Correlation between Anti-CCP Titer and Body Mass Index Score in Rheumatoid Arthritis Patients in Cipto Mangunkusumo Hospital

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Abstract

Background Rheumatoid Arthritis (RA) is a chronic systemic inflammation that attacks and damages joints of upper and lower extremities. RA causes morbidity and disability, hence, affects the quality of life. Chronic inflammation, as the disease progressing causes lowering of body mass index in RA patients. Titer of anti-CCP is specific for RA which indicates the progressivity and severity of the disease. Study about anti-CCP titer and body mass index has not been done in Indonesia. Therefore, this study done to understand the correlation between anti-CCP titer and body mass index score in rheumatoid arthritis patients in Cipto Mangunkusumo hospital.

Method The design of this study is cross-sectional study with 42 samples. The data included anti-CCP titer, body weight, height, and body mass index are collected from patients' medical records.

Result RA patients in Cipto Mangunkusumo hospital in 2012-2016 with negative and positive anti-CCP titer consecutively are 28.6% and 71.4%. The result of this correlation study is p>0.05; r-0.03.

Conclusion In conclusion, there is no correlation between anti-CCP titer and body mass index score in RA patients in Cipto Mangunkusumo hospital **Keywords**: Anti-CCP; Body Mass Index; Rheumatoid Arthritis

Introduction

Rheumatoid Arthritis (RA) is a chronic systemic inflammation that attacks and damages joints of upper and lower extremities.[1,2] RA causes morbidity and disability, hence, affects the quality of life and also raise mortality risk.[1] Various studies have been carried out over the last 100 years to discover the etiology and characteristics of RA.[1] Although the exact etiology of RA is still unclear, yet strong evidence suggests that autoimmunity is one of the causes.[3] Other study states that genetic factor is one of the predisposing factor of RA.[1,3]

There are more than 20 million people in the world who suffer from RA. Rheumatoid arthritis is the most common inflammatory arthritis of 0.5-1% of the world's population.[2] The prevalence of RA in Indonesia is <0.4%, with incidence rate in women and men is 2.5: 1.4. This disease can occur at different ages, with the most common age is between 40 to 70 years, and the incidence increases with age.[2]

Serological test to diagnose RA is usually seen from rheumatoid factor (RF).[2] RF is detected in 70-80% of RA patients and used as RA diagnosis markers.[2] However, these antibodies are not specific to RA. It can be detected in other diseases and in 3-5% of normal person .[2] In recent years the study of antibody cyclic citrullinated peptide (CCP) shown it has highly specific and predictive to RA because it can be detected several years before clinical manifestations appears and associated with joint destruction.[2,5] Anti-CCP can be used to evaluate the disease's progressivity, it means when anti-CCP was high, progression of the disease was high too.[1-2,5]

Systemic inflammation in patients with active chronic disease such as RA correlates significantly with weight loss (thereby significantly affecting body mass index), which is called rheumatoid cachexia in RA patients.[6] A study found that radiographic images of joint damage were fewer in patients with higher body mass index. It was also mentioned that the mortality rate in RA patients decreased with increasing of body mass index.[6]

Genetic factors play a role in the occurrence of RA disease, and the progressivity of RA may be affected by the body mass index score.[3,4] Similarly, anti-CCP could describe the disease's activity. Studies about correlation between anti-CCP and body mass index in RA patient have not been done in Indonesia.

Method

This is cross-sectional study. Subjects of this study are RA patients in Cipto Mangunkusumo hospital (both in Center of Cipto Mangunkusumo hospital and Kencana cluster Cipto Mangunkusumo hospital), all of subjects were evaluated by analyzing their medical records who have fulfilled the inclusion criteria, such as patients who have been diagnosed with RA> 12 months based on ACR / EULAR 2010 criteria, is ≥18 years old, with medical record contained anti-CCP titer and body mass index (BMI) score (with maximum BB examination in 3 months after/before anti-CCP titer test). The exclusion criteria of this study are patients with other diseases that may cause changes

in body mass index score, such as diabetes mellitus, cancer, and other chronic diseases.

