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Systemic Inflammations in Non Obese and Obese Uncontrolled Asthma

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Abstract: ***Background: Asthma is a chronic airway inflammation. There is increasing evidence confirming in severe or asthma systemic inflammation can occur. Spillover of inflammatory mediators into the circulation is generally considered to be the source of this systemic inflammation. Obesity is well known to be associated with systemic inflammation too. Both asthma and obesity often occur in the same individual. We examined the independent and synergistic associations of asthma uncontrolled and obesity with systemic inflammation using high-sensitivity C-reactive protein (hs-CRP). Methods: This was an observational study with cross-sectional approach in 48 asthma subjects with aged 18 – 55 years old without diabetes, cardiovascular disease, hypertension and non smoker. The study was performed in the Hasanuddin Teaching Hospital South Sulawesi Indonesia. Asthma control was assessed using asthma control test (ACT). Results: Mean of hs-CRP levels were significantly higher in uncontrolled asthma than controlled asthma (4.23 ± 3.11 vs 0.92 ± 0.61 ; p=0.001). The high hs-CRP levels were most found in uncontrolled asthma patients than controlled asthma. Obese Subject with uncontrolled asthma have higher hs-CRP levels compared to obese subject with controlled asthma (p=0.026). In non obese subject with uncontrolled asthma have also siginificant higher hs-CRP compared to non obese controlled asthma (p=0.005). Hs-CRP level significantly higher in uncontrolled asthma both in obese and non-obese subject. Hs-CRP levels in asthma subject were not influenced by age (p=1.000), gender (p=0.822), family history of asthma (p=0.117), long duration of asthma (p=0.117) and used of steroid. (p=0.358). Conclusion: Uncontrolled Asthma associated with systemic inflammation both in obese and non obese subject. These findings underline a potensial CVD risk in asthma especially with uncontrolled status.***

Keywords: Uncontrolled, Asthma, Obese, non obese persistent

1. Introduction

Asthma is 1 of 10 major causes of morbidity & mortality in Indonesia. The Indonesian National Household Health Survey in 1995 reported asthma was 5th rank of 10 cause of morbidity as well as bronchitis & emphysema. Asthma prevalence in Indonesia around 5-7%.(1) Asthma is a chronic airway inflammation. There is increasing evidence confirming in severe or persistent asthma systemic inflammation can occur. Spillover of inflammatory mediators into the circulation is generally considered to be the source of this systemic inflammation.(2) There was a direct correlation between the serum levels of hs-CRP and severity of asthma.(3) Since 2006 Asthma management recommendations were based on the level of asthma control rather than disease severity. Uncontrolled asthma considered to have more systemic inflammation rather than controlled asthma. Obesity is well known to be associated with systemic inflammation too (4). Both asthma and obesity are proinflammatory conditions that are prevalent and often occur together in the same individual(5). Because of the large number of individuals who have both the conditions, a more complete understanding of the independent and synergistic associations of degree of asthma control and obesity with systemic inflammation will help to clarify the role of asthma in CVD risk assessment in non obese and obese individuals. Inflammatory markers such as high-sensitivity C reactive protein (hs-CRP) shows a strong association with CVD risk in adults. Elevated levels of hs-CRP are now considered as an independent risk factor for CVD in adults (6) In this study, we aimed to examine the independent. and synergistic associations of degree asthma control and obesity with systemic inflammation, using hs-CRP levels.

2. Materials And Methods

This case-control study was performed from Januari to June 2014 in Teaching Hospital of Hasanuddin University. Forty eight patients were diagnosed with bronchial asthma according to clinical and functional criteria established by GINA were included in this study. We excluded subjects with conditions that could affect CRP measurement for reasons other than asthma, such as patients with respiratory tract infection, smokers, patients with a history of renal, hepatic, cardiovascular, and collagen vascular, diseases, cancer, COPD, Diabetes.

In this study, we evaluate the correlation between the serum levels of hs- CRP in patients with different levels of asthma control based on ACT scores and spirometric. We classified according to ACT score, uncontrolled asthma if ACT <20 and Controlled Asthma if ACT Score ≥20. The following information was collected for each patient: age, gender, asthma medication and history of hospitalization during a year prior to current presentation. The validated Indonesian version of ACT was administered to the subjects.(20) Spirometry was performed and prebronchodilatory FEV1 was measured. Blood samples for CRP measurement were taken after 4 hours of fasting.hs-CRP levels were analyzed with ELISA method using the commercial kit. We divided the level of hs-CRP to high hs-CRP if the level ≥3 mg/l and low hs-CRP if <3 mg/l.

The study was approved by the Ethics Committee of Medical Faculty of Hasanuddin University. All patients provided written informed consent. SPSS statistical software version 17 was employed for data analysis. Descriptive statistics were used to summarize the demographic characteristics of patients. t-test was used to test the significance of differences

between mean hs-CRP levels among the groups. Correlations between data were analyzed with Fisher Exact test and Chi Square test A p-value of <0.05 was considered significant.

3. Results

A total of 48 asthmatic patients and participated in this study. The mean age was 34.96 ±11 (range 22 to 55 years). There were 34 females and 14 males.

Table 1: Comparison of mean hs-CRP

Degree of Asthma control	n	Mean	Standard deviation	p
Uncontrolled	27	4.23	3.11	0.001
Controlled	21	0.92	0.61	

3.1 Independent t test

hs-CRP level was significantly higher in uncontrolled asthmatic patients (4.23 mg/l) as compared to the controlled asthmatic group (0.92 mg/l) (table 1).

