwald, Hauser, Fauci, Longo, Kasper, & Jameson, 2004) . Malnutrition can cause a decrease in body mass, decline, organ dysfunction, and a reduction in the number of lymphocytes and the immune system (Macpherson, De Agüero, & Ganal-Vonarburg, 2017)(Sobotka, Allison, Furst, Meier, Pertkiewicz, & Soeters, 2004) .

The World Health Organization (WHO) states that infection is one of the leading causes of death in mothers and is one of the causes of premature infant mortality (Maternal mortality, 2019). In Indonesia, the most significant cause of maternal mortality during 2010-2013 was an infection, which ranked third. In 2013, the incidence of infection was 7.3, which was higher when compared to 2012, which was 5.6% (Kemenkes, Pedoman Manajemen Pelayanan Kesehatan, 2014).

In 2019, the Regency/City Data Recapitulation showed the number of maternal deaths in South Sulawesi Province as many as 144 cases (Dinkes, 2019). From the Maros District Health Office data in 2019, it was estimated that 20% of pregnant women experienced obstetric complications. The maternal mortality rate in 2019 was 45 people.

Pregnant women are suggested to consume enough Vitamin C every day to maintain a healthy body and antioxidants for the mother and fetus. The minimum amount of vitamin C a mother needs per day is 85 mg (Kemenkes, Profil Kesehatan Indonesia tahun 2017, 2018). Research conducted by Astriningrum et.al said that the average intake of vitamin C for pregnant women did not meet the standard requirements (Astriningrum,

Hardinsyah, Nurdin, & Muharam, Intake of folic acid, vitamin B12 and vitamin C among pregnant women in Indonesia based on Total Diet Study, 2017).

Pregnant women need a good intake of nutrients to meet their nutritional needs. Food intake during pregnancy is different from intake before pregnancy (Macpherson, De Agüero, & Ganal-Vonarburg, 2017)(Syari, Serudji, & Mariati, 2015). Based on the nutritional adequacy rate, pregnant women need additional macro and micronutrients in each trimester of pregnancy (Permenkes, 2019). Micro and macronutrients are needed to help improve the system. The minimum amount of macronutrientneeded per day are carbohydrates (400 grams), protein (70 grams), and fat (67.3 grams), while the protein adequacy of pregnant women is less than 80% of the protein adequacy rate (Nutritional Adequacy Rate).

Moringa leaf or honey supplementation can be given to pregnant women and provides health benefits for both mother and baby. Several studies have shown that Moringa leaf supplementation significantly increases hemoglobin levels, increases maternal weight, reduces stress and cortisol levels, and increases blood levels of antioxidants (Hadju, Dassir, Sadapotto, Putranto, Marks, & Arundhana, 2020).

Moringa is food ingredients that are rich in nutrients for the body. It contains many nutritional compositions, including protein, fat, carbohydrates, fiber, various vitamins, calcium, magnesium, phosphorus, potassium, copper, iron, sulfur, phenolic acid, β-carotene, Vitamin C, potassium, selenium, zinc, and essential amino acids (Gopalakrishnan, Doriya, & Kumar, 2016)(Valdez-Solana, et al., 2015)(Rumbold, Fletcher, & Daniels, 2012).

Honey plays a vital role in the activation of antibacterial, anti-inflammatory and can boost the immune system (Pais-Chanfrau & Trujillo-Toledo, 2016)(Nguyen, Panyoyai, Kasapis, Pang, & Mantri, 2019). The study results stated that Moringa leaf extract contains polyphenolic compounds, flavonoids, and phenols as antioxidant components that act as free radical scavengers (Nguyen, Panyoyai, Kasapis, Pang, & Mantri, 2019). Other research also reveals that this superfood contains iron, vitamin A, vitamin B, vitamin C, vitamin E, calcium, amino acids, protein, and iron (Nurdin, Imam, Thahir, & Hadju, 2018)(Nadimin, Hadju, As'ad, & Buchari, 2015)(Hastuty, Hadju, & Ariyandy, 2020).

