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Bioscientia Medicina: Journal of Biomedicine & Translational Research

eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscimed.com

Relationship between Interleukin 6 Serum Levels and Degree of Depression in Systemic Lupus Erythematosus Patients Internal Disease in Dr. Moh Hoesin Palembang

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ARTICLE INFO

Keywords:
IL-6
Systemic Lupus Erythematosus (LES)
Depression

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/bsm.v5i2.224

ABSTRACT

Introduction. Systemic Lupus Erythematosus (LES) is a chronic autoimmune inflammatory disease affecting many organ systems with varied clinical manifestations, disease course and prognosis. One of the clinical manifestations that can occur is depression as much as 25%. In LES patients, there is an increase in proinflammatory cytokines, one of which is IL-6, which often associated with contributing to the pathophysiology of depression. The purpose of this study was to determine the relationship between serum IL-6 levels and the degree of depression in LES patients at RSUP DR. Mohammad Hoesin Palembang. **Methods**, analytic observational study in the form of correlation test with cross sectional design which was conducted in the Internal Medicine room RSUP DR. Mohammad Hoesin Palembang from May 2019 to March 2020. The number of study subjects was 40 samples who were LES patients with depression who had been calculated using the BDI (Beck's Depression Inventory). All subjects were examined for serum IL-6 levels and evaluated for factors that influence it. **Results**, there were 40 study subjects aged 18-56 years. The median degree of depression was 16 with a range of values from 10 to 40. There were 17 people (42.5%) with mild depression degree, 14 people (35%) moderate depression, and 9 people (22.5%) major depression. In LES activities, there were 5 people (12.5%) with light LES activities, 20 people (50%) with moderate LES activities, and 15 people (37.5%) with heavy LES activities. The median serum IL-6 level was 11.57 pg / mL with a value range of 1.1-50pg / mL. There was a significant correlation between the degree of depression and LES activity ($p = 0.004$; $r = 0.444$) and between serum IL-6 levels and the degree of depression ($p = 0.025$; $r = 0.169$). However, there was no significant correlation between serum IL-6 levels and LES activity ($p = 0.057$; $r = 0.304$). **Conclusion**, there is a relationship between serum IL-6 levels and the degree of depression in LES patients at Dr. Moh. Hoesin Palembang with a very weak correlation.

1. Introduction

Systemic Lupus Erythematosus (LES) is a chronic autoimmune inflammatory disease affecting many organ systems with various clinical manifestations, disease course and prognosis.[1-3] Genetic, immunological, hormonal and environmental factors play a role in the pathophysiology of LES.[1,3] According to the *World Health Organization* (WHO), the number of LES worldwide reaches five million sufferers, and each year more than 100 thousand new cases are found.[4] LES affects 1 to 12 people per 5.000 worldwide. Meanwhile in Indonesia, based on data from the Ministry of Health, in 2017 there were 2.166 LES sufferers, with a death rate of 550 patients due to LES. LES disease is more common in women than men, namely 2:1 to 15:1.[5-10] LES causes many manifestations, one of which is psychological

depression by 25%.[7]

Depression is one of the most common forms of psychosomatic disorders in LES sufferers. According to Lijuan Zhang, in 2017, by conducting a systematic review of 59 studies worldwide, there was a prevalence of depression of 5 - 76% in LES patients.[1,3] This figure is much higher than the incidence rate of depression in the general population where the prevalence of depression in the adult population in United States is estimated at 17.8%. The LES state accompanied by depression can exacerbate the patient's perception of the symptoms of the disease, reduce the quality of life, worsen the clinical outcome of LES, decrease adherence to medication and increase health costs.[7]

In LES disease there are various kinds of cytokines involved such as IL-6, IL-2, IL-4, IL-23, TNF-α, TGF-β, and IL-17.[12] Increased proinflammatory cytokines including TNF-α, interleukin (IL) -1 and IL-6, as a response to viral infection and chronic stress, can cause sick behavior characterized by fatigue, sleep disturbances, irritability, loss of appetite, depressed mood and even social withdrawal.[8] In addition to psychosocial factors due to long-term treatment, complaints related to disease and loss of productivity that reduce the quality of life of LES patients, it is estimated that the proinflammatory cytokines in LES also contribute to the pathophysiology of depression. IL-6 activator on the HPA axis, which is characterized by increased cortisol production and depressed mood.[9]

