

Immunoglobulin-E and Thyroid-Stimulating Hormone Receptor Antibody in Graves' disease with Atopy

Inmunoglobulina E y el receptor del anticuerpo de la hormona estimulante de la tiroides en la enfermedad de Graves con atopia

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SUMMARY

Background: Graves' disease is known to have a high recurrence rate with recent evidence linked pollen allergy as one of the factors that might induce relapse in Graves' disease. Therefore, it was argued that IgE might play a role in inducing relapse of Graves' Disease. This study aims to investigate the correlation between IgE and Thyroid-Stimulating Hormone Receptor Antibody (TRAb) in Graves' disease respondents with a history of atopy.

Methods: A cross-sectional study was conducted in 2012. Blood samples were collected using a 5 mL sterile syringe, put on EDTA tubes, and analyzed for Routine Blood Count, IgE level, and TRAb level. Stool examination and skin prick test data were also collected from the respondents to determine the history of atopy.

Results: A total of 131 respondents participated in

this study, consisting of 28 males (20.6 %) and 103 females (79.4 %). In the group with a history of atopy, the average atopy duration was 26.5 years, and the most common types of atopy were allergic rhinitis (42.6 %), food allergy (32.3 %), asthma (16.1 %), and drug allergy (8.8 %). IgE level and TRAb level among respondents with a history of atopy were significantly higher than those without a history of atopy (407 vs. 23.9 for IgE; 9.2 vs. 1.4 for TRAb). We found a positive correlation between IgE level and TRAb level among respondents with a history of atopy ($r=0.580$; $p<0.0001$).

Conclusion: This study found a significant correlation between IgE level and TRAb level among Graves' disease respondents with atopy history.

Keywords: Atopy, graves' disease, immunoglobulin-E, thyroid-stimulating hormone receptor antibodies.

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RESUMEN

Antecedentes: *Se sabe que la enfermedad de Graves tiene una alta tasa de recurrencia con evidencia reciente que relaciona la alergia al polen como uno de los factores que podrían inducir una recaída en la enfermedad de Graves. Por lo tanto, se argumentó que la IgE podría desempeñar un papel en la inducción de la recaída de la enfermedad de Graves. Este estudio tiene como objetivo investigar la correlación entre la IgE y el receptor del anticuerpo de la hormona estimulante de la tiroides (TRAb) en los encuestados con enfermedad de Graves con antecedentes de atopía.*

Métodos: *Se realizó un estudio transversal en 2012. Se recolectaron muestras de sangre usando una jeringa estéril de 5 mL, se colocaron en tubos con EDTA y se analizaron para el recuento sanguíneo de rutina, el nivel de IgE y el nivel de TRAb. También se recopilaron datos de exámenes de heces y pruebas cutáneas de los encuestados para determinar el historial de atopía.*

Resultados: *Un total de 131 encuestados participaron en este estudio, compuesto por 28 hombres (20,6 %) y 103 mujeres (79,4 %). En el grupo con antecedentes de atopía, la duración media de la atopía fue de 26,5 años, y los tipos más frecuentes de atopía fueron rinitis alérgica (42,6 %), alergia alimentaria (32,3 %), asma (16,1 %) y alergia a fármacos (8,8 %). El nivel de IgE y el nivel de TRAb entre los encuestados con antecedentes de atopía fueron significativamente más altos que aquellos sin antecedentes de atopía (407 frente a 23,9 para IgE; 9,2 frente a 1,4 para TRAb). Se encontró una correlación positiva entre el nivel de IgE y el nivel de TRAb entre los encuestados con antecedentes de atopía ($r = 0,580$; $p < 0,0001$).*

Conclusión: *Este estudio encontró una correlación significativa entre el nivel de IgE y el nivel de TRAb entre los encuestados con enfermedad de Graves con antecedentes de atopía.*

Palabras clave: *Atopía, enfermedad de Graves, inmunoglobulina E, anticuerpos receptores de la hormona estimulante del tiroides.*

INTRODUCTION

Graves' disease is an autoimmune disorder characterized by the production of Thyroid-Stimulating Hormone Receptor Antibody (TRAb) which activates and causes excessive thyroid hormone synthesis and release. Graves' disease is the most common cause of hyperthyroidism, a typical presentation among females aged 40 – 60 years (1). Although the prevalence among

general populations was around 1 % - 1.5 %, Graves' disease is known to have a high recurrence rate. One study described a recurrence rate of 50 % during the 4-year follow-up course among patients with Graves' disease (2).