Research conducted by Hasriani et al. in 2020 illustrates that Moringa leaf tea plus Fe tablets effectively suppress leukocyte levels of pregnant women (Hasriani, Nontji, Hadju, As'ad, Singrang, & Bahar, 2020). In addition, Kartika Sari Senas and YunitaLinawati show a significant effect of forest honey on lymphocyte proliferation improvement in male Wistar rats (Senas & Linawati, 2012).

In another study conducted by Rakhman et al. in 2020, based on in vitro test, Moringa-Honey decided safe for consumption by experimental animals (Rakhman, Hadju, & Bahar, 2020). An analysis in the Hasanuddin University Laboratory illustrates those carbohydrates, protein, fat, vitamin C, and zinc are more than regular Honey. Thus, it is safe for consumption by pregnant women. Currently, there is no research examining the Moringa-Honey (Honey from bees fed Moringa juice) on the pregnancy.

2.Objectives Of The Study

This study aimed to determine the effect of Moringa-Honey on Leukocyte Levels and Total Lymphocyte Count in pregnant women.

3.Research methodology

This research was conducted in Maros District, approximately 33.40 km from Makassar, the capital city of South Sulawesi Province, Indonesia. The area of Maros of 1619.11 km2, with 353,121 residents. It consists of 14 sub-districts and has 14 Public Health Centers (in Indonesian is: Pusat Kesehatan Masyarakat, abbreviated as Puskesmas). Turikale Health Center and Lau Health Center were chosen as the main places to conduct this research, involving all pregnant women aged 20-27 weeks who were registered at those two Health Center from February to April 2021.

3.1. Intervention materials

Moringa oleivera was purchased from the Antang regional market, Makassar City, freshly picked and gathered from the Gowa District, South Sulawesi Province. The eaves were washed and blended until smooth. Then, it was mixed with one kg of sugar dissolved in 500 ml of water. Furthermore, the Moringa juice was given to the bees that have been caged in mosquito nets located at the Faculty of Forestry, Hasanuddin University, Makassar. Later, Honey was harvested every two weeks to meet the needs of researchers by putting the existing Honey into a jerry can.

The harvested Moringa-Honey was then put into the Faculty of Mathematics and Natural Sciences Laboratory, Hasanuddin University. There, the results obtained that Moringa-Honey contains protein (8700 ppm), fat (100 ppm), polyphenols (610ppm), carbohydrates (802,600 ppm), flavonoids (289,822 ppm), vitamin C (670 ppm), Fe

(307.22 ppm), calcium (302.86 ppm), sodium (705.8 ppm), magnesium (84.51 ppm), potassium (1400 ppm), phosphorus (300 ppm), zinc (2,4428 ppm), and Antioxidant inhibitory (53.16%).

Moringa-Honey had also been tested for its toxicity content by the Faculty of Pharmacy, Hasanuddin University, Makassar, with an LC50 value of 614.58 g/mL. This Honey is classified as low toxicity (LC50 > 500 g/mL), so it is safe for consumption by pregnant women.

3.2. Experiment Design

It was a Randomized Control Trial (RCT) that randomly allocated participants into one of two existing groups. Eligibility criteria were 20-27 weeks gestation, parity one to three, and singleton fetus. Those who were eligible (n=36) were randomly allocated into two groups. The randomization sequence was made by hand, and field researchers carried out the allocation to each group, and mothers were asked to take a small rolled-up piece of paper that contained the words A or B from a can. If the mother took the paper containing the letter A, the mother would receive Honey from bottle A and vice versa. Mother was given 100 ml of Honey in a bottle coded A and B according to the letter taken at the randomization. The treatment given in letters A and B was only known by the main researcher.

