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Correlation of Serum Immunoglobulin-E Level with Allergic Rhinitis Severity Based on Symptoms Classification

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ABSTRACT

Background: Allergic rhinitis (AR) is defined as an Imunoglobulin-E (IgE) -mediated reactions to inhaled allergens in atopic individual, with symptoms including runny nose, itchy nose, nasal congestion, and sneezing. Serum IgE was a reliable diagnostic marker for allergic rhinitis. This study aimed to reveal the correlation between IgE levels and the severity of allergic rhinitis symptoms according to the Allergic Rhinitis and Its Impacts on Asthma (ARIA) classification.

Subject and Methods: A cross-sectional observational study was conducted involving 45 patients diagnosed with allergic rhinitis at the Otorhinolaryngology outpatient clinic. Subjects were identified through clinical evaluation, blood screening, and skin prick tests. Serum total IgE levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. Allergic rhinitis severity was categorized according to the ARIA classification into mild and moderate groups. Data were analyzed using the Chi-square test, and the association was presented as prevalence ratio (PR) with a 95% confidence interval (CI).

Results: Forty-five patients with allergic rhinitis comprised of 30 females (66.70%) and 15 males (33.30%). The average IgE levels examination results were 204.24 IU/ml, with 23 subjects (48.89%) classified as standard, while those with higher-than-normal IgE levels were 22 subjects (53.49%). The Pearson chi-square test showed a significant correlation between higher-than-normal IgE levels and ARIA severity (PR = 1.65; 95% CI = 1.03–2.64; p = 0.045)

Conclusion: Elevated serum IgE levels were significantly associated with greater allergic rhinitis severity based on ARIA classification and may serve as a useful supporting marker for disease severity assessment.

Keywords: ARIA, ELISA, IgE, allergic rhinitis.

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BACKGROUND

Allergic rhinitis (AR) is defined as an IgE-mediated reactions to inhaled allergens in atopic individual, with symptoms including runny nose, itchy nose, nasal congestion, and sneezing (Small, Keith and Kim, 2018). In numerous nations, the incidence of AR has increased and varied during the previous decade(Chong and Chew, 2018). Its estimated global prevalence ranges from 10% to 25%. In middle-income countries, AR and asthma incidence rates have grown since the 1960s (Ayanoğlu, 2021). The prevalence of AR in Bandung city, Indonesia, was reported as 38.2% of young adults. Male and female share an equal

proportion of prevalence, whereas, in children, AR is more prevalent among boys (An *et al.*, 2015; Sudiro and Lestari, 2015). These incidents are connected to lifestyle, dietary habit, environment, socio-economic level, climatic variance, disease awareness, or medication management (Sudiro and Lestari, 2015).

IgE-mediated inflammation triggered by allergens causes these AR symptoms. It is implied that environmental factors are more influential than genetic factors. One of the criteria used to diagnose AR is the development of symptoms following inhalation of the allergen that induced sensitization. Additional criteria include the patient's medical record, physical assessment, and the correlation between allergy tests and exposure history (Shoormasti *et al.*, 2018). According to the severity and length of symptoms, patients with AR are treated with Allergic Rhinitis and Its Impacts on Asthma (ARIA)-recommended medicine or pharmacological therapy.

Based on the guidelines, treatment is administered until the patient's symptoms have resolved. The optimal period of therapy for symptom remission and prognostic markers must be determined using factors such as IgE level. Additionally, to acquire an AR diagnosis, the IgE examination can be utilized as a factor in choosing the choice of therapy and provides the basis for preventative actions against variables that trigger an increase in IgE levels, if they are associated with the severity of the disease. Precise biomarkers such as IgE are required to predict the length of therapy (Klimek *et al.*, 2019; Bousquet *et al.*, 2016).

Previous research showed several factors contribute to the development of IgE, including environmental pollution, cigarette smoke, house dust, recurrent viral infections, the family number in the household, obesity, and a family history of atopy. Meanwhile, the preventive factors are living in rural area, vaccinations, breast milk, and birth history (Stemeseder *et al.*, 2017). This study examined the correlation between IgE levels and the allergic rhinitis severity, to determine what factors could prevent IgE production stimulation.