According to a metanalysis of 24 studies conducted by Dowlati et al and 29 studies by Liu et al, there were significantly higher concentrations of TNF-α and IL-6 in people with depression than in healthy controls.[6,7,10,11] This is in line with studies that conducted by Emilia et al that there is a role for TNF-α in LES patients who experience depression.[13] Likewise, a study conducted by Margarida et al where there was an increase in IL-6 in LES and RA patients who experienced depression.[14] As for other studies, namely that no relationship was found between psychosocial measurements and levels of cytokines (IL-6, IL-10, TNF-α IFN-γ and IL-8) in depressed patients who took medication and in controls in LES patients.[15]

From the research results and findings above, it can provide an understanding that LES and depression may have a common pathophysiological pathway that causes the two diseases to influence each other. Currently, there are very few publications about the relationship between IL-6 and the degree of depression in LES sufferers, especially in Indonesia. So that the more evidence obtained, the stronger the basis for conducting further studies to assess the role of IL-6 compared to other factors in the condition of LES patients who experience depression.

2. Methodology and samples

This type of research is an analytic observational study in the form of a correlation test with a *cross sectional* design. This research was conducted in the Internal Medicine section Dr. Mohammad Hoesin (RSMH) Palembang from May 2019 to March 2020. The study sample was patients who had been diagnosed with systemic lupus erythematosus at RSMH Palembang who had depression who were selected by *consecutive sampling* technique. The inclusion criteria of this study were LES patients who experienced depression through screening using BDI at RSMH Palembang, aged 18-60 years, who were willing to participate in the study by signing an *informed consent*. While the exclusion criteria for this study were patients who had psychotic disorders, were receiving antidepressant therapy, were pregnant and breastfeeding, were receiving hormonal contraceptive therapy, were undergoing CBT, and refused to participate in the study.

Procedure

For all research subjects included in the inclusion criteria:

1. Explanation of filling out the BDI questionnaire, then followed by taking demographic data, including age, gender, education, occupation, religion, duration of suffering from LES, type of drug consumed
2. Then do a physical examination including height and weight, body mass index (BMI)

3. Blood draw to check serum IL-6 levels.
4. Calculation of LES disease activity is performed using the MEX SLEDAI score.
5. Data is processed and analyzed using the program *statistical package for the social sciences* (SPSS) version 22 for Windows.

3. Results

There were 40 LES patients who included the inclusion and exclusion criteria as the sample. The results of the data normality test using Shapiro Wilk showed that most of the data were not normally distributed so that they were presented with a median (minimum-maximum) and normally distributed data were on nutritional status so that they were presented with mean ± standard deviation (SD). This study was dominated by a sample aged 18-40 years of 36 (90%) patients, 4 of whom were male. The youngest age in this study was 18 years and the oldest was 56 years.

This study was also dominated by an unemployed sample of 24 (60%) patients, 9 (22.5%) patients were students, 4 (10%) were civil servants and 3 (7.5%) patients were self-employed. The majority of the samples in this study had a normal nutritional status of 25 (62.5%), with an average BMI value of 21.24 ± 2.57. The duration of LES was predominantly> 12 months in 22 (55%) patients. The lowest LES duration was 1 month and the longest was 156 months. LES activity was calculated using the MEX-SLEDAI score. It was obtained that the sample with mild LES activity was 5 (12.5%) patients, moderate was 20 (50%) patients and severe there were 15 (37.5%) patients. The lowest score of the subject was 1 and the highest score in this study was 12.

Subjects were grouped based on the number of immunosuppressants, namely with one immunosuppressant as many as 6 subjects (15%), two immunosuppressants as many as 24 subjects (60%) and three suppressants as many as 10 subjects (25%). Only 1 subject received intravenous therapy, namely cyclophosphamide according to the specified cycle and at the time of the examination was undergoing a second series of cyclophosphamide. The degree of depression was dominated by samples with mild depression degrees of 17 (42.5%) followed by 14 (35%) samples with moderate depression and 9 (22.5%) patients experiencing major depression.

