Hypoglobulinemia Frequency in Adult Patients with Allergic Rhinitis

**Abstract**

Objective: Allergic rhinitis (AR) is an immunoglobulin E (IgE)-mediated inflammation of the nasal mucosa. Allergic rhinitis is an important disease due to its high prevalence, effect on quality of life and socio-economic impact. It is known that hyper-immunoglobulin E syndrome and Wiskott-Aldrich syndrome have an atopic component. We aimed to investigate the humoral deficiency by evaluating Ig levels in adult patients with AR. Material and Methods: One hundred eighty-seven patients (Female/male: 112/75) who admitted to our clinic with allergic rhinitis diagnosis were included in the study. Skin prick test (SPT) was performed in all patients for mites, pollens, animal dander, molds, insects, histamine, and negative controls (ALK-Abello, Spain). Serum total IgE, IgG, IgA and IgM were measured by nephelometry (Siemens Dade Behring BNII Nephelometer). Immunoglobulin deficiency was defined as two standard deviations less than mean value for that specified age. Results: Five patients (2.67%) had IgA deficiency and four patients (2.13%) had IgM deficiency. None of the patients had IgG deficiency. Conclusions: There may be an association between AR and IgA or IgM deficiency in adult patients.

Key Words: Rhinitis, allergic, perennial; rhinitis, allergic, seasonal; acquired immunodeficiency syndrome

Rhinitis is an inflammation of the nasal mucosa, and it is characterized by rhinorrhea, nasal obstruction, sneezing, nasal itching, and post-nasal drainage. Allergic rhinitis is the inflammation of the nasal mucosa that is mediated by IgE after exposure to an allergen. Non-allergic rhinitis (NAR) occurs as a result of infections, hormonal disorders, medications, anatomical defects, and physical agents. The symptoms of NAR are similar to AR. AR is an important disease, due to its high prevalence and effect on quality of life and socio-economic status. Its prevalence is between 10.0-30.0% and 20.0-50.0% of AR patients have asthma. Allergic rhinitis has been reported as a risk factor in developing asthma. Chronic rhinosinusitis is a persisting disease characterized by inflammation of one or more sinuses at least 12 weeks duration. Specific antibody deficiency was reported in patients with chronic rhinosinusitis.

The association between some primary immune deficiencies (PID) and allergic diseases has been established. It is known that hyper-immunoglobulin E syndrome and Wiskott-Aldrich syndrome have an atopic component.
n some type of humoral immunodeficiencies, atopy is higher than in the normal population, but the mechanism is still unknown. The prevalence of atopic and allergic diseases in patients with selective IgA deficiency is higher than in the normal population. Most patients with common variable immune deficiency (CVID) have allergic respiratory tract diseases. However, atopy has not been well defined in these patients due to lower total and specific IgE levels.

The aim of this study was to investigate humoral deficiency by evaluating Ig levels in adult patients with AR.

### MATERIAL AND METHODS

One hundred eighty-seven patients who admitted to our clinic between January 2014 and June 2014 with allergic rhinitis diagnosis were included in the study. This study was designed as retrospective clinical study. Written informed consent was obtained from all patients for skin prick test (SPT). Skin prick test was performed in all patients for mites, pollens, animal dander, molds, insects, histamine, and negative controls (ALKAbello, Spain). Antihistamines were suspended at least 7 days before testing. These tests were performed on the volar surface of both fore-arms, with results recorded after 15 minutes. The results were considered positive when the mean wheal diameter was at least 3 mm larger than that produced by the control. Allergen sensitization was defined as having positive SPT for at least one allergen. Serum total IgE, IgA, IgM and IgG were measured by nephelometry (Siemens Dade Behring BNII Nephelometer). Immunoglobuline deficiency was defined as two standard deviations less than mean value for that specified age. Patients with Ig deficiency had at least two levels of Ig measurement and the mean levels were recorded.

### STATISTICAL ANALYSIS

The patients demographic data, laboratory results and skin prick testing of all patients were extracted from patients’ medical records. The statistical datas were evaluated by using the SPSS (Statistical Package for Social Sciences) version 13.0 (Chicago, IL, USA) running under Windows XP. Descriptive data were displayed as mean, standard deviation, minimum, maximum, and percentage values.

### RESULTS

A total of 187 patients with allergic rhinitis were evaluated. The mean age was 30.57±9.6 years (range 15-56). One hundred twelve of them were female (59.8%) and 75 were male (40.1%). The mean duration of the disease was 48.36±42.09 months (Table 1). Results of SPT of the patients are given in Table 2.

The mean total IgE was 231.55 IU/ml (reference range: 0-100 IU/ml) and 118 patients (63.10%) had raised serum total IgE levels. The mean IgA level was 2.10 g/l (reference range: 0.7-4 g/l) and 5 patients (2.67%) had an IgA deficiency. The level of each IgG subclass was within the normal range among those patients with IgA deficiency. The mean IgM level was 1.21 g/l (reference range 0.4 to 2.3 g/l) and 4 patients had an IgM deficiency (2.13%). The mean IgG level was 12.16 g/l (reference range: 7-16 g/l) and all patients had normal IgG level (Table 3).