The study began on February 3, until April 30 of 2021. Pregnant women at 20-27 weeks of gestation who came to the public health centers were screened for eligibility in the study. Four field researchers screened 80 mothers: 50 were eligible to participate in the study and were divided into two groups, 25 people consumed MK (Moringa-Honey), and 25 people consumed MB (Regular Honey).

During the intervention, 4 subjects dropped out (1 respondent of Honey in bottle B and 3 respondents of Honey in bottle A) due to family problems and refused to continue consuming Honey. Furthermore, the remaining 46 respondents of this study were divided into 24 pregnant women consuming Honey in bottle B and 22 pregnant women consuming Honey in bottle A. Data for this subject were included in the analysis.

There were two interventions in this study, the provision of Moringa-Honey and Regular Honey. Both interventions were put into the same bottle with a capacity of 100 ml each. Mothers were instructed to take 15 ml of Honey in the morning and one Fe tablet at night for 8 weeks of intervention. So, each mother in one group received 1 bottle of 100 ml Moringa-Honey (daily dosage of 15 ml/per day), while in the other group, each mother received 1 bottle of 100 ml Regular Honey (daily dosage of 15 ml/per day).

At the end of each week, adherence to the intervention was assessed by field researchers by checking the amount of Honey left in the bottle. The amount of Honey consumed and the reason for the mother's refusal was written on a standard form. Field investigators sent a short electronic message to the mother every morning for a reminder of Honey consumption. Mothers were asked to respond to the messages, or field workers would call to encourage honey consumption. All mothers included in the analysis were finished all given Honey (100%).

3.3. Outcome variables

The main outcome variables measured before and after the intervention were leukocyte levels and total lymphocyte count, measured by the analysts. Maternal characteristics were assessed at baseline using a standardized questionnaire, including the family's economic status, such as the education and occupation of the mother and husband, monthly family income, and the number of family members.

Leukocyte levels and total lymphocyte count were calculated using a hematology analyzer. Blood sampling was done at the Turikale Health Center. About 3 ccs of blood were taken and put into the tub, then examined using a hematology analyzer. According to the standard, the normal value of Leukocytes is 3,200/µl-10,000/µl, and the total lymphocyte is 1,700/µl-3,500/µl.

3.4. Statistical Analysis

Collecting data was using a questionnaire and processed using SPSS for windows version 26. The respondent characteristics were analyzed using Chi-Square, changes in each group (before and after the intervention) were analyzed using the Paired t-Test, while the differences between groups were analyzed using the independent t-Test.

3.5. Ethical Approval

Ethical approval for this research was granted by the Ethics Committee of the Faculty of Medicine, Hasanuddin University, Makassar, Indonesia, in May 2021 with protocol number UN4.14.1/TP.02.02/2021. Each mother gave written consent during study enrollment.

4.Results

Table 1 data shows that most Moringa-Honey (MK) group respondents were aged 20-25 years old, while in the Regular Honey (MB) group were aged 26-30 years old. The majority of pregnant women had a high school/vocational high school education level, were housewives, had more than 1 child, and had monthly income was in the sufficient category. The statistical test results of the difference between the two groups at the beginning of the study showed no difference in age, last education, occupation, and income between the MK and MB groups. Those were indicated by p-value >0.05. While in gravida, a significant difference between MK and MB was a p-value of 0.045 ($\alpha < 0.05$).

Table 1. Frequency Distribution of Respondents Characteristics

Characteristics	Control		Intervention		p value
	N	%	n	%	
Age					
20 – 25	8	18.1	10	20.8	0.230
26 – 30	12	27.2	8	16.6	
31 -35	2	4.8	6	12.5	
Parity					
Primigravida	7	14.5	2	4.1	0.045
Multigravida	15	31.2	22	45.8	
Education					
Elementary School	3	6.8	8	16.6	0.398
Secondary School	7	15.9	4	8.3	
High/Vocational School	11	25.0	10	20.8	
Diploma	0	0.0	1	2.0	
Bachelor	1	2.2	1	2.0	
Job					
Housewife	22	50	21	43.7	0.401
Self-employed	0	0	1	2.0	
Midwife	0	0	1	2.7	
Teacher	0	0.0	1	2.0	
Income					
High	0	0	2	4.1	0.343
Enough	20	45.4	19	39.5	
Low	2	4.5	3	6.2	