Serum IL-6 levels in the study sample were dominated by increased IL-6 levels by 31 (77.5%) patients, while samples with normal IL-6 levels were 9 (22.5%) patients. The examination of the mean serum IL-6 level in this study showed a median result of 11.97 pg / mL where the minimum level was 1.10 pg / mL and a maximum of 50 pg / mL.

The degree of depression in LES patients can be seen in Table 2. Judging by age, samples aged 18-40 years had mild depression as many as 17 (42.5%) and 14 (35%) patients had moderate depression and 9 (22, 5%) patients had severe depression. There were 3 (7.5%) patients aged 41-60 years who had mild depression and 1 (2.5%) other patients had moderate depression. Female patients with mild depression were 14 (35%) patients and moderate depression had a sample of 13 (32.5%) patients and 9 (22.5%) patients had severe depression. In male patients, 3 (7.5%) and 1 (2.5%) patients had moderate depression.

In the BMI based group, patients were predominantly normal BMI with mild depression as much as 12 (30%), 9 (22.5%) patients had moderate degrees and 4 (10%) patients with severe degrees. In samples with BMI 23-24.9 with mild depression as much as 2 (5%), 1 (2.5%) patients had moderate degrees and 3 (7.5%) patients with severe degrees. In samples with BMI > 25 with mild depression as much as 1 (2.5%), 2 (5%) patients had moderate degree and 1 (2.5%) patients with severe degree.

Based on the type of work, there were 3 students (7.5%), 2 civil servants (5%) and the most in the non-working group were 9 people (22, 5%). Most years of suffering from LES were in the group> 12 months as many as 6 people (15%) and those <12 months were as many as 8 people (20%).

Most LES activities were LES with moderate activity as many as 6 people (15%), light activity by 1 person (2.5%) and heavy activities by 7 people (17.5%). In major depression, it was found that all patients with

heavy LES activity were associated with depressive symptoms. Apart from the association with LES activity, the use of immunosuppressants is also associated with depressive symptoms.

Serum IL-6 levels in LES patients can be seen in Table 4. Judging at the age of the sample, it was dominated by IL-6 levels that increased by 28 (77.8%) samples at 18-40 years of age and 3 (75%) samples at 41-60 years old. Based on gender, there were 3 (75%) men and 28 (77.8%) women who had elevated levels of IL-6. In terms of nutritional status, there is 1 person who has a low BMI, 24 (80%) samples with normal BMI, 3 (60%) samples with BMI overload and 3 (75%) samples with obese BMI have increased IL-6.

In this study, there were 15 (83.3%) patients with LES duration < 12 months and 16 (72.7%) patients with lesion duration > 12 months experienced increased IL-6. Judging by the results of the MEX SLEDAI calculation, there are 5 (83.3%) samples with MEX SLEDAI scores of light activity, and each of the 13 samples in moderate activity and strenuous activity had IL-6 levels increased in their bodies. The results of the *Chi square* analysis showed that there was no significant relationship between IL-6 levels and LES patients. Of all the characteristic variables, there is no statistically significant correlation.

The analysis of the relationship between serum IL-6 levels and the degree of depression can be seen in Table 4.In this study, it was dominated by elevated serum IL-6 levels where at mild degrees there were 12 (38.7%) patients, at moderate degrees there were 14 (45.2%) patients and 5 (16.1%) patients had a severe degree. The results of the *chi square* analysis showed that there was a significant relationship between IL-6 and depression, but the strength of the correlation was very weak (p = 0.025, R = 0.169).

Table 1. Characteristics of LES patients who experience depression

General characteristics of the sample	N (%)	Means ± SD	Median (min-max)	P
Age (y.o)			30.50 (18 - 56)	0.028
• 18 – 40	36 (90%)			
• 41 – 60	4 (10%)			
Sex				
• Male	4 (10%)			
• Female	36 (90%)			
Profession				0.000
• College student	9 (22.5%)			
• Civil servants	4 (10%)			
• Does not work	24 (60%)			
• Entrepreneur	3 (7.5%)			
Nutritional status		21.24 ± 2.57		0.611
• Less	5 (12.5%)			
• Normal	25 (62.5%)			
• Over / Obese	10 (25%)			
LES duration (months)			19 (1 - 156)	0.000
• 1-12 months	18 (45%)			
• > 12 months	22 (55%)			
MEX SLEDAI			5 (1 – 12)	0.001
• Light	5 (12.5%)			
• Moderate	20 (50%)			
• Heavy	15 (37.5%)			
Total Immunosuppressants			2 (1 – 3)	0. 000