The etiology of recurrence in Graves' disease is still unknown, recent evidence linked pollen allergy as one of the factors that might induce relapse in Graves' disease (3). Pollen allergy is one of the diseases related to Immunoglobulin-E (IgE) synthesis. It was argued that IgE might play a role in inducing relapse of Graves' Disease. IgE levels were elevated in 29 % of those with Graves' disease.

Although the incidence of increased IgE levels was smaller than in patients with bronchial asthma (63 %) or pollen allergy (40 %), the mean value of IgE increase in subjects suffering from Graves' disease was equal in subjects suffering from bronchial asthma, and even greater when compared to people with pollen allergy. Therefore, it appears that elevated IgE levels are associated with Graves' autoimmune disease (3).

Previous studies have found that 30 %-40 % of people with Graves' disease have elevated levels of immunoglobulin-E (IgE). Some evidence also suggests a link between autoimmune thyroid disease and allergic responses. Several findings that might support this argument are 1) IgE was found in thyroid tissue and ocular muscle in subjects with Graves' disease, 2) Recurrence of Graves' disease was linked to allergic rhinitis, 3) Several studies reported an IgE class of thyroid peroxidases autoantibodies among subjects with Hashimoto Thyroiditis and Graves' disease, and 4) A significant increase of IgE level in 29 % - 40 % subjects with Graves' disease. Studies also revealed that the remission rate in patients with Graves' disease associated with an increase in IgE levels is lower than in patients with Graves' disease with normal IgE levels (3-5).

However, no study had been conducted to confirm whether IgE is correlated directly with Graves' disease progression. This study aims to compare the IgE level and TRAb level among Graves' disease subjects based on atopy status.

METHODS

Study Design

This was a cross-sectional study conducted from April to August 2012 at the Endocrinology outpatient clinic, Dr. Soetomo General Hospital, Surabaya, Indonesia. Subjects were Graves' disease patients aged 18 years and above that have fulfilled the diagnostic criteria and received Propylthiouracil (PTU) treatment for at least eight weeks. Using sample size calculation, we obtained the minimum requirement was 38 responses (6). Consecutive sampling was conducted until the minimum number is fulfilled. This study followed the principles of Helsinki's Declaration and also received permission from Dr. Soetomo General Hospital Ethical Committee before it began (ethical clearance o.0050/LOE/301.4.2/VI/2012). All respondents had given their informed consent before their inclusion in the study. Details that might disclose the identity of the respondents were omitted.

Data Collection

We obtained respondents through interviews using a structured questionnaire which consisted of sociodemographic data, disease condition, treatment data, and allergy history. The physical examination was then conducted to obtain information on respondents' vital signs (blood pressure, heart rate, respiration rate, and body temperature) using standardized protocols.

Blood samples were collected using a 5 mL sterile syringe, put on EDTA tubes, and analyzed for Routine Blood Count, IgE level, and TRAb level. Stool examination and skin prick test data were also collected from the respondents to determine the history of atopy.

Data Analysis

Acquired data were compiled and analyzed using IBM SPSS for Windows ver. 20.0. Demographical data were presented in frequency tables, while IgE and TRAb level was expressed as mean \pm standard deviation. Correlation between IgE and TRAb level in respondents with atopy were analyzed using Spearman rank-order.