The data in Figure 1 shows that the two groups were given Moringa-Honey and Regular Honey had the energy nutrients, carbohydrates, fats, protein, iron, vitamin C, vitamin E, calcium, and folic acid below 80% of the minimum RDA set. Furthermore, the nutrient analysis test had a statistical value of $p > 0.05$, which means that both groups had an equivalent nutritional intake before being given treatment.

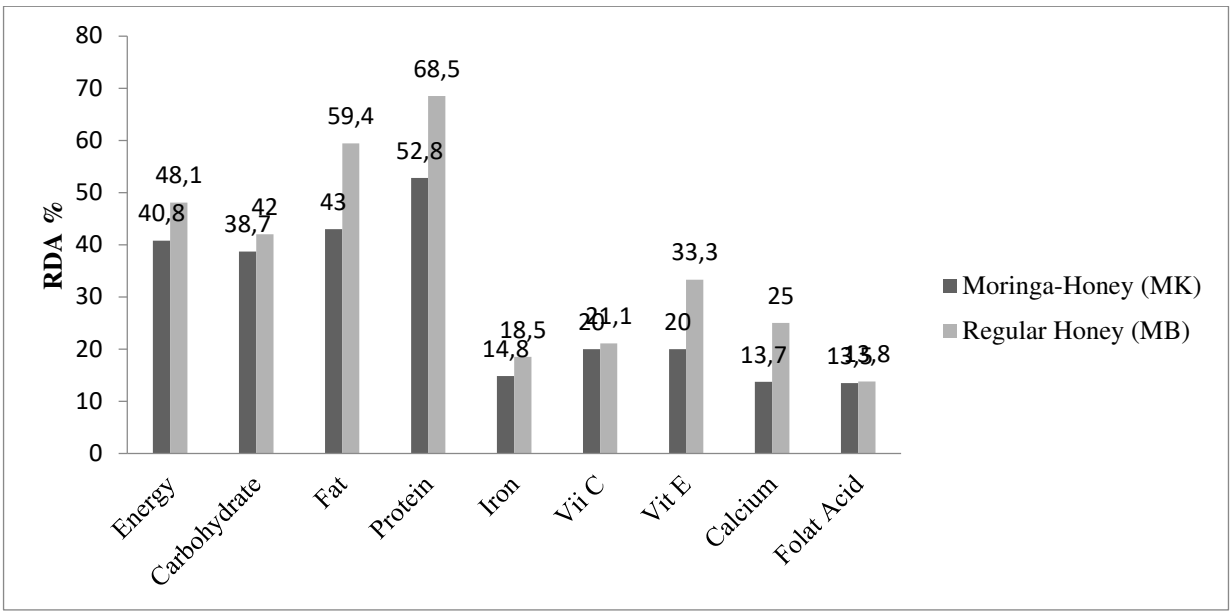

Figure 1. Overview of Respondents' Basic Nutritional Adequacy Rate

Based on Table 2, it can be seen a significant drop in leukocyte levels after the intervention in both groups given Moringa-Honey and Regular Honey. In the group of Moringa Honey, the average difference before and after the intervention was 1225/µL. Meanwhile, in the respondents who were given Regular Honey, the average difference before and after the intervention was 1154/µL. The p-value between the two groups was 0.252 (α> 0.05), which means that the reduction in leukocyte levels between both groups was not significant.

Furthermore, there was no change in the total lymphocyte count in both groups. In the group given Moringa-Honey, the average TLC before the intervention was 1795/µL, and after the intervention was 1820/µL with a p-value of 0.833 (α> 0.05). In respondents who were given Regular Honey, the average TLC before intervention was 1826/L and after the intervention was 1846/µL, p-value 0.856/µL (α > 0.05).