• 1	6 (15%)		
• 2	24 (60%)		
• 3	10 (25%)		
Depression Degree		16 (10 – 40)	0.000
• Light	17 (42.5%)		
• Moderate	14 (35%)		
• Heavy	9 (22.5%)		
IL-6		11.97 (1.10 – 50)	
• Normal	9 (22.5%)		
• Increase	31 (77.5 %)		

Table 2. Degree of depression based on characteristics

Characteristics	Degree of depression			Total n = 40 (n%)
	Easy	Moderate	Severe	
Age (yo)				
• 18 – 40	14 (35 %)	13 (32.5%)	9 (22.5%)	36 (90%)
• 41 – 60	3 (7.5%)	1 (2.5%)	0 (0%)	4 (10%)
Sex				
• Male	3 (7.5%)	1 (2.5%)	0 (0%)	4 (10%)
• Female	14 (35%)	13 (32.5%)	9 (22.5%)	36 (90%)
Profession				
• College student	5 (12.5%)	3 (7.5%)	1 (2.5%)	9 (22%)
• Civil servants	1 (2.5%)	2 (5%)	1 (2.5%)	4 (10%)
• Does not work	8 (20%)	9 (22.5%)	7 (17.5%)	24 (60%)
• Entrepreneur	3 (7.5%)	0 (0%)	0 (0%)	3 (7.5%)
BMI				
• Less	2 (5%)	2 (5%)	1 (2.5%)	5 (12.5%)
• Normal	12 (30%)	9 (22.5%)	4 (10%)	25 (62.5%)
• More	2 (5%)	1 (2.5%)	3 (7.5%)	6 (15%)
• Obesity	1 (2.5%)	2 (5%)	1 (2.5%)	4 (10%)
LES duration				
• <12 months	7 (17.5%)	8 (20%)	3 (7.5%)	18 (45%)
• > 12 months	10(25%)	6 (15%)	6 (15%)	22(55%)
MEX SLEDAI				
• Light	3 (7.5%)	1 (2.5%)	1 (0%)	5 (12.5%)
• Moderate	10 (25%)	6 (15%)	4 (0%)	20 (50%)
• Severe	4 (10%)	7 (17.5%)	4 (40%)	15 (37.5%)
Total Immunosuppressants				
• 1	4 (10%)	1 (2.5%)	1 (2.5%)	6 (15%)
• 2	11 (27.5%)	8 (20%)	5 (12.5%)	24 (60%)
• 3	2 (5%)	5 (12.5%)	3 (7.5%)	10 (25%)

* Chi square test, p value is significant if p <0.05

Table 3. Distribution of serum IL-6 levels based on characteristics

Characteristics	IL6		P
	Normal	Increased	
Age (yo)			0.900
• 18 – 40	8 (22.2%)	28 (77.8%)	
• 41 – 60	1 (25%)	3 (75%)	
Sex			0.900
• Male	1 (25%)	2 (75%)	
• Female	8 (22.2 %)	28 (77.8%)	
BMI			0.731
• Less	0 (0%)	1 (100%)	
• Normal	6 (20%)	24 (80%)	
• More	2 (40%)	3 (60%)	
• Obesity	1 (25%)	3 (75%)	
Old LBS			0.424
• <12 months	3 (16.7 %)	15 (83.3%)	
• > 12 months	6 (27.3%)	16 (72.7%)	
MEX SLEDAI			0.419
• Light	1 (16.7%)	5 (83.3%)	
• Moderate	6 (31.6%)	13 (68.4%)	
• Heavy	2 (13.3%)	13 (86.7%)	

* Chi square test, p value is significant if p <0.05

Table 4. Correlation between IL-6 and degree of depression

IL-6 Level	Degree of depression			P	r
	Mild	Moderate	Severe		
Normal	6 (66.7%)	2 (22.2%)	1 (11.1%)	0.025	0.169
Increased	12 (38.7%)	14 (45.2%)	5 (16.1%)		