Table 2: Variables Correlates with high hs-CRP

Variabels		hs-CRP				
		high		Low		p
		N	%	N	%	
Age (years)	<35 yo	9	33.3	18	66.7	1
	≥35 yo	7	33.3	14	66.7	
Gender	Man	5	35.7	9	64.3	0.822
	Woman	11	32.4	23	67.6	
Duration	> 5 years	15	36.6	26	63.4	0.358
	≤ 5 years	1	14.3	6	85.7	
Family of asthma	Yes	11	28.2	28	71.8	0.117
	No	5	55.6	4	44.4	
Use steroid oral	Yes		23.1	10	76.9	0.358
	No	13	37.1	22	62.9	
Obesity	Obese	11	55	9	45	0.007
	Non-obese	5	17.9	23	82.1	

3.2 Chi Square test

There were no difference distribution of hs-CRP in correlation with ages, gender, duration of asthma,Family history of asthma, history of using oral steroid. But there were significant differences in the distribution of hsCRP levels in correlation to obesity (table 2). Obese patients more likely to have high hs-CRP levels than non-obese (55.0 % vs 17.9 %). In other words that obesity also has a significant correlation with hsCRP levels. Therefore, obesity has a significant correlation with hsCRP levels , then the results of the previous analysis showed a significant association between asthma control status with hs-CRP levels need to be repeated to control the obesity factor with stratified analysis. (table 3)

Table 3: Distribution of Level hsCRP according to the degree Asthma controlled and Obesity

Obesitas	Status Kontrol Asma	hsCRP				p
		≥ 3		<3		
		n	%	n	%	
Obese	Uncontrolled asthma	11	68.80%	5	31.30%	
	Controlled asthma	0	0.00%	4	100.00%	
	Total	11	55.00%	9	45.00%	0.026
Non-Obese	Uncontrolled asthma	5	45.50%	6	54.50%	
	Controlled asthma	0	0.00%	17	100.00%	
	Total	5	17.90%	23	82.10%	0.005

3.3 Fisher Exact Test

In obese patients we found that patients with uncontrolled asthma significantly more likely to have high hsCRP levels compared to patients with controlled asthma 68.8 % vs 0.0 % ($p < 0.05$). We found also that non - obese patients with uncontrolled asthma significantly more likely to have high hsCRP levels compared to patients with controlled asthma 45.5 % vs 0.0 % ($p < 0.01$). This study shows a significant association between asthma control status with systemic inflammation. Patients uncontrolled asthma have a high RP in obese patient also non obes.

4. Discussion

This study was a cross sectional and conducted on 48 subjects. According to ACT score the subjects were divided to 27 subjects with controlled asthma and 21 subjects with uncontrolled asthma. The mean levels of hs-CRP were significantly higher in uncontrolled asthma than controlled asthma ($p < 0.001$).

The previous study by killic in 30 patients with a diagnosis of asthma and 30 healthy subjects and ACT score and pulmonary function tests was performed.hs-CRP levels were higher in subjects with asthma compared to controls ($p = 0.002$).(7) This research obtains hs-CRP levels in poorly controlled asthma group (ACT < 20) was significantly higher than the controlled asthma group (ACT ≥ 20) . Hs-CRP levels showed a significant relationship with ACT ($p = 0.00$, $r = -0.91$) and the severity of asthma ($p = 0.04$, $r = 0.38$) The study concludes hs - CRP is a marker of potential and associated with the severity and control of asthma. The results also get a significant increase in hs-CRP levels in serum in moderate persistent asthma compared with mild persistent asthma.

Other study by Zietkowsi in 62 atopic asthma patients and was divided in 3 groups: 19 with mild to moderate persistent asthma , 23 patients with unstable asthma , and 15 healthy subjects as controls . The study concluded hs-CRP levels were significantly higher in Extra Breath Condensated and serum examination in unstable asthma compared with stable asthma .(8)

This research obtain significant correlation between hs-CRP levels and obesity ($p < 0.01$) . Obese subjects more likely to have high levels of hs - CRP than non- obese , ie 55.0 % vs. 17.9 % . Therefore, obesity has a significant relationship with hs-CRP levels , the results of previous analyzes which showed a significant relationship between the degree of asthma control with hs-CRP levels need to control the obesity factor in the analysis of stratification . The analysis found high levels of hs - CRP in subjects uncontrolled asthma are obese ($p = 0.020$) and non - obese ($p = 0.05$) . This suggests there is a significant relationship between the degree of asthma control with hs-CRP levels

Amina et al found a corelation between increasing body mass index with the level of hs-CRP . Delgado et al showed that obesity increased the normal function of the adipocyte tissue causing systemic proinflammatory state, with increasing concentrations of several cytokines and chemokines.(9) Some mediators are synthesized and secreted

by cells of the adipocyte tissue such as IL - 6 , IL - 10 , eotaxin , TNF - α , TGF - β , CRP , leptin and adiponectin.(10) This study obtains the relationship between asthma control and hs-CRP levels . Distribution of hs-CRP levels were significantly higher in uncontrolled asthma subjects both in obese and non-obese . So that hs -CRP can be used to help evaluate the progress of asthma control. We hypnotized there is association between control asthma with cardiovascular risk. Sabatine et al hs-CRP levels on the subject of stable coronary heart disease and an increase in hs - CRP get 1-3 mg / l significantly increased risk of cardiovascular death , myocardial infarction or stroke were 1.39 times (95 % CI : 1 , 06 to 1.81 , p = 0.016). hs - CRP > 3 mg / L increased risk of 1.52 (95 % CI : 1.15 to 2.02 , p = 0.003) . The increase in hs - CRP as well as a predictor of heart failure (p = 0.001) and the incidence of diabetes (p = 0.001) . (11)

In conclution uncontrolled Asthma was associated with systemic inflammation both in obese and non obese. These findings underline the need of a multifaceted approach to address CVD risk in asthma uncontrolled.

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