

## THE DIFFERENCE IN TOTAL IMMUNOGLOBULIN E LEVELS AND EOSINOPHIL COUNTS AMONG ELDERLY INDIVIDUALS WITH AND WITHOUT ALLERGIC DISEASES

*Perbedaan Kadar Immunoglobulin E Total dan Jumlah Eosinofil pada Lansia  
dengan dan tanpa Penyakit Alergi*

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### ABSTRAK

Penyakit alergi dapat terjadi pada lansia dengan gejala yang dapat memburuk akibat adanya proses immunosenesens. Kadar IgE total dan jumlah eosinofil dapat digunakan sebagai pemeriksaan tambahan untuk penyakit alergi. Penelitian ini bertujuan untuk mengetahui perbedaan kadar IgE total dan jumlah eosinofil pada lansia dengan dan tanpa penyakit alergi. Penelitian observational analitik ini dilakukan pada lansia usia 60-80 tahun di RSUP DR. M. Djamil Padang selama Januari-Juni 2024. Sampel dikelompokkan menjadi kelompok lansia dengan penyakit alergi dan kelompok lansia tanpa penyakit alergi. Pengambilan sampel dilakukan secara consecutive sampling, melibatkan 52 partisipan (masing-masing 26 dengan dan tanpa penyakit alergi). Kadar IgE total dan jumlah eosinofil diperiksa dengan menggunakan sampel darah vena. Analisis data menggunakan uji Mann-Whitney. Hasil penelitian menunjukkan median kadar IgE total pada kelompok alergi sebesar 1.741,1 kIU/L (minimum 517,7 kIU/L; maksimum 4843 kIU/L), sedangkan kelompok non-alergi 177,1 kIU/L (minimum 14 kIU/L; maksimum 800 kIU/L). Median jumlah eosinofil pada kelompok alergi sebesar 378 sel/ $\mu$ L (min: 100; maks: 950), sedangkan kelompok non-alergi 61,5 sel/ $\mu$ L (min: 17; maks: 189). Terdapat perbedaan signifikan kadar IgE total dan jumlah eosinofil antara lansia dengan dan tanpa penyakit alergi ( $p < 0,001$ ). Lansia yang mengalami Alergi menunjukkan kadar IgE dan jumlah eosinofil lebih tinggi dibandingkan lansia yang tidak alergi.

**Kata kunci:** alergi, imunoglobulin E total, immunosenesens, kadar eosinofil, lansia

### ABSTRACT

Allergic diseases can occur in the elderly, with symptoms that may worsen due to the process of immunosenescence. Total IgE levels and eosinophil counts can be used as supplementary examinations for allergic diseases. This study aims to determine the differences in total IgE levels and eosinophil counts in elderly individuals with and without

allergic disease. This observational-analytical study was conducted on elderly individuals aged 60–80 years at DR. M. Djamil General Hospital, Padang, from January to June 2024. Samples were divided into two groups: elderly with allergic disease and elderly without allergic disease. Sampling was performed by consecutive sampling, involving 52 participants (26 with allergic disease and 26 without). Total IgE levels and eosinophil counts were measured using venous blood samples. Data analysis was conducted using the Mann–Whitney U test. The results showed that the median total IgE level in the allergic group was 1,741.1 kIU/L (minimum 517.7 kIU/L; maximum 4,843 kIU/L), while the non-allergic group had a median of 177.1 kIU/L (minimum 14 kIU/L; maximum 800 kIU/L). The median eosinophil count in the allergic group was 378 cells/ $\mu$ L (min: 100; max: 950), whereas the non-allergic group had a median of 61.5 cells/ $\mu$ L (min: 17; max: 189). There were significant differences in total IgE levels and eosinophil counts between elderly individuals with and without allergic disease ( $p < 0.001$ ). Elderly individuals with allergies exhibit higher IgE levels and eosinophil counts compared to elderly individuals without allergies.