* Chi square test, p value is significant if p <0.05. The strength of correlation is very weak if r <0.2, weak if r = 0.2-0.4, moderate if r = 0.41-0.6, high if r = 0.61-0.8 and very high if r> 0.8

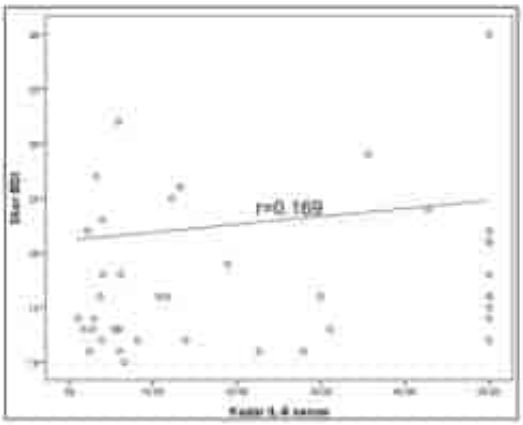

Figure 9. IL-6 Scatter Plot and BDI Score

4. Discussion

This study used a sample of 40 subjects, predominantly aged 18–40 years, 36 (90%) patients and 36 of them were women. The youngest age in this study was 18 years and the oldest was 56 years. This is appropriate based on a survey conducted by Prof. Handoko et al in Malang which shows a figure of 0.5% of the total population. As many as 60% of LES patients have disease onset between the ages of 16-55 years, 20% before 16 years, and 15% after 55 years.[16] In line with this study, Istiqomah et al found that the age of the sample was dominated by the age of 20–41 years. women.[17] This result is in accordance with the theory that LES affects women more than men. 16 This occurs because estrogen and prolactin increase autoimmunity, activate B cell factor production, modulate lymphocytes and activate pDC. On the other hand, androgens have a protective role.[18]

As many as 90% of women suffered from depression in this study. This is due to hormonal changes, especially during puberty, before menstruation, after pregnancy and in perimenopause. Depression in women also occurs due to exposure to environmental stressors and women have a lower threshold for stressors when compared to men. In addition, the complex interactions between gonad hormones and neurotransmitters also increase women's vulnerability to experience depression.[19]

Depression is more common in early adulthood with an average onset of about 20-40 years. In this study, depression occurred at the age of 18-40 years as many as 36 subjects (90%). The most common cause is social factors.[20]

The average BMI value in this study was 21.24 ± 2.57 with the most distribution being normal BMI, as many as 25 subjects (62.5%) experienced depression. In this study, there was no significant relationship between BMI and depression. This is the same as a study conducted by Fonseca which did not have a significant relationship between depression and BMI and between LES and BMI.[21] According to Speed et al, BMI cannot describe the composition of fat and protein in a person's body. If the excessive BMI is fat, then the composition of the excess fat can play a role in the pathogenesis of depression but if the excessive BMI is not fat, the probability of a person suffering from depression is low.[22]

Based on occupation, 24 (60%) patients were unemployed, 9 (22.5%) patients were students, 4 (10%) were civil servants and 3 (7.5%) patients were self-employed. Based on the occupation group, 24 (60%) of the unemployed experienced depression, but there was no significant relationship between work and depression level. In the study of Maneeton et al., LES patients who did not work had a higher incidence of depression than those who worked. In this study, 17 subjects with depression who did not work found LES subjects (60.7%). The unemployment condition is one of the worst factors to occur and worsening mental health.[20]

In this study, the duration of LES was predominantly > 12 months in 22 (55%) patients. The lowest LES duration was 1 month and the longest was 156 months. The LES group with an event duration of > 12 months had a higher incidence rate of depression and a higher degree of depression than those with an event duration of 1-12 months. LES activity was calculated using the MEX-SLEDAI score. It was found that the sample mostly with moderate LES activity were 20 (50%) patients. In the LES activity group and the degree of depression, there was a significant relationship between depressive symptoms and LES activity. These results are not consistent with a study conducted by Maneeton et al. Which found no significant association between depressive symptoms and LES activity using the MEX-SLEDAI score in 40 patients with LES and depression. LES activity in the study of Maneeton et al. Found a MEX-SLEDAI score of 4.1 ± 4.1. [1] Jacobs et al. Who measured LES activity with MEX-SLEDAI also did not find an association between depressive symptoms and LES activity.[23] However based on a study conducted by Emilia et al., It was reported that there was an association between depressive symptoms and MEX-SLEDAI. This is due to LES and depression occurs due to inflammation that occurs due to the formation of pro-inflammatory cytokines[13]