### TABLE 1: Demographic features of the patients.

<table>
<thead>
<tr>
<th>Number of patients (n = 187)</th>
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</thead>
<tbody>
<tr>
<td>Mean age (year)</td>
</tr>
<tr>
<td>Female / Male</td>
</tr>
<tr>
<td>Duration of the disease (months)</td>
</tr>
</tbody>
</table>

### TABLE 2: Results of skin prick test of the patients (n=187)

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Positive result n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollens III (Avena, Hordeum, Triticum, Secale)</td>
<td>124 (66.31)</td>
</tr>
<tr>
<td>Pollens IV (Dactylis, Festuca, Lolium, Phleum, Poa)</td>
<td>117 (62.56)</td>
</tr>
<tr>
<td>Mite (D. pteronyssinus)</td>
<td>51 (27.27)</td>
</tr>
<tr>
<td>Mite (D. farinae)</td>
<td>50 (26.73)</td>
</tr>
<tr>
<td>Olive (Olea europaea)</td>
<td>96 (19.25)</td>
</tr>
<tr>
<td>3 -Trees mix (Alnus, Betula, Corylus)</td>
<td>19 (10.16)</td>
</tr>
<tr>
<td>Cat dander</td>
<td>19 (10.16)</td>
</tr>
<tr>
<td>German cockroach</td>
<td>11 (5.88)</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>10 (5.34)</td>
</tr>
<tr>
<td>Dog dander</td>
<td>6 (3.20)</td>
</tr>
</tbody>
</table>
DISCUSSION

Allergic rhinitis is a serious disease with high prevalence and significantly impairs the quality of life. The relationship between some primary immune deficiencies and AR has been well established. Atopy is frequently detected in patients with antibody deficiency compared with normal population. We aim to investigate humoral deficiency by evaluating Ig levels in adult patients with AR. In our study, 5 of all patients had IgA deficiency and 4 of all patients had IgM deficiency while there was no patients with IgG deficiency.

IgA deficiency is the most common PID characterized by an isolated low level serum IgA while other immunoglobulin levels are normal. Serum IgA level of less than 7 mg/dl is defined as selective IgA deficiency. When serum IgA level is higher than 7 mg/dl but less than 2 standard deviations are defined as partial IgA deficiency. The partial IgA deficiency is quite common. In our study, 5 patients with IgA deficiency had results consistent with partial IgA deficiency.

The incidence of IgA deficiency varies between countries and is reported to be 1:163 in Spain, 1:252 in Nigeria, 1:875 in England, 1:965 in Brazil, 1:2.600-1:5.300 in China, and 1:223-1:1000 in the USA. In our study we found IgA deficiency in 2.67% of the allergic rhinitis patients.

While the disease is asymptomatic in 85-90% of the patients, some patients may experience recurrent sinopulmonary infections, gastrointestinal infections, allergic diseases, autoimmune diseases, and malignancy. There was no sign of recurrent infections, autoimmune disease or malignancy in our patients with IgA deficiency. Atopy was reported in 50% of pediatric patients with selective IgA deficiency. There is a wide spectrum of clinical findings such as airway inflammation (94%), asthma (84%), atopic dermatitis, allergic rhinitis, and conjunctivitis in IgA deficiency.

Although the prognosis of IgA deficiency is good, this disease may rarely advance into CVID. So, regular clinical and immunologic follow-up is recommended for patients with IgA deficiency.

Chronic rhinitis is common in patients with CVID. It may be allergic in patients with CVID due to their own or family history of atopy. Since the production of Ig is quite impaired in patients with CVID, it is difficult to make a diagnosis of IgE mediated allergic disease. The atopy may not be defined well. Total serum IgE and specific IgE levels of these patients may be low. Our study included patients with positive skin test. No patient were defined with IgG deficiency in our study.

Primary IgM deficiency is a rare PID disease. The frequency of the disease is unknown, although various rates have been reported such as 0.03%, 1.68% and 0.07%. Infections are common in pediatric population, while malignancies, allergic, autoimmune diseases are rare. Recurrent lower and upper respiratory tract infections are common in adult patients and allergic, autoimmune diseases are also frequent. Associations between malignancies and IgM deficiency have also been reported. In a study, 25% of selective IgM deficiency patients had allergic rhinitis/asthma. Asthma (47%) and allergic rhinitis (36%) were reported in patients with selective IgM deficiency. We evaluated IgM levels in patients with allergic rhinitis and IgM deficiency was found in 2.13% of the patients. Four patients with IgM deficiency in our study had results consistent with partial IgM deficiency. None of our patients had signs of autoimmune disease, malignancy, or infection. We considered low levels of IgM associated with allergic rhinitis.

In conclusion, association between AR and IgA or IgM deficiency in adult patients. Partial IgA and IgM deficiency accompanied with allergic rhinitis in our study. However, IgA deficiency may rarely advance into CVID. Regular clinical and immunologic follow-up is recommended for patients with IgA deficiency.
Conflict of Interest

Authors declared no conflict of interest or financial support.

Authorship Contributions

Idea/Concept: Constructing the hypothesis or idea of research and/or article: Songül Çildağ; Design: Planning methodology to reach the conclusions: Songül Çildağ, Taşkin Şentürk, Gökhan Sargın; Control/Supervision: Organizing, supervising the course of progress and taking the responsibility of the research/study: Songül Çildağ, Taşkin Şentürk, Gökhan Sargın; Data Collection and/or Processing: Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments: Songül Çildağ; Analysis and/or Interpretation: Taking responsibility in logical interpretation and conclusion of the results: Songül Çildağ, Taşkin Şentürk, Gökhan Sargın; Literature Review: Taking responsibility in necessary literature review for the study: Songül Çildağ; Writing the Article: Taking responsibility in the writing of the whole or important parts of the study: Songül Çildağ, Taşkin Şentürk, Gökhan Sargın; Critical Review: Reviewing the article before submission scientifically besides spelling and grammar: Songül Çildağ, Taşkin Şentürk, Gökhan Sargın; References and Fundings: Providing personnel, environment, financial support tools that are vital for the study: Songül Çildağ; Materials: Biological materials, taking responsibility of the referred patients: Songül Çildağ.

REFERENCES