**Keywords:** allergy, elderly, eosinophil counts, immunosenescence, total immunoglobulin E

## INTRODUCTION

The World Allergy Organization defines allergy as a hypersensitivity reaction mediated by immunological mechanisms, involving both Immunoglobulin E (IgE) and non-IgE pathways. The reaction occurs due to exposure to allergens such as food products, dust, animal dander, and others, beginning with the sensitization phase [1]. The sensitization phase is the initial stage of hypersensitivity reactions, during which an individual is first exposed to an allergen [2]. The allergen acts as an antigen, stimulating B cells to produce IgE with the help of T helper cells. Immunoglobulin E then binds to mast cells or basophils through Fc $\epsilon$  receptors. Upon re-exposure to the same antigen, the antigen binds to the IgE already present on the surface of mast cells or basophils. This allergen-IgE interaction triggers mast cell or basophil degranulation, leading to the release of mediators such as histamine, which causes hypersensitivity reaction symptoms. The symptoms vary, ranging from skin redness (allergic dermatitis, erythrodermic urticaria) to lower respiratory tract inflammation accompanied by wheezing (asthma) [2]. Total immunoglobulin E serves as an index for assessing allergic diseases [3].

For many years, the measurement of serum total IgE levels has been an important tool in the evaluation of patients with suspected allergic diseases. Total IgE testing is a simple, cost-effective, and reliable screening tool for allergic diseases [4]. A study conducted by Man-Li Chang et al. (2015) on patients with allergies at the Hospital of Harbin Medical University, China, found that total IgE testing has a sensitivity of 88.9%, making it useful for allergy screening at a low cost [3]. Allergy sufferers not only experience an increase in total IgE but also an increase in eosinophil count. Eosinophils are proinflammatory granulocytes associated with parasitic infections and allergic diseases, such as asthma, allergic rhinitis, and allergic dermatitis.[5] Eosinophil examination is performed using venous blood samples analyzed with a hematology analyzer based on the principle of laser-based (optical) flow cytometry, with normal eosinophil levels being less than 3%. Eosinophil testing has a sensitivity of 70.4% and a specificity of 66.7% in detecting allergies [6].

Allergic diseases are classified into several groups based on the ICD (International Statistical Classification of Diseases)- 11, including eye and respiratory system conditions (asthma, hypersensitivity pneumonitis, rhinitis, rhinosinusitis, conjunctivitis), skin and mucous membrane conditions (dermatitis, urticaria, erythroderma), digestive system conditions (gastrointestinal hypersensitivity reactions to food), anaphylaxis, and

multisystem diseases (drug allergies, food allergies, hymenoptera venom allergies) [7]. The global prevalence of allergic diseases is rapidly increasing in both developing and developed countries [2]. The elderly population consists of individuals aged 60 years and above, as defined by Law No. 13 of 1998 [8]. The number of elderly individuals is rising rapidly, with many countries experiencing a drastic increase in aging populations [9]. Indonesia has officially entered the aging population phase since 2021, when the percentage of elderly individuals surpassed 10%. West Sumatra is among the eight provinces in Indonesia classified as having an aging population, with 10.79% of its residents being elderly as of 2022 [10].

Elderly individuals undergo an aging process that leads to changes in the body's physiological systems. One of the most significant changes is immunosenescence. Immunosenescence is a condition of immune system dysregulation that occurs gradually due to aging, affecting both innate and adaptive immune responses [11]. The main characteristics of immunosenescence include an imbalance in lymphocyte subpopulations (a decrease in naïve lymphocytes), thymic involution with reduced new T-cell generation, and hematopoietic stem cell dysfunction. These changes increase susceptibility to infections and make the immune system more prone to inflammation, autoimmune diseases, and allergic conditions. Additionally, stress experienced by the elderly can influence various aspects of mast cell function, particularly skin mast cells, triggering the release of inflammatory mediators such as histamine, Vascular Endothelial Growth Factor (VEGF), cytokines, nitric oxide, and proteases. These inflammatory mediators can contribute to allergic reactions [11],[12].