In this study, the relationship between depression and LES activity was found. This can be seen from the results of the Spearman correlation test with moderate correlation strength ($r = 0.388$, $p = 0.013$). In a study conducted by Palagini et al, there were 17 studies on depression in the LES reporting 8 studies that analyzed the relationship between depression and LES activity. Five studies suggest an association between depression severity and disease severity. Previous research conducted by Emilia et al. Found that there was a significant relationship between the level of LES disease activity and the level of depression. The higher the LES activity, the higher the level of depression experienced.[3]

The highest number of immunosuppressants was in the sample that received 2 immunosuppressants (methylprednisolone and other immunosuppressants), namely 24 people (60%). This study is not much different from the research of Istiqomah et al in 2018 which also found that the average LES patient who had worked with treatment was predominantly <1 year to 5 years and the most immunosuppressant types were 2 types of drugs.[17] Consistent with this study and previous research, Zuadi *et al* in 2018 also found that the average LES patient was those who actively worked with MEX-SLEDAI, which was dominated by the moderate category and the majority of the sample (80%) consumed 2 types of immunosuppressants. Zuadi also found that 66.7% of his sample had moderate-severe depression.[24] Based on Lang et al's study, depression was associated with chronic corticosteroid use so that it resulted in disruption of corticosteroid receptor signaling. In this study, there was a relationship between depressive symptoms and the number of immunosuppressants consumed by the *Spearman* test. There was a significant correlation with the strength of the weak correlation ($r = 0.347$, $p = 0.028$). Researchers did not evaluate the number of immunosuppressants used in the past month. It is advisable to do research from the beginning of the patient using corticosteroids or research by calculating the mean number of corticosteroids used by the patient. This can occur because one of the causes of depression due to increased cortisol, so that the pathogenesis of depression is multifactorial.

In this study, the median BDI score was 16 with the highest score of 40 and the lowest score of 10. Most depressive symptoms were in the mild depression group, namely 17 people (42.5%), 14 people (35%) in the moderate depressive symptom group and 9 people (22.5%) experienced major depression. These results were not much different from Jacobs et al. In 102 patients with LES reporting a mean BDI score of 10.2 and Postal et al in 153 LES patients reporting a BDI score of 17.08 ± 13.02.[25]

LES is an autoimmune, multisystem, and connective tissue disorder with several neuropsychiatric manifestations. The results of Kwan et al's report found that 19 neuropsychiatric syndromes, mood disorders, anxiety and depression were most frequently experienced by LES patients.[26] Eldeiry et al's study also found no significant association between age, race, BMI and the degree of depression in LES patients. However, Eldeiry found a significant association in female LES patients who experienced skin discoloration compared to those who did not.[27] Jordan et al also found reduced quality of life in LES sufferers which led them to become depressed, so that mental assistance from family and those around them is urgently needed.[28]

In this study, the number of research subjects was about 40 people with an overall mean level of IL-6 of 11.97. The minimum value of IL-6 responder serum levels is 1.10 pg / mL and the maximum value is 50 pg / mL. Serum IL-6 levels in the sample of this study were dominated by elevated serum IL-6 levels (> 3.93) by 31 (77.5%) patients, while samples with normal IL-6 levels were 9 (22.5%). Dowlati et al. Studied significantly higher serum IL-6 levels ($p < 0.00001$) in depressed subjects compared with control subjects (492 depressed / 400 non depressed) with an overall WMD (*weighted mean difference*) (95% confidence interval) 1,78 pg / ml (1.23 to 2.33).[10]

Serum IL-6 levels in the study subjects based on age found in the 18-40 year age group increased by 28 (77.8%) while in the 41-60 year age group increased by

3 (75%). In the study of Gomez et al. Demonstrated that IL-6 regulates age-related defects in macrophages by altering proinflammatory cytokines[29]

