

# **Correlation of Smoking Intensity Scores and Total Serum Immunoglobulin E Level in Adult Male Smokers**

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# ABSTRACT

Background: Exposure to cigarette smoke causes an increase in the T-helper 2 immune response and elevates the formation of IgE by B cells and activation of eosinophils. *Objectives:* This study aims to determine the correlation between smoking intensity scores measured using the Brinkman Index and total serum Immunoglobulin E level. *Methods:* The study used an analytical cross-sectional design in a population of adult male smokers according to inclusion and exclusion criteria. This study evaluated the smoking intensity score on total serum Immunoglobulin E expression with control for age, gender, history of atopy, infection, and use of corticosteroids. Serum total IgE levels were examined by immunoradiometric assay using venous blood samples. Data were analyzed using correlation tests and multivariate analysis, linear regression tests with p <0.05 which was significant. *Results:* The study included 95 samples with a mean sample age of 31.38 ± 1.98 years. The mean Brinkman Index was  $103.74 \pm 74.47$  with a mean total serum IgE level of  $247.58 \pm 354.58$ kU/L. Of the total sample, there were 47 samples (49.5%) who were obese and 26 samples (27.4%) consumed alcohol. The correlation between the Brinkman index and IgE level based on the Spearman correlation test was obtained with a p-value <0.001. Multivariate linear regression analysis showed that the B coefficient value of the Brinkman Index was 0.880 with a p-value of <0.001. Meanwhile, no significant relationship was found between confounding variables and total serum IgE levels. *Conclusion:* The study found a strong correlation between total serum IgE levels in adult male smokers and the Brinkman Index. The higher the Brinkman Index, the higher the total serum IgE level.

Keywords: Brinkman index; total serum IgE level

# INTRODUCTION

Cases of allergic diseases are increasing throughout the world and not only in developed countries.<sup>1</sup> One of the causes of increasing cases of allergies is lifestyle changes, including smoking.<sup>2</sup> In Indonesia, tobacco use is still relatively high among adults and teenagers. In 2007, as many as 23.7% of Indonesia's population had a smoking habit. The prevalence of smoking in adolescents aged 10-19 years increased from 7.2% in 2013 to 9.1% in 2018.<sup>3</sup> The majority of smokers who use tobacco products, including ecigarettes, are individuals under 35 years of age.<sup>4</sup> Research shows that smoking habits affect IgE levels. Cigarette smoke causes an increase in the T-helper 2 (Th-2) immune response, thereby increasing the production of cytokines IL-4, IL-13, and IL-5 which play a role in the formation of IgE by B cells and activation of eosinophils. IgE will sensitize mast cells and basophils by binding to the high-affinity receptor FccRI on the cell surface. When the FccRI-IgE complex is formed, it will cross-link with the allergen so that the cells experience degranulation and release vasoactive amines, lipid mediators, chemokines, and other cytokines.

Immunoglobulin E (IgE) as a key mediator of allergic diseases will increase in patients with allergic rhinitis, asthma, and atopic dermatitis.<sup>5</sup>

Based on literature studies, smoking habits are correlated with increasing total serum IgE levels which has an impact on increasing the incidence of allergic diseases. This study aims to find a correlation between smoking intensity scores and total serum IgE levels in adult male smokers.

# SUBJECT AND METHOD

The study used an analytical cross-sectional design in a population of adult male smokers according to inclusion and exclusion criteria. This study evaluated the smoking intensity score on total serum Immunoglobulin E expression in adult male smokers. This research was conducted at the Udayana Faculty of Medicine University/ Prof. dr. I.G.N.G. Ngoerah General Hospital by taking a serum sample at the polyclinic. Examination of total serum IgE levels will be carried out at the Pramita Clinical Laboratory.