The prevalence of allergies in the elderly ranges from 5-10% and continues to increase [13]. Age-related changes due to immunosenescence can worsen nasal congestion, itching, sneezing, and rhinorrhea, which are characteristic symptoms of allergic rhinitis [14]. This condition is caused by a reduction in mucociliary clearance due to the decreased number and activity of cilia in the upper respiratory tract. Additionally, there is a decline in mucosal barrier function, immune response dysregulation, and inflammation in the airways [16]. Several anatomical and physiological changes in the nose can influence the severity of rhinitis symptoms. Weakening of the fibrous connective tissue in the nasal cartilage and atrophy of collagen fibers lead to a drooping nasal tip. These changes reduce nasal airflow, making nasal congestion common in the elderly [14].

Aging also affects the skin, leading to loss of hydration, atrophy of the dermis and epidermis, changes in skin barrier function, and reduced immune response, increasing the risk of urticaria and dermatitis. Itching, often accompanied by nonspecific skin manifestations, is common in the elderly. Therefore, if an elderly individual presents with pruritus or chronic urticaria, systemic diseases should be considered as potential underlying causes [5]. An additional diagnostic test that can be performed for allergic diseases is the total IgE level examination [12].

A study conducted by Manuprita Sharma et al. (2019) on 113 individuals with allergic rhinitis and 42 individuals as a control group compared total IgE levels across different age groups. The results showed that the 51-75 age group had an average total IgE level of approximately 781.25 IU/mL, which was higher than the 26-50 age group (approximately 729.69 IU/mL) and the control group (96.62 IU/mL) [15]. These findings differ from a study conducted by Suaad A. Brakhas et al. (2016), which examined 77 individuals over 50 years old with asthma, where only 4 participants had total IgE levels around 249.6 IU/mL. In this study, the total IgE levels in individuals over 50 years old were lower than those in younger age groups but still higher than the control group, which had an average total IgE level of 30 IU/MI [16].

The differences between these two studies may be due to the unequal sample sizes of the control and case groups among the elderly, making it difficult to determine the

impact of immunosenescence on total immunoglobulin E levels in elderly individuals with allergic diseases [17]. Based on this background, the author is interested in conducting a study on the differences in total immunoglobulin E levels and eosinophil counts in elderly individuals with and without allergic diseases. This study aims to analyze the differences in total IgE levels and eosinophil counts between elderly individuals with and without allergic diseases.

## **METHODS**

### **Study design**

This research was an observational-analytic study using a cross-sectional method, in which independent and dependent variables are examined simultaneously. The study was conducted at RSUP DR. M. Djamil Padang in the Internal Medicine, Allergy Immunology, Pulmonology, Geriatrics, ENT, Dermatology, and Pulmonary outpatient clinics, as well as in the Internal Medicine, ENT, Dermatology, and Pulmonary inpatient wards. The research was carried out over six months (from January 2024 to June 2024).

### **Population and sample**

The population in this study consists of elderly patients who meet the inclusion criteria, including elderly patients aged 60–80 years who have been diagnosed with an allergic disease and those who have not been diagnosed with an allergic disease by a specialist based on clinical assessment and medical records. The exclusion criteria for this study are patients with parasitic or fungal infections, malignancies, autoimmune diseases, cognitive disorders, or those receiving high-dose corticosteroid therapy and immunosuppressants. The sampling method used was consecutive sampling, with the minimum sample size calculated using the Lemeshow formula, resulting in 24 participants in the elderly group with allergic diseases and 24 participants in the elderly group without allergic diseases.

### **Data collection**

Elderly patients who agree to participate in the study, as evidenced by signing the informed consent form, will undergo total IgE examination through venous blood sampling. A total of 2 cc of blood will be collected and placed in a clinical chemistry tube (yellow-capped tube), and an additional 1 cc of blood will be placed in an EDTA (Ethylenediaminetetraacetic acid) tube (purple-capped tube) for eosinophil count analysis. The blood samples will then be stored and transported in a cooler box at a temperature of 2–8°C to Prodia Laboratory in Padang for analysis using the ELISA method for total IgE levels and a hematology analyzer for eosinophil count. The blood samples will be left at room temperature for 2 hours or overnight at 2–8°C, then centrifuged at 3000 rpm for 10–15 minutes. After processing, the samples can be stored at -80°C until they are used for result analysis.