RESULTS

A total of 131 respondents were included in this study, consisting of 28 males (20.6 %) and 103 females (79.4 %). Respondents were then further categorized based on a history of atopy; age distribution was shown in Table 1. In the group with a history of atopy, the average atopy duration was 26.5 years, and the most common types of atopy were allergic rhinitis (42.6 %), food allergy (32.3 %), asthma (16.1 %), and drug allergy (8.8 %).

Table 1.
Respondent Age Distribution

	Without Atopy n = 63	With Atopy n = 68
Mean age (years)	42.2	45.4
Age group		
< 20 years	0 (0)	1 (1.5)
20 – 29 years	8 (12.6)	6 (8.8)
30 – 39 years	18 (28.5)	13 (19.1)
40 – 49 years	19 (30.1)	16 (23.5)
50 – 59 years	14 (22.2)	23 (33.8)
60 – 69 years	4 (6.6)	8 (11.8)
> 69 years	0 (0)	1 (1.5)

We analyze the laboratory data collected from the respondent. We found that the mean total IgE level in respondents with and without a history of atopy consecutively 407 IU/mL and 23.9 IU/mL. Total TRAb level in respondents with and without a history of atopy consecutively 9.2 IU/mL and 1.4 IU/mL. It was found that both IgE level and total TRAb level in respondents with a history of atopy are higher than respondents without a history of atopy.

We further analyze the correlation between IgE level and TRAb level in respondents with a history of atopy. It was found that TRAb level was positively correlated with IgE level ($r=0.580$; $p<0.0001$).

DISCUSSION

Graves' disease is a polygenic disease that occurred due to interaction between genetic susceptibility, environmental factors, and endogenous factors (7). Interaction between these factors remained unclear and researches are needed to shed some light on this topic. This study agreed with previous studies that showed Graves' disease affects females 4 – 5 times more likely than males, with the age group of 30 – 50 years old being the most susceptible to this disease (8). This study found that 51.9 % of respondents with Graves' disease had a history of atopy. This finding is in accordance with a previous study that reported 30 % - 50 % of respondents with Graves' disease have at least one type of atopy (7-9). Regarding the IgE level among respondents with and without a history of atopy, this study was in accordance with a previous study (9), which shows that IgE level in subjects with a history of atopy was significantly higher than subjects without a history of atopy. It was argued that respondents with a history of atopy would synthesize a higher level of IgE as a response toward environmental allergens. In comparison, those without a history of atopy will synthesize other antibody types such as IgG and IgM in a higher level while only a small number of IgE (10). This study found that the TRAb level in respondents with a history of atopy was significantly higher than those without a history of atopy.

In Sato's study, Graves' disease subjects with above average IgE levels will have significantly higher TRAb levels than those with normal IgE levels. Sato's study also revealed that before receiving methimazole therapy, TRAb levels in Graves' disease patients who experience elevated IgE levels are higher than those with Graves' disease patients with normal IgE levels. However, while receiving methimazole therapy, even though both groups experienced a decrease in TRAb levels, the decrease was significantly developed in the group of Graves' disease patients with normal IgE levels. Another previous study also showed a positive correlation between IgE level and TRAb level in Graves' disease subjects with a positive history of asthma and allergic rhinitis (11). We further explore the correlation

between IgE level and TRAb level in this study. Using the Spearman-rank order test, we found a positive correlation between IgE level and TRAb level among respondents with atopy history.

This study has several limitations. Firstly, this study was only conducted in a single center, which may not represent Indonesia or Surabaya population. Second, there was a limited amount of funds available for this study, which caused fewer parameters to be examined in this study. Therefore, the authors recommend further study in Graves' disease subject with a history of atopy to obtain an optimal treatment result and prevent recurrence in the future.

CONCLUSION

We found that IgE level and TRAb level in Graves' disease respondents with a history of atopy were significantly higher than those without a history of atopy. We also found a positive correlation between IgE level and TRAb level in Graves' disease respondents with a history of atopy. The result of this study may be used to investigate further the correlation between Graves' disease and history of atopy.

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Not applicable.

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