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The sample selection in this study was random consecutive sampling involving students from the Udayana Faculty of Medicine planned sample size was reached. Inclusion criteria in this study: 1. Male Smoker subjects aged 25 - 35 years. 2. Currently studying at the Udayana Faculty of Medicine. Subjects with the following conditions were excluded: 1. Subjects with a history of bacterial, viral, or parasitic infections in the last month, 2. Subjects with a history of atopy, 3. Subjects receiving corticosteroid therapy, 4. Refuse to participate after Informed Consent.

Descriptive statistical analysis was used to describe the overall characteristics of the subjects and research variables. The normality test aims to assess the distribution of smoking intensity score variable data with total serum IgE levels. The normality test was carried out using the Shapiro-Wilk test. The correlation test aims to assess the correlation between smoking intensity scores and total serum IgE levels. The correlation test is carried out by making a scattered plot and then carrying out a correlation test using Pearson correlation if the data distribution for the two variables is normally distributed. If one or both variables are not normally distributed then Spearman rank correlation is used. The multivariate analysis test aims to assess correlation by considering confounding factors. The test was carried out using linear regression. The results of the correlation test obtained a correlation coefficient which shows the direction and strength of the correlation. Conclusions are made based on the p-value with an  $\alpha$  limit of 0.05. The entire data analysis process was carried out using the IBM SPSS version 26.0.

#### RESULT

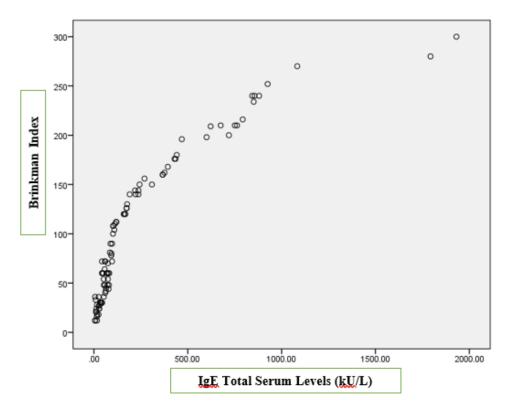
In this study, there were 95 subjects involved. The mean age of the subjects was  $31.38 \pm 1.98$  years. The mean age when the subjects first started smoking was  $21.89 \pm 3.68$  years with the mean length of time the subjects smoked was  $9.55 \pm 3.80$  years. The type of cigarette most commonly used was white cigarettes, namely 53 subjects (55.8%). Of the total research subjects, there were 47 subjects (49.5%) with obesity. A total of 26 subjects (27.4%) consumed alcohol. The average Brinkman Index was  $103.74 \pm 74.47$  with an average IgE level of  $247.58 \pm 354.58$  kU/L. Detailed characteristics of the research subjects can be seen in Table 1 below.

#### TABLE 1: Basic characteristics of research subjects.

Variable	Result	
Age, mean ±SD, year	31,38 ± 1,98	
Age of starting smoking, mean ±SD, year	21,89 ± 3,68	
Smoking Habit Duration, mean ±SD, year	9,55 ± 3,80	
Amount cigarettes per day, mean ±SD	10,73 ±5,99	
Cigarette		
Tobbaco mix with clovers	24 (25,3)	
Tobbaco	53 (55,8)	
Tobbaco mixed with clovers and electric cigarette	6 (6,3)	
Tobbaco and electric cigarette	12 (12,6)	
Obesity, n (%)		
Yes	47 (49,5)	
No	48 (50,5)	
Alcohol Consumption, n (%)		
Yes	26 (27,4)	
No	69 (72,6)	
Brinkman Index, mean ±SD 103,74 ±74		
IgE Total Serum Levels, mean ±SD, kU/L	247,58±354,58	

The correlation between the Brinkman Index and IgE levels based on scattered plots obtained a positive correlation with a linear R2 of 0.787 (Figure 1).

Based on the Spearman correlation test, a strong correlation was obtained (r=0.975) with a p-value <0.001.



**FIGURE 1**: Scattered plot of correlation between Brinkman index and IgE Total Serum Levels (r= 0.975; R2= 0.787; p <0.001).