### **Data analysis**

Categorical data, including patient characteristics such as age, gender, current medical history, past medical history, and treatment history, are presented in the form of frequency and percentage. Numerical data, specifically total IgE levels and eosinophil count, are tested for normality using the Shapiro-Wilk test. The normality test results indicate a non-normal distribution; therefore, total IgE levels and eosinophil count are presented as median (minimum-maximum). The data are then analyzed using the Mann-Whitney test. A p-value of <0.05 is considered significant, indicating a meaningful difference in total IgE levels between elderly patients with and without allergic diseases.

### **Ethical statement**

This study has received ethical clearance from the research ethics committee with the approval number DP.04.03/D.XVI.XI/246/2024. Subjects who meet the inclusion criteria are given an explanation of the study's objectives and the procedures they will undergo during the research. After understanding the information and agreeing to participate,

subjects are asked to fill out and sign an informed consent form. Participation in the study is entirely voluntary, and subjects are free to decline if they do not agree.

## RESULT

This study involved 52 elderly, consisting of 26 individuals in the allergy group and 26 in the non-allergy group. The characteristics of the study respondents are presented in Table 1. Table 1 shows that males were more prevalent in the allergy group, while females were more common in the non-allergy group. The most common age group was the young elderly (aged 60–69 years) in both the allergy and non-allergy groups. Most respondents were homemakers in both groups. A family history of allergies was reported by only 50% of respondents in the allergy group, whereas none of the respondents in the non-allergy group had a family history of allergies.

**Table 1. Characteristics of Study Respondents**

Variable	Allergy group Total (%)	Non-allergy group Total (%)
Gender		
Man	14 (53,8)	10 (38,5)
Woman	12 (46,2)	16 (61,5)
Age		
Young elderly (60 – 69 <sup>th</sup> years old)	19 (73,1)	17 (65,4)
Middle elderly (70 – 79 <sup>th</sup> years old)	7 (26,9)	9 (34,6)
Job		
Housewife	10 (38,5)	14 (53,8)
Civil Servant	2 (7,7)	0 (0)
Entrepreneur	5 (19,2)	5 (19,2)
Farmer	1 (3,8)	3 (11,5)
Retiree	5 (19,2)	3 (11,5)
Worker	3 (11,5)	1 (3,8)
Family History of Allergies		
Yes	13 (50)	0 (0)
No	13 (50)	26 (100)
History of Smoking Habits		
Yes	7 (26,9)	10 (38,5)
No	19 (73,1)	16 (61,5)
Nutritional Status		
Malnutrition	5 (19,2)	3 (11,5)
No Malnutrition	21 (80,8)	23 (88,5)
Fungsional Status		
Independent	14 (53,8)	11 (42,3)
Mild Dependent	3 (11,5)	9 (34,6)
Moderate Dependent	9 (34,6)	6 (23,1)
Severe Dependent	0 (0)	0 (0)
Comorbidity		
Diabetes Mellitus Type II	5 (19,2)	5 (19,2)
<i>Community Acquired Pneumonia</i>	5 (19,2)	8 (30,8)
Hypertension	6 (23,1)	3 (11,5)
Dyspepsia Syndrom	1 (3,8)	4 (15,4)
<i>Chronic Heart Failure</i>	4 (15,4)	3 (11,5)
Others	5 (19,2)	3 (11,5)
Distribution of Allergy Classification		
Eyes and Respiratory Tract	9 (34,6)	
Skin and Mucous Membranes	11 (42,3)	
Multisystem	6 (23,1)	