Table 2. Differences in Leukocyte and Total Lymphocyte Levels of respondents before and after giving Moringa honey and Regular Honey

Variables		n	Mean ± SD		*P* Value	Difference Mean ± SD	P value
			Pretest	Posttest			
Leukocyte level	Intervention	24	9454 ± 2276	8229 ± 2098	0,011	-1225 ± 2182	0,252
	Control	22	9986 ± 1884	8831 ± 2067	0,002	-1154 ± 1559	
Total Lymphocyte Levels	Intervention	24	1795 ± 549	1820 ± 530	0.833	25 ± 575	0,932
	Control	22	1826 ± 471	1846 ± 529	0.856	20± 521	

5.Interpretation of the result

This study showed a significant decrease in leukocyte levels before and after the intervention in both groups, Moringa-Honey (MK group) and Regular Honey (MB group). A greater slope of leukocyte levels was found in the group given Moringa Honey than the group was given Regular Honey. Also, there was no change in the total lymphocyte count in either the Moringa honey or Regular honey groups.

The reduction in leukocytelevelsoccurred in the MK and MB groups because Honey contains vitamin C and flavonoids (antioxidants) to overcome inflammation. The elevation in free radicals in the body will damage healthy cells and trigger inflammation (Prakasa, 2015). Furthermore, vitamin C and flavonoids contained in Honey will bind to free radical electrons so that inflammation stops.

Antioxidants work by donating one electron to oxidant compounds so that the activity of these oxidant compounds can be inhibited. There are two antioxidants, enzymatic antioxidants, and non-enzymatic antioxidants. Enzymatic antioxidants include superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) enzymes. Meanwhile, non-enzyme antioxidants include glutathione (GSH), vitamins C, vitamin E, β-carotene, flavonoids, isoflavones, flavones, anthocyanins, catechins, isocatechins, and lipoic acid (Santoso, Canada, Latson, Alladi, Lucci, & Coleman, 2000)(Crevel, 2001).

The exaggerated free radicals in the body can damage more healthy cells and DNA, which leads to the disease occurrence. Damaged cells can quickly damage other cells. It may cause premature birth, congenital disabilities, and even dangerous for the pregnancy continuity.

The slope in leukocyte levels was more significant in the MK group because Vitamin C and flavonoids in Moringa-Honey were better than Regular Honey. Vitamin C and flavonoids in Moringa-Honey are 670 ppm and 289,822 ppm. Meanwhile, Regular Honey contains Vitamin C of 460 ppm and flavonoids of 167.82 ppm.

The results of this study are in line with research conducted by Luthfiyah through an in vitro study in 2012, local Moringa leaf powder in West Nusa Tenggara could normalize the number of leukocytes and lymphocytes in rats with insufficient protein-energy (Luthfiyah, 2012). In addition, research conducted by Hasriani et al. in 2020, giving Moringa leaf tea plus Fe tablets was also effective in reducing leukocyte levels of pregnant women (Hasriani, Nontji, Hadju, As'ad, Singrang, & Bahar, 2020).

The total leukocyte count increases significantly in response to infection, trauma, inflammation, and certain diseases. Factors influencing leukocyte counts in healthy adults include gender, hormonal environment, genetic inheritance, stress levels, diet, nutrition, and lifestyle (e.g., tobacco-induced inflammatory changes, chronic psychological disorders) (Venkatalakshmi, Vadivel, & Brindha, 2016).

Total lymphocyte count is an indicator to assess the immune system. One of the nutrients that play a role in boosting the immune system is zinc. The mineral zinc is required for the metabolic activity of 300 of the body's enzymes and is considered essential for cell division and the synthesis of DNA and protein. These enzymes are involved in the metabolism of proteins, carbohydrates, fats, and alcohol. Zinc is also essential for tissue growth, wound healing, maintenance of immune system function (Askary, Jahan, Sabbagh, Jahani, Dourandish, & Kamachali, 2011).

