Egyptian Journal of Medical Microbiology Volume 30 / No.3 / July 2021 59-63 Online ISSN: 2537-0979

ORIGINAL ARTICLE

Correlation between serum IL-23 and serum total IgE levels in allergic rhinitis patients

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Key words:
Allergic rhinitis, serum IL-23, serum total IgE.

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ABSTRACT

Background: *Allergic rhinitis (AR) is an immunoglobulin E (IgE) mediated inflammatory chronic disorder of the nasal mucosa caused by contact to allergens which affects a significant percentage of population. Th17 cells might be involved in the acute phase of the allergic reaction. Th17 cells are regulated by IL-23, which is a member of the IL-12 cytokine family. IL-23 was suggested to be a pivotal cytokine involved in the pathogenesis of AR and may become a novel target in the treatment of AR.* ***Objective:*** *Here we investigate the role of serum IL-23 and its correlation with serum total IgE level in AR.* ***Methodology:*** *This case control study included the investigation of 48subjects. Blood samples were collected for measuring serum IL-23 and total IgE levels by ELISA.* ***Results****: positive correlation was found between IL-23 and total IgE serum level in AR patients.* ***Conclusion:*** *Positive correlation was found between serum IL-23 and serum total IgE levels in allergic rhinitis patients.*

INTRODUCTION

Allergic rhinitis (AR) is a worldwide health proplem that affects nearly 10–20% of whole population, therefore AR can be the most prevalent chronic non contagious disease [1]. In adults, the prevalence of AR varies from 10% to 30%, while in children it is nearly 40% [2]. When atopic individuals are exposed to allergen, they produce allergen specific (IgE). These IgE antibodies bind to IgE receptors on mast cells in the respiratory mucosa and to basophils in the peripheral blood. When the same allergen is then inhaled, the IgE antibodies became connected to the cell surface by allergen. This leads to release of chemical mediators, which produce the symptoms of allergic rhinitis [3,4]. Th17 cells might be involved in the process of neutrophil infiltration that occurs during the acute phase of the allergic reaction [5]. Th17 cells are regulated by IL-23, which is a member of the IL-12 cytokine family. IL-23 is a heterodimer comprising the p19 and p40 subunits, and is secreted by dendritic cells in response to immune danger, moreover, It may contribute to the differentiation of macrophages [6].

IL-23 is a newly discovered cytokine that resembles IL-12 structurally and functionally [7]. It is a composite cytokine composed of subunits IL-23p19 and p40 linked through a disulfide bond, its receptor complex is composed of IL-12RB1(which is also shared with IL-12) and IL-23R [8]. It is produced by various innate immune cells including DCs, macrophages, B cells and endothelial cells[9]. It is a proinflammatory cytokine, its action is dependent mainly on IL-12RB1, a type 1 transmembrane receptor that physically associates with the p40-domain and promotes its signaling [8]. It is involved in promoting Th17 differentiation and proliferation via stimulation of the naive CD4 T cells to differentiate into Th17 [10,11]. It plays a pivotal role in the pathogenesis of many autoimmune and inflammatory diseases [12]. IL-23 drives Th17, which produce IL-17 family cytokines IL-17A and IL-17F [13]. IL-17 producing T helper cells (Th17 cells) and regulatory T cell (Treg cells) provided new understanding of the molecular mechanisms convoluted with immunological disorders, predominantly Th17 cells, have been contributed to the pathogenesis of classically recognized Th2-mediated allergic disorders [14].

This study will investigate the correlation between serum IL-23 and serum total IgE levels in AR patients.

METHODOLOGY

Patients:

This case control study included 48 subjects (24 in case group and 24 in control group). The mean age in case group was 25.3±3.7 and 24.6± 3.1 in control group. They were enrolled from the Allergy and Immunology Unit, Medical Microbiology and Immunology Department, Faculty of Medicine, Zagazig University, Egypt. Inclusion criteria; included patient consent and adult patients more than 20 years with typical nasal symptoms and positive skin prick test. Exclusion criteria; included patient refusal, pediatric age group, malignancy, Patients diagnosed with AR associated with rhino sinusitis.

Diagnosis of allergy was verified by a history of exposure to allergens, family history for allergic

diseases and careful clinical examination for typical nasal symptoms which include congestion, watery rhinorrhea, nasal itching, sneezing and post-nasal drip.