Respondents with a history of smoking accounted for only 26.9% in the allergy group and 38.5% in the non-allergy group. The majority of respondents, as shown in Table 1,

had good nutritional status (not malnutrition) and were functionally independent in both the allergy and non-allergy groups. The most common comorbid disease in the allergy group was hypertension, while in the non-allergy group, it was Community-Acquired Pneumonia. In the allergy group, the types of allergic diseases experienced by respondents included allergies affecting the eyes and respiratory tract (bronchial asthma), skin and mucous membranes (urticaria, erythroderma, irritant contact dermatitis), and multisystem allergies (drug eruption, drug allergy reactions). However, the most prevalent type of allergic disease was skin and mucous membrane allergies, with a prevalence of 42.3%. Total IgE levels in elderly individuals with and without allergic diseases can be seen in Tables 2.

**Table 2. Difference in Total IgE Levels Between the Allergy and Non-Allergy Group**

Category	Group with Allergies		Group without Allergy		<i>p-value</i>
	Median	Minimum – Maximum	Median	Minimum – Maximum	
Total IgE (kIU/L)	1741,1	517,7 – 4843	177,1	14 – 800	<0,001

The total IgE levels in the allergy group, as shown in Table 2, had a median value of 1741.1 kIU/L, with a minimum level of 517.7 kIU/L and a maximum level of 4843 kIU/L. These results indicate that the total IgE levels in the allergy group are higher than the normal range (<150 kIU/L). The total IgE levels in the non-allergy group had a median value of 177.1 kIU/L, with a minimum level of 14 kIU/L and a maximum level of 800 kIU/L. Most IgE levels in the non-allergy group remained within the normal range. The data analysis results shown in Table 2 indicate a difference in total IgE levels between the allergy group and the non-allergy group, with the allergy group exhibiting higher total IgE levels than the non-allergy group. This difference is statistically significant, with a *p*-value of <0.001. The eosinophil counts in elderly individuals with and without allergic diseases can be seen in Tables 3.

**Table 3. Difference in Eosinophil Counts Between the Allergy and Non-Allergy Group**

Category	Group with Allergies		Group without Allergy		<i>p-value</i>
	Median	Minimum – Maximum	Median	Minimum – Maximum	
Eosinophil counts (sel/ $\mu$ L)	378	100 – 950	61,5	17 – 189	<0,001

The eosinophil counts in the allergy group, as shown in Table 3, had a median value of 378 sel/ $\mu$ L, with a minimum level of 100 sel/ $\mu$ L and a maximum level of 950 sel/ $\mu$ L. These results indicate that the eosinophil counts in the allergy group are higher than the normal range (50-400 sel/ $\mu$ L). The eosinophil counts in the non-allergy group had a median value of 61,5 sel/ $\mu$ L, with a minimum level of 17 sel/ $\mu$ L and a maximum level of 189 sel/ $\mu$ L. Most eosinophil counts in the non-allergy group remained within the normal range. The data analysis results shown in Table 3 indicate a difference in eosinophil counts between the allergy group and the non-allergy group, with the allergy group also exhibiting higher eosinophil counts than the non-allergy group. This difference is statistically significant, with a *p*-value of <0.001.

## DISCUSSION

This study included 52 elderly participants equally divided into allergy (elderly patients diagnosed with allergic diseases by a specialist) and non-allergy groups (elderly patients not diagnosed with allergic diseases by a specialist), with strict exclusion criteria to minimize confounding factors affecting IgE levels and eosinophil counts.

### Characteristics of Study Respondents

The allergy group had a slightly higher proportion of males, consistent with previous studies suggesting hormonal influences on allergic disease prevalence in elderly males.