Honey contains several types of minerals, including calcium, magnesium, potassium, iron, and zinc. Based on the results of laboratory universitas Hasanudddin tests by examining the zinc content in Moringa honey and ordinary Honey, it was found that the zinc content was more in Moringa honey than ordinary Honey. However, in this study, there was no increase in TLC due to honey intervention. Researchers also gave tablets to add blood to the research respondents. Zakiah et al. said that Moringa leaf extract capsules plus royal jelly could significantly reduce the average MDA levels (Zakiah, Hadju, & Ariyandy, 2020).

Zn absorption occurs in the duodenum, ileum, and jejunum and only slightly in the colon or stomach, and the most significant is in the ileum. Zn absorption is about 30 to 60%, influenced by the amount and balance of other minerals. Factors that influence the absorption of Zn include methionine, histidine, cysteine, citrate, picolinate. Meanwhile, those that inhibit the absorption of Zn include cadmium (Cd), cuprum (Cu), phosphorus (P), iron (Fe), and oxalate. In addition, the high calcium content and the presence of phytic acid can inhibit the absorption of Zn. This substance will bind Zn so that The gastrointestinal tract cannot absorb zinc. Therefore, the adequacy and balance of these minerals are important to consider in consuming foods and supplements (Widhyari, 2012). On a low-zinc diet, folic acid can inhibit zinc absorption and In high-zinc diets, there is a small inhibitory effect on zinc absorption (Hansen, Samman, Madsen, Jensen, Sørensen, & Sandström, 2001)(Milne, Canfield, Mahalko, & Sandstead, 1984).

Research conducted by Richard reveals that consumption of a high-calcium diet can significantly reduce net zinc absorption (Bourke, Berkley, & Prendergast, 2016).

Inhibited zinc absorption will cause zinc deficiency, suppressing immunity where there is a reduced number of antibody-forming cells in the spleen and impaired lymphocyte cell activation. In addition, zinc deficiency also results in reduced phagocytosis (Fiaccadori, Lombardi, Leonardi, Rotelli, Tortorella, & Borghetti, 1999). In addition, deficiency of lymphocytes in the body can reduce protection from infection, predispose to chronic inflammation of growth hormone, increase inflammatory metabolism at birth, metabolic defects and decrease maternal immune transfer factors, and increase exposure to pathogenic microbes (Zulaikhah, 2017).

Research conducted by Gunarsa in 2015 showed a relationship between malnutrition and total lymphocyte count. Malnutrition can lower the total lymphocyte count in hospitalized patients (Gunarsa, Simadibrata, Syam, Timan, Setiati, & Rani, 2015). Another study conducted by Najera in 2004 showed that well-nourished respondents without bacterial infection had more TLC than well-nourished respondents infected with bacteria, and malnourished respondents were infected with bacteria (Nájera, González, Toledo, López, & Ortiz, 2004). The study conducted by Fiaccadori by comparing the TLC of well-nourished, moderately malnourished, and poor-nourished respondents described the same thing: the total lymphocyte count was greater in respondents with good nutrition, while the lowest TLC amount was owned by respondents with poor nutrition (Fiaccadori, Lombardi, Leonardi, Rotelli, Tortorella, & Borghetti, 1999). Research conducted by Santoso in 2000 said that well-nourished patients had more lymphocyte counts than malnourished patients (Santoso, Canada, Latson, Alladi, Lucci, & Coleman, 2000).

The mechanism of lymphocyte reduction in malnutrition has not been clearly elucidated but is most likely related to thymic atrophy (Nájera, González, Toledo, López, & Ortiz, 2004). One of the nutrients associmuharamated with the cause of lymphoid thymus atrophy is zinc deficiency.

6.Conclusion

A significant drop in leukocyte levels in both groups and a greater reduction occurred in the group given Moringa-Honey. There was no change in the total lymphocyte count in either the Moringa-Honey or Regular honey groups.

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