Skin test:

Allergen extracts for skin test: Different Coca's extracted antigens were used from the Allergy and Immunology Unit, Medical Microbiology and Immunology Department, Faculty of Medicine, Zagazig University, these were: House dust mites, tobacco leaf, wool, cotton, mixed fungi, hay dust, date palm pollen, rye grass. The allergen was eluted for a time, and then the solid material was filtered out, leaving an aqueous solution. Saline as a negative control and histamine as positive control were used. Interpretation of the tests after 15 – 20 minutes of application, with a positive result defined as a wheal ≥3 mm diameter.

Skin prick test was performed on the volar aspect of the forearm. The skin was disinfected by 70% ethyl alcohol and left to dry before test. Forearm was coded with a marker pen corresponding to the allergens being tested along with the positive and negative controls. Marks were at least 2 cm apart. A drop of each allergen solution, negative and positive controls was placed beside each mark. A small prick through the drop was made to the skin using sterile prick lancet. After 15-20 minutes, the drops were wiped off and each wheal and flare were carefully outlined with a pen. With a positive reaction to an allergen, the skin became itchy within a few minutes and then became red and swollen with a wheal in the centre. A wheal of 3 mm or greater indicated the presence of specific IgE to the allergen tested [15,16] .

Serum total IgE concentration was measured by ELISA (ELISA KIT, IMMUNOSPEC, Canoga Park, CA, 91303).

Serum IL-23 concentration by (ELISA): was also measured by ELISA (ELISA KIT, INOVA No. 18, Keyuan Road, Daxing Industry Zone, Beijing, China).

Ethical Considerations:

A written informed consents were obtained from the study participants. Approval by IRB research committee of Zagazig Faculty of Medicine was also included.

Statistical analysis:

Data was analyzed by IBM SPSS Statistics 25 and was presented as means and range. Chi-square test was used to compare two groups regarding the distribution of different variables. Probability values (p) of <0.05 were considered significant.

RESULTS

Table 1: Skin test results of AR patients and control groups.

Skin test	Studied groups		χ 2	P value
	Case group	Control group		
Positive	24(100%)	1 (4.2%)	44.16	0.002
Negative	0 (0%)	23 (95.8)		

χ 2 : Chi square test.

There was a statistically significant difference between both groups regarding skin test results (p<0.001).

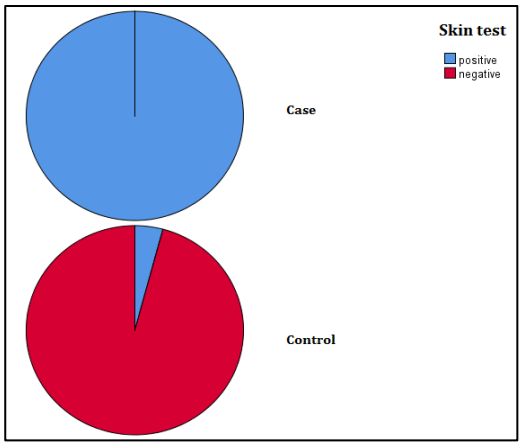

Fig. 1: A pie chart representing skin test results of AR patients and control groups

Table 2: Correlation between serum levels of IL-23 and total IgE in AR patients

Variable	Correlation coefficient®	P
IL-23 and total IgE in AR patients	**0.768****	**0.001**

(R): Pearson correlation

There was a positive correlation between total IgE and IL-23 serum level in AR patients (p= 0.001).

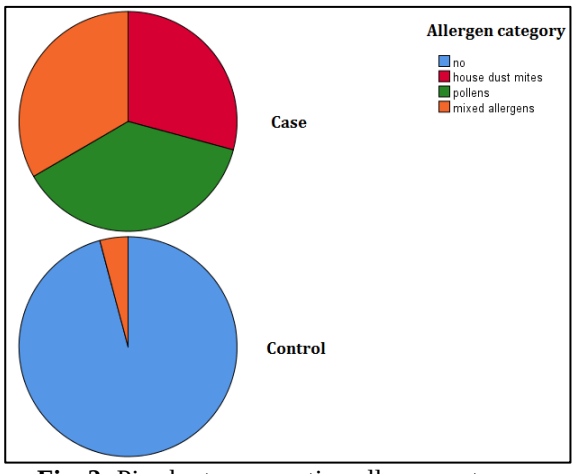

Fig. 2: Pie chart representing allergen category distribution among AR patients and control groups.