Serum IL-6 levels based on BMI increased in a group of less than 1 (100%) people, at normal BMI as many as 24 (80%) people, BMI over 3 (60%) people and obesity as many as 3 (75%) people. Interleukin-6 is mainly produced by macrophages and adipose, plasma IL-6 levels will be increased in obesity. Approximately 30% of plasma IL-6 levels are derived from adipose tissue and its release is influenced by the sympathetic nervous system. The correlation test between BMI and IL-6 levels in this study showed no significant relationship (p = 0.731; n = 40). This is consistent with a study conducted by Safitri et al, namely that there is no difference in IL-6 levels in obesity or not (p = 0.925).[30]

Based on the duration of suffering from LES, the study subjects were grouped into two, namely less than 12 months and more than 12 months. IL-6 levels in the group suffering from LES for less than 12 months were 15.55 (1.71-50) pg / mL and increased by 15 (83.3%) people. At LES duration of more than 12 months, the median IL-6 levels were 11.22 (1.10-50) pg / mL and increased by 16 (72.7%) people. The correlation between serum IL-6 levels and LES duration was also not significant (p = 0.424).

Based on LES activity, serum IL-6 levels were grouped into three groups, namely light, moderate and heavy activity. In the light activity group serum IL-6 levels were 3.49 (2.97-50) pg / mL, the moderate LES activity was 6.305 (1.10-50) pg / mL and in severe LES activity was 35.60 (3.24-50) pg / mL. IL-6 is the main cytokine as a balance regulator between Th17-Treg which plays a major role in the pathophysiology of SLE and disease activity.[31]. In this study, IL-6 did not have a significant relationship with LES activity (p = 0.419), but there was a significant increase in IL-6 levels in a state of severe LES activity. This is similar to the study conducted by Thanadetsuntorn where IL-6 did not have a significant correlation with SLEDAI-2K, but IL-6 levels were significantly increased in active LES patients. 32 In line with this study, Familia et al also stated that there was no significant relationship between IL-6 levels and LES patients. 52 Familia et al concluded that the pathophysiology of LES shifted to a new paradigm emphasizing the imbalance between Th17 and Treg.[33]

Correlation analysis was used to assess the strength of correlation and its direction. Correlation analysis in this study used Chi square analysis. Interpretation is seen from the strength of correlation (r), p value, and correlation directions. Interpretation of the strength of correlation (r) is very weak (r <0.2), weak (r = 0.2-0.4), moderate (r = 0.4-0.6), strong (r = 0.6 -0.8), and very strong (r> 0.8). The interpretation of the p value is that there is a significant correlation (P <0.05) and there is no correlation (P> 0.05). The results of the Chi square analysis in this study showed that there was a significant relationship between IL-6 and depression in LES patients, but the strength of the correlation was very weak (p = 0.025, R = 0.169).

The meta-analysis study conducted by Ding et al found a significant relationship with the strength of the positive correlation between IL-6 levels in LES patients.[34] In line with this study, Familia et al also found a significant association with a weak positive correlation between IL-6 levels and the degree of depression in LES patients.[35] Interleukin-6 (IL-6) is a multifunctional proinflammatory cytokine, which can be secreted from endothelial cells, macrophages, lymphocytes, dendritic cells and fibroblasts. IL-6 can directly induce maturation of naïve B cells into plasma cells and facilitate differentiation of cytotoxic T cells by regulating IL-2 and IL-2R. Because of this function, IL-6 enhances systemic autoimmunity and pathological inflammatory responses[33]

Yuk et al and Pacheco et al 2017 reported that patients with LES had higher serum IL-6 levels than healthy controls. In addition, Yuk et al concluded that IL-6 levels in LES patients correlate with the degree of depression and mood disorders in the sufferers.

5. Conclusion

This study was conducted on LES patients with depression at Dr. Moh. Hoesin Palembang, which is

dominated by 15-40 years old with the most female sex. The majority of the samples obtained were non-working, nutritional status was dominated by normal BMI, the duration of LES suffered was more in the > 12 months group with the most MEX SLEDAI scores on moderate activity, the number of immunosuppressants was dominated by 2 types of immunosuppressants and most of the study samples had levels Serum IL-6 is increased (> 3.93). In this study, there was a significant relationship between serum IL-6 levels and the degree of depression in LES patients at RSMH Palembang with a weak correlation strength.

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