The calculation of the samples number was performed by a single proportion hypothesis test. The sampling method used was the consecutive sampling. Furthermore, the normality of the data is checked by using Saphiro Wilk test. If the results of the data are normally distributed, correlation bivariate analysis will be performed by Pearson test. If the data are not normally distributed, the correlation bivariate analysis will be performed by Spearman test[7,8]

Result

Data obtained in this study is 42. Characteristic of subjects is presented in Table 1. Result of correlation test is presented in Table 2 and Table 3.

Tabel 1. Samples Demographic Data

Variable	Frequency (n)	Percentage (%)
Gender		
Woman	39	92.8
Man	3	7.2
Age group		
>18-19 years	0	0
20-29 years	4	9.5
30-39 years	7	16.7
40-49 years	7	16.7
50-59 years	17	40.5
≥60 years	7	16.7
Anti-CCP Titer		
Negative	12	28.6
Positive	30	71.4
Body Mass Index Score		
Underweight	2	4.8
Normal	14	33.3
Overweight	18	42.9
Obese	8	19

Tabel 2. Median Score of Anti-CCP Titer dan Body Mass Index Score

Variable	Result
Anti-CCP Titer	32.2 (1.08–800)*
Body Mass Index Score	23.5 (15.9–30.7)*

*:not normally distributed data, data presented in median (range)

Tabel 3. Result of Correlation Spearman's Test

	Anti-CCP Titer (N=42)	
	r	p
Body Mass Index Score	-0.03	0.851

The anti-CCP titer and body mass index score were abnormal based on the normality test results. Therefore, the correlation test used Spearman test. In this study, the result of p value was 0.851 (p> 0.05). Thus, statistically there was no correlation between anti-CCP titer and body mass index score.

The r value obtained was -0.03, so it can be interpreted that the anti-CCP titer is inversely correlated with the body mass index score with very poor correlation.

Discussion

In this study, the number of female is more than men. This is consistent with the epidemiologic datawhich stated prevalence of RA in women is higher than in men.[9] The result was consistent with study conducted by Sotoudehmanesh et al which has the percentage of female 84.4%.[10] The other study conducted by Symmons et al, obtained the ratio of RA in men and women consecutively 1.5:3.6. [11]

Sex hormones play a role in immune response.[12] Estrogen plays a role in humoral immunity, while androgens and progesterone act as immune suppressors. Higher estrogen levels in women may cause RA is more occur in women than in men.[12,13]

In this study, the median age of the sample is 49.5 years. This value corresponds to incidence of RA which increases in fourth to sixth decade of life.[2] This value is also in accordance with research conducted by Symmons et al, which found the prevalence of RA is high in individuals aged> 40 years. [11] This value is different from the research done by Cutolo which found the most common RApatients are > 70 years old, although RA could be appeared at different ages. [12]

In this study, the data obtained 71.4% from total samples with a positive anti-CCP titer. This is consistent with a study by Pruijn et al[5] that received a seropositive anti-CCP result of 70% of a total of 17,359 samples tested for anti-CCP. The distributions of weight are obese group (19%), overweight (42.9%), normal (33.3%), and underweight (4.8%). This result is different from the research conducted by Baker et al[14], which obtained sample with normal and underweight group (42.1% total), with overweight sample (33.5%) and obese (24.3%).

Correlation between Anti-CCP Titer and Body Mass Index Score There was no correlation between anti-CCP titer and body mass index score (p>0.05). Moreover, r value is -0.03, it can be interpreted that the anti-CCP titer sample is inversely correlated with the body mass index score with a very weak association. Then, the probability result caused by chance (coincidence) r = -0.03 is 85%.