Adeeb B. Bulkhi et al. (2020) reported that the prevalence and morbidity of allergic diseases, particularly asthma, increase in males after the fifth decade of life [18]. This is associated with the role of sex hormones, particularly testosterone, which helps inhibit smooth muscle contraction in the airways and reduces inflammation, thereby decreasing the incidence of asthma. However, in elderly males, testosterone levels decline, leading to a resurgence in asthma prevalence. A study conducted by Xin Wang et al. (2022) reported that the prevalence of dermatitis and eczema was also higher in elderly male patients compared to females, with a percentage of 56% versus 44%. However, this also depends on the characteristics of aging skin. A decrease in water and sebum levels in the skin can be a risk factor for dermatitis and eczema in the elderly. Additionally, elderly individuals who are more active outdoors may be at higher risk of exposure to allergens during activities and work, which can trigger dermatitis [19].

The majority of participants in both groups were young elderly (60–69 years). There has been no detailed explanation as to why the young elderly group experiences allergies more frequently than other elderly groups until now. However, some studies related to their higher activity levels and greater exposure to allergens, as reflected by their diverse occupations including farming, labor, entrepreneurship, and civil service [12].

A family history of allergies was present in only 50% of the allergy group. This indicates that indicating that elderly individuals without such history can still develop allergies. This may result from continuous exposure to antigens, which drives allergy progression through repeated stimulation. In individuals without allergies, Th1 cells tend to be more dominant than Th2 cells [20]. Th1 cells play a role in suppressing the immune response to allergens, whereas Th2 cells contribute to the development of allergy symptoms by producing IgE antibodies and releasing histamine and inflammatory mediators, which are key components of allergic reactions. In individuals with allergies, Th1 cells are not strong enough to produce sufficient interferon-gamma (IFN- $\gamma$ ) to counterbalance Th2 activity. As a result, IL-4 is actively produced by Th2 cells, leading B cells to produce IgE, which triggers allergic reactions [20]. Aging also affects the release of mast cells and basophil mediators in response to chemoattractant signals, as well as the activation of mast cells and basophil mediators [12].

Elderly individuals also experience immunosenescence, which leads to dysregulation of the immune system. The main characteristics of immunosenescence include an imbalance in lymphocyte subpopulations (naïve lymphocyte dysregulation), thymic involution with dysregulation in the generation of new T cells, and hematopoietic stem cell dysfunction. These changes result in immune system dysregulation, increasing the risk of inflammation, autoimmune diseases, and allergic diseases. Stress can impair mast cell function, especially in the skin, causing the release of inflammatory mediators such as histamine, VEGF, cytokines, nitric oxide, and proteases, which may trigger allergic reactions [11],[12].

Hematopoietic stem cells also undergo aging, where the bone marrow hematopoietic compartment is gradually replaced by adipose tissue with increasing age. This process increases the risk of DNA damage, Reactive Oxygen Species (ROS) accumulation, and epigenetic changes. In this condition, myeloid progenitor cells increase, while lymphoid progenitor cells decrease, leading to myeloproliferative disorders and impaired B and T cell development, which can disrupt the adaptive immune system [12].

The aging process, which affects changes in body function in the elderly, can be observed through their functional status. Although most respondents had an independent functional status, some had a moderate dependency, including 34.6% in the allergy group and 23.1% in the non-allergy group [10],[11]. A study conducted by Nejari et al reported that elderly individuals with asthma symptoms, particularly those accompanied by dyspnea, experience a decline in quality of life [21].

### **Total IgE Levels and Eosinophil Counts in Elderly Individuals With and Without Allergic Diseases**

Based on Table 2, the median total IgE level in the allergy group was 1741.1 kIU/L (range 517.7 kIU/L - 4843 kIU/L). This result indicates an increase in total IgE levels exceeding the normal range in the allergy group (normal total IgE level <150 kIU/L). In contrast, the median total IgE level in the non-allergy group was 177.1 kIU/L (range: 14 kIU/L - 800 kIU/L). This result shows that there was no increase in total IgE levels beyond the normal range in the control group.