SUBJECTS AND METHOD

1. Study Design

This was a cross-sectional study carried out at the Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Indonesia.

2. Population and Sample

The study population consisted of students from the Faculty of Medicine and Health Sciences. Using consecutive sampling, 45 students with clinical manifestations of allergic rhinitis who met the inclusion criteria and had positive skin test results were enrolled, while students with comorbidities or complications were excluded.

3. Study Variables

The main variables in this study included the classification of allergic rhinitis based on symptom severity and duration, as well as serum IgE levels. Allergic rhinitis was categorized according to ARIA-WHO classification into: Intermittent, Persistent, Mild, and Moderate.

4. Operational Definition of Variables

Allergic rhinitis severity was defined based on symptom classification using the ARIA-WHO questionnaire, which categorizes the condition into intermittent (symptoms occurring less than four days per week or less than four weeks) and persistent (symptoms occurring more than four days per week and lasting more than four weeks), as well as mild and moderate severity. Serum Immunoglobulin E (IgE) levels were measured from venous blood samples using the ELISA method. IgE

levels were expressed on a numerical scale, while allergic rhinitis severity was categorized according to ARIA-WHO classification. The correlation between serum IgE levels and allergic rhinitis severity was analyzed to determine the association between these variables.

5. Study Instruments

Data were collected using the ARIA-WHO questionnaire to assess allergic rhinitis classification. Laboratory examination of serum IgE levels was conducted using the ELISA method from venous blood samples. Standardized procedures were applied to ensure consistency in data collection.

6. Data analysis

Data were analyzed using the Chi-Square test to determine associations between variables. Statistical significance was set at $p < 0.05$. The analysis was performed using appropriate statistical software.

7. Research Ethics

Research ethical issues, including informed consent, anonymity, and confidentiality, were carefully addressed throughout the study process. Ethical clearance approval was obtained from the Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, under No. 239/EP-FKIK-UMY/IV/2017.

RESULTS

1. Sample Characteristics

The subject of this study was 45 students, consisted of 30 females (66.70%) and 15 males (33.30%). Eight students had asthma as comorbidities (17.70%), and 37 (82.30%) had no asthma nor comorbidities. Environmental exposure and atopic genetic history could be seen in Table 1.

Table 1. Sample characteristics of correlation of serum Immunoglobulin-E level with allergic rhinitis severity based on symptoms classification

Characteristics		N	%
Gender	Male	15	33.30
	Female	30	66.70
Asthma history	Yes	8	17.70
	No	37	82.30
Cigarette exposure	Yes	15	33.30
	No	30	66.70
Family atopy	Yes	26	57.70
	No	19	42.30

2. IgE levels examination and RA classification

The results of the IgE levels examination showed an average data of 204.24 IU/ml after being grouped based on normal values ≤100 IU/ml. Respondents with normal IgE levels were 23 (51.11%), while students with high IgE levels were 22 (48.89%). Based on a questionnaire, the classification of allergic rhinitis results was shown in Table 2.

Table 2. The result of IgE levels examination and RA classification

Characteristic	Category	n	%
IgE levels	Normal	23	51.11
	Increased	22	48.89
ARIA classification	Mild intermittent	11	24.44

Characteristic	Category	n	%
	Moderate intermittent	20	44.44
	Mild persistent	4	8.89
	Moderate persistent	10	22.22

3. The relationship between increased levels of IgE and the severity based on ARIA classification

The Chi-square test was used to determine the correlation between elevated IgE levels and severity in allergic rhinitis patients. The chi-square test yielded a significant ($p<0.05$) (PR = 1.65; 95% CI = 1.03–2.64; p= 0.045) (Table 3). There was a substantial correlation between the rising levels of IgE and ARIA classification severity.