The results of this study are in accordance with research conducted by Baker et al[15] which explained that there was no interaction between CCP seropositivity with statistical changes in body mass index score. It was also mentioned that there were several confounding factors that may affect one or both variables in the sample of the study, such as drug use, smoking habits, and initial weight before illness.[15]

Study conducted by Curtis et al[16], found that there was body weight increasing in RA patients who took prednisone (doses of 14─16 mg/day).[16] It was also mentioned that the disease activity in the sample group was low.[16,17] This statement was different from study conducted by Baker et al[15], which found that there was no association between prednisone use and weight gain in RA patients. However, it caused prednisone

dose which used in the sample group was low (7 mg/day). Therefore, different results may be obtained if the prednisone dose is increased.[15]

In a study conducted by Baker et al[15] found that MTX therapy reduced the risk of BMI degradation when it compared with non-MTX as controls.[15] Based on study conducted by Brown et al[18], patients who took anti-TNF therapy had BMI repair. However, this result different from study by Baker et al[15] which found no association between anti-TNF and weight gain. In addition, therapy using infliximab for six months also causes reduce anti-CCP titers.[19]

Research samples used in the Baker et al[15] study were patients who had undergone pharmacological therapy such as MTX and/or anti-TNF. This may explain the absence of correlation between anti-CCP titer and body mass index score, which is due to an improvement in body mass index score along with RA treatment.

Smoking is a risk factor of RA.[20] Chronic inflammation in lung mucosa caused by cigarette, it play role in RA initiation as an environmental trigger.[21-23] In a study conducted by Baker et al[15] there was found that smoking habits were associated with weight loss.[13] Study conducted by Clair et al[24] and Audrain-McGovern et al[25] found that there was a significant increase in body weight in patients who did not smoke and patients who quit smoking. Nicotine in cigarettes may play a role in suppressing hunger.[25]

Based on a research conducted by Baker et al[15], weight gain is still occured in RA patients until they reach age 50, and it will decrease over age.[15] Weight loss is more common in the elderly, it may be caused by systemic cytokines and hormones which play a role in satiety.[26]

High BMI score in early disease associated with greater weight loss.[15]In this study result, the majority of samples are overweight and obese, there is no weight loss. However, it can not be proven because the researchers did not take the patient's initial weight data before the onset of the disease began.

Higher or lower body mass index is caused by many factors, such as physical activity, socio-economic status, nutrition, educational level, alcohol consumption, contraceptive use of oral contraceptives in women, psychosocial factors, and television viewing habits.[27-28]

Physical activity is associated with lower BMI.[29] In RA patients, physical activity may improve condition of cardiorespiratory system, muscle mass, decrease fat mass, and increase body strength and body function without exacerbating disease activity or worsening joint damage.[30] Therefore, American College Sports Medicine recommends physical activity for at least 30 minutes per day several times a week.[31] In general, RA patients have low physical activity. This condition caused by joint stiffness, pain, metabolic changes which causes muscle weakness and decrease muscle mass. [31-33]

The socio-economic status is positively associated with body mass index. The socio-economic status is related to lifestyle such as physical activity and nutrition.[27] A study conducted by Handayani[34] in Tangerang, Indonesia, in elderly, higher amounts of energy/calories were consumed in individuals with higher incomes. The study found that socio-economic status was positively correlated with body mass index score.[34] Economic status is also related to physical activity. Individuals in low economic status are associated with higher physical activity.[27]

Study Limitation

In this study, sample's weight loss was measured by total body weight or BMI score. However, according to Masuko[35], BMI score is poor to describe the muscle/protein loss that occurs in rheumatoid cachexia. Body Lean Mass (total mass reduced by fat mass) should be used in this research. Body lean mass can be measured by using waist circumference data or other gauges.

From the discussion, there are many factors that can affect the weight score and also anti-CCP titer. In this study, the researchers aren't consider whether the patient is taking drugs or not and period of treatment. Retrieval time of anti-CCP in this study is heterogeneous, while pharmacological procedures can affect both weight and anti-CCP titer.

Conclusion

Based on the results, it can be concluded that nutritional status of patients with rheumatoid arthritis in Cipto Mangunkusumo hospital from 2012 to 2016 is obese (19%), overweight (42.9%), normal (33.3%), and underweight (4.8%). The percentage of rheumatoid arthritis patients in Cipto Mangunkusumo hospital from 2012 to 2016 with negative and positive titer were 28.6% and 71.4% consecutively. There is no correlation between anti-CCP titer and body mass index score in rheumatoid arthritis patients in Cipto Mangunkusumo hospital in 2012-2016. We recommend using body lean mass to measure weight changes and to analyze the confounding factors, such as drug use, smoking activity, nutrition, and socio-economic factors as future research variables.

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