These findings are consistent with a study conducted by Suaad A. Brakhas et al. (2016), which reported a significant increase in total IgE levels in patients over 50 years old suffering from allergic diseases, including asthma, rhinitis, and urticaria. The role of IgE is not only to provide protective immunity against parasitic infections but also to mediate hypersensitivity reactions that contribute to the pathogenesis of allergic diseases. Current studies support the role of IgE in mediating, sustaining, and assessing the severity of allergic responses in allergic patients, as evidenced by the increased IgE levels in the allergy group compared to the non-allergy group [16].

Based on Table 3, the median eosinophil counts in the allergy group were 378 sel/ $\mu$ L (range: 100 sel/ $\mu$ L – 950 sel/ $\mu$ L). This result indicates an increase in eosinophil counts exceeding the normal range in the allergy group (normal eosinophil counts 50-400 cells/ $\mu$ L). In contrast, the median eosinophil counts in the non-allergy group were 61.5 50-400 sel/ $\mu$ L (range: 17 sel/ $\mu$ L – 189 sel/ $\mu$ L). This result shows that there was no increase in eosinophil counts beyond the normal range in the control group.

Immunoglobulin E (IgE) is an antibody synthesized and released by B lymphocytes of the immune system through the interaction of genes, cytokines, and the environment. The allergy mechanism occurs due to intracellular signaling processes involving allergens. Allergens bind to IgE receptors with high-affinity Fc $\epsilon$ RI on mast cells, basophils, and monocytes. This process can induce mast cell degranulation and cross-linking between IgE bound to mast cells or basophils with allergens. The stimulus transmits a signal to activate the cyclic nucleotide system, increasing the cGMP-to-cAMP ratio, allowing Ca<sup>++</sup> ions to enter the cell. Ultimately, this leads to the release of various inflammatory mediators stored in mast cell granules, including histamine, Eosinophil Chemotactic Factor of Anaphylaxis (ECF-A), and Neutrophil Chemotactic Factor (NCF) [22],[23]. Th2 cells play a crucial role in allergic responses by releasing eosinophils [23]. Individuals with a family history of allergies may experience an increase in total circulating IgE levels, reaching up to ten times the normal value, which significantly raises the risk of developing allergies [24].

Some patients in the non-allergic group had total IgE levels exceeding the normal range, as seen from the maximum total IgE level reaching 800 kIU/L in this study. Several factors may contribute to this condition, including:

1. Changes in the Immune System in the Elderly. Aging leads to alterations in the immune system, which may result in a decreased ability to respond to new pathogens and increased reactivity to previously encountered antigens, even without showing characteristic symptoms [25].
2. Elderly individuals may experience conditions such as chronic infections and gastrointestinal inflammation that can elevate total IgE levels, even though these conditions may not be recorded in medical records [26]. Gastrointestinal inflammation, such as peptic ulcers caused by *Helicobacter pylori* infection, is associated with a dominant Th1 cell response that activates macrophages and enhances bactericidal activity by inducing cytokine expression, including interferon- $\gamma$  (IFN- $\gamma$ ), interleukin-18 (IL-18), IL-12, and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). Meanwhile, cytokines secreted by Th2 cells, such as IL-4, increase IgE production and contribute to hypersensitivity reactions [27].

3. Elderly individuals who smoke may have elevated total IgE levels. Cigarette smoke contains harmful substances that trigger pro-inflammatory responses. Smoking leads to neutrophil and macrophage accumulation in lung tissues, inducing airway inflammation, which results in increased total IgE levels and eosinophil counts. Smoking has been linked to a higher risk of allergic responses. Current studies show significant differences in total IgE levels between smokers and non-smokers, indicating that smoking can elevate IgE levels, potentially triggering allergic reactions due to immune system dysregulation [12], [28].
4. Total IgE levels can increase up to ten times the normal value in elderly individuals with a history of allergies, which raises the risk of developing allergic reactions later in life [12].