Table 3. Chi-square test results in the relationship between increased levels of IgE and the severity based on ARIA classification

IgE Levels	Mild ARIA n (%)	Moderate ARIA n (%)	Total	PR (95% CI)	p
Normal	11 (50.0)	11 (50.0)	22	1.00	—
Increased	4 (17.4)	19 (82.6)	23	1.65 (1.03–2.64)	0.045
Total	15	30	45		

DISCUSSION

The results of this study showed that allergic rhinitis prevalence in young females is higher than in young males. It was similar with the study by Fröhlich *et al* (2017) which reported that allergic rhinitis was coexisting with asthma, and showed a clear male predominance in childhood, and seemed to switch to female predominance in adolescent. These results were different from another study of allergic rhinitis prevalence in adolescence which reported that when they reach adulthood (18-79 years) there was no difference in prevalence between gender (Rosário and Murrieta, 2021). But according to allergic sensitization cohort study, it was found that the cumulative IgE plasma levels of young male adults (56.8%) with allergic rhinitis were considerably higher than those of young female adults (50.9%)(Paula Couto *et al.*, 2014).

Our cross-sectional study revealed a prevalence of allergic rhinitis according to WHO ARIA classification, that 31 (68.9%) of subjects as intermittent, and 14 subjects (66.67%) as persistent, whereas based on severity, the majority 30 subjects (66.7%) was in the moderate-severe level.

These results were slightly lower than another study reporting the duration of complaints of intermittent allergic rhinitis was 91%, and moderate severity was 71% (Stemeseder *et al.*, 2017). Deb *et al* (2014) reported that 42% of patients with allergic rhinitis in Kolkata had mild symptoms, and 57.5 % had moderate to severe symptoms. Another study by Srivastava, Shamanna and Viswanatha (2018) with 80 participants, showed 36 reporting mild symptoms, 32 moderate symptoms, and 12 severe symptoms.

The chi-square test in our study revealed a correlation between elevated IgE levels and the severity of allergic rhinitis (RP= 3.71; 95% CI= 0.62 to 0.65; p= 0.045). Corsico *et al* (2017) reported differences in specific IgE levels between patients with mild intermittent AR and mild persistent disease (p = 0.05), mild intermittent with moderate persistent disease (p=0.001), moderate intermittent

with moderate persistent disease (p = 0.01), and mild persistent with moderate persistent disease (p= 0.05). Several studies reported the association of elevated levels of IgE on allergic diseases in general, including asthma (Ciprandi *et al.*, 2016), and the respiratory tract of hyperresponsiveness (Samitas *et al.*, 2018) and with decreased lung function (Rengganis *et al.*, 2018).

Allergic rhinitis is characterized by the degranulation of IgE-mediated mast cells and the release of mediators, which sets off a very quick reaction that causes sneezing, palate itching, nasal congestion, runny nose, and possibly eye symptoms like itchy, red, watery, and burning eyes. Later on, inflammatory responses with eosinophilic infiltration could happen.

Thus, a person's quality of life may be impacted by the symptoms of allergic rhinitis (Widiatmaja et al., 2024). A cumulative dose-response relationship was found between smoking and higher total IgE levels associated with Dermatophagoides farinae, insect, and dog allergies. In addition, smoking has been identified as a predictor of elevated IgE levels, and specific IgE levels to certain allergens (Kim et al., 2017). Therefore, cigarette smoke exposure should be minimized to reduce the incidence of allergic sensitization and the intensity of AR symptoms (Kwon et al., 2016).

This study's findings suggested that evaluating patients' IgE levels during clinical examination was essential for providing optimal therapy, and also for predicting their prognosis in AR. Serum IgE was a reliable diagnostic marker for allergic rhinitis. The correlation between the severity of allergic rhinitis and the duration of optimal treatment for a complete symptom remission was ensured by choice of medications. Understanding the nature of the condition for immunotherapy requires the ability to assess IgE levels in allergen extracts, pure proteins, and novel allergens (Platts-Mills et al., 2016) . The knowledge of serum IgE level at the initial therapy, supported the present study which investigated the effectiveness of immunotherapy, the symptoms and quality of live scores in the second-year treatment, which showed significant improvement compared to the baseline (Fujioka et al., 2022).

In conclusion, there was a correlation between elevated total IgE blood levels and the severity in allergic rhinitis patients. The relationship between IgE concentration and some allergy severity may assist physicians in preventing AR by identifying the trigger and prescribing an appropriate therapy, especially in patients with a genetic history of allergic disorders.

AUTHORS CONTRIBUTION

AW contributed to the conceptualization, data collection, data analysis, manuscript drafting, and revision of the study.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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