Multivariate linear regression analysis was performed to evaluate the independent relationship between the Brinkman Index and IgE levels. The B coefficient value obtained from the Brinkman Index is 0.880 with a p-value of <0.001.

These results show that every 1 increase in the Brikman Index score is associated with an increase in IgE levels of 0.880 kU/L. Meanwhile, no significant relationship was found between confounding variables and IgE levels (Table 2).

Variable	B coefficient	SE	95% CI	P value
Brinkman Index	0,880	0,236	3,721-4,658	<0,001
Age	-0,006	8,813	-18,660-16,357	0,896
Obesity	-0,067	38,216	-128,561-23,284	0,172
Alcohol	-0,015	35,071	-80,321-59,028	0,762

TABLE 2: Linear regression test between the Brinkman Index and IgE levels after controlling for confounders.

\*R<sup>2</sup> (Model) = 0,782; p<0,001.

# DISCUSSION

This study found that the average age of smokers was  $31.38 \pm 1.98$ . This data is consistent with research conducted in 2020 in Bali, with the average age of smokers being 37.13 years with ages ranging from 20 to 79 years.<sup>6</sup> In Italy, the age of male smokers is  $47.1 \pm 20.8$  years, this average is not much different from Korea which reports the average age of adult smokers to be 47 years old.

Nearly half of the subjects with obesity in this study were found to be 49.5%, this is in accordance with a study by Taylor (2019) that increasing the intensity and severity of smoking is associated with an increase in BMI.<sup>7</sup>

In this study, the highest mean IgE levels were found in smokers (602.16 kU/L). This is in accordance with

other study which stated that IgE levels in smokers it range from 100 to 870 kU/L.<sup>8</sup> The average Brinkman Index was the highest in this study (178.21). Analysis of the relationship between the Brinkman Index and IgE showed a significant relationship in this study (p<0.001). The relationship between the two was found to have a positive correlation where the higher the Brinkman Index, the IgE levels in the blood will increase.

In this study, it was also found that every 1 increase in the Brikman index score was associated with an increase in IgE levels of 0.880 kU/L. Meanwhile, no significant relationship was found between confounding variables, namely age, obesity, and alcohol habits, with IgE levels. The results of this study are not in line with the study of Carballo et al., which found that obesity and metabolic syndrome

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components were associated with high levels of total IgE concentrations.<sup>9</sup> This study also found that the results of multivariate analysis (linear regression) showed that there was a relationship between metabolic syndrome, in the form of abdominal obesity and hyperglycemia, with total serum IgE after adjusting for confounding factors, namely history of atopy, age, gender, alcohol consumption, smoking, and physical activity (respective p values, p = 0.011 and p = 0.002 ). This can occur because obesity and metabolic syndrome are stated to be pro-inflammatory conditions which can cause an imbalance in cytokine production with Th2 dominance and this condition supports IgE synthesis.<sup>9</sup> The findings of this study are also not in line with the study of Lomholt et al., which succeeded in showing that there was a significant relationship between high alcohol consumption and IgE levels.<sup>10</sup>

The results of this study are in line with the study of Stemeseder et al which succeeded in showing that only smoking habits had a significant relationship with the risk of developing IgE sensitization compared to other lifestyle factors, such as alcohol consumption, exposure to passive smoke or air pollution, time spent outside, physical activity, stress or sleep.<sup>11</sup>

Thus, the smoking habit is not only associated with a process of irritation by the content of toxins, chemicals, and oxidant free radicals but also with allergic sensitization and increased total serum IgE production.

The limitation of this study was not being able to objectively evaluate research participants who experienced viral, bacterial, or parasitic infections as a variable controlled by the design due to limited costs.

#### CONCLUSION

This study found differences in total serum IgE levels in adult male smokers based on smoking intensity scores. An increase of 1 smoking intensity score is associated with an increase in IgE levels of 0.880 kU/L. no significant relationship was found between confounding variables: age, obesity, and alcohol habits, with IgE levels.

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