#### **Difference in Total IgE Levels and Eosinophil Counts in Elderly Individuals With and Without Allergic Diseases**

Statistical analysis showed that there was a significant difference in total IgE levels between the allergy group and the non-allergy group, with an increase in total IgE levels exceeding normal in the allergy group ( $p < 0.001$ ). Elderly individuals undergo immunosenescence, which can affect both the innate and adaptive immune systems [20]. Immunosenescence leads to damage or dysfunction in immune organ structures and dysregulation of both innate and adaptive immunity due to aging. In the elderly, adaptive immune function becomes dysregulated, leading to an increase in pro-inflammatory responses, a phenomenon known as inflammaging. Inflammaging is caused by continuous antigen exposure and defects in T and B cells [29]. According to epidemiological data, there is a decline in total IgE levels and allergen sensitization in older adults. However, in elderly individuals with a history of allergies, the immunosenescence process does not affect the decline in total IgE levels, allowing IgE levels to remain elevated [12],[18]. This is evident in the study results, which show a median total IgE level of 1741.1 kIU/L in the allergy group.

This finding is supported by a study conducted by Anja Mediaty et al. (2005), which reported that total IgE production decreases in older adults, except in those with a history of allergies, whose IgE levels remain high, and their tendency for allergic reactions persists into old age [3]. Another study by Mara De Amici et al. (2013) also reported that total IgE levels do not decline with age but instead increase, peaking in the oldest subgroup (aged  $>85$  years). This phenomenon is attributed to regulatory dysfunction occurring during the aging process [30].

Likewise, the eosinophil count also shows an increase in the allergic group. Olga Prokunina et al. (2023) reported an increased number of eosinophils in both younger patients ( $879.6 \pm 1253.2$  cells/ $\mu$ L) and older patients ( $705 \pm 571$  cells/ $\mu$ L) with allergies, with no statistically significant difference between the two groups ( $p = 0.518$ ). Older patients with asthma in the study exhibited similar levels of Th2 inflammation compared to the younger cohort, despite the presence of immunosenescence in the elderly [5].

Eosinophils are pro-inflammatory granulocytes associated with allergic diseases. Cytokine signaling can support a feedback loop activation between Group 2 innate lymphoid cells (ILC-2) and eosinophils. ILC-2 cells play a crucial role in communication between tissues and inflammatory cells by responding to IL-25, IL-33, and thymic stromal lymphopoietin (TSLP) signals originating from tissues, thereby promoting a Th2 response via secretion of IL-4 [31].

Th2 cells support the activation and survival of eosinophils by releasing various molecules, particularly IL-5. Conversely, eosinophils help sustain the Th2 response through production of IL-25. Additionally, eosinophils contribute to the adaptive humoral response by releasing plasma cell survival factors such as IL-6 or A Proliferation Inducing Ligand (APRIL), and by recognizing IgG and IgE via their surface receptors [31], [32].

Mast cells respond to the release of major basic protein (MBP) from eosinophils, which is a key trigger of acute inflammation in various inflammatory conditions. Mast cells also further activate eosinophils by releasing prostaglandins such as prostaglandin D2 (PGD2), chemokines such as CCL5, and leukotrienes. These interactions contribute to the elevated eosinophil counts observed in patients with allergic diseases.[32]

The strength of this study lies in the fact that there is limited research examining differences in total IgE levels and eosinophil counts in elderly patients with allergic diseases. Additionally, the number of participants was balanced between the allergy and non-allergy groups. However, this study has some limitations, including the lack of consideration for confounding factors such as comorbidities, smoking history, and nutritional status, which could introduce bias in the study results. Moreover, undiagnosed chronic infections in elderly participants, such as fungal or parasitic infections, could also contribute to bias. A deeper understanding is necessary to assess the impact of smoking habits on total IgE levels and eosinophil counts. Future research should further investigate the relationship between total IgE levels and eosinophil counts in elderly individuals with allergies, comorbidities, smoking history, and nutritional status.

## CONCLUSION

Total IgE levels and eosinophil counts in elderly individuals with allergies showed an increase. Some elderly individuals without allergies also experienced elevated total IgE levels. This study demonstrates a significant difference in total IgE levels and eosinophil counts between elderly individuals with allergies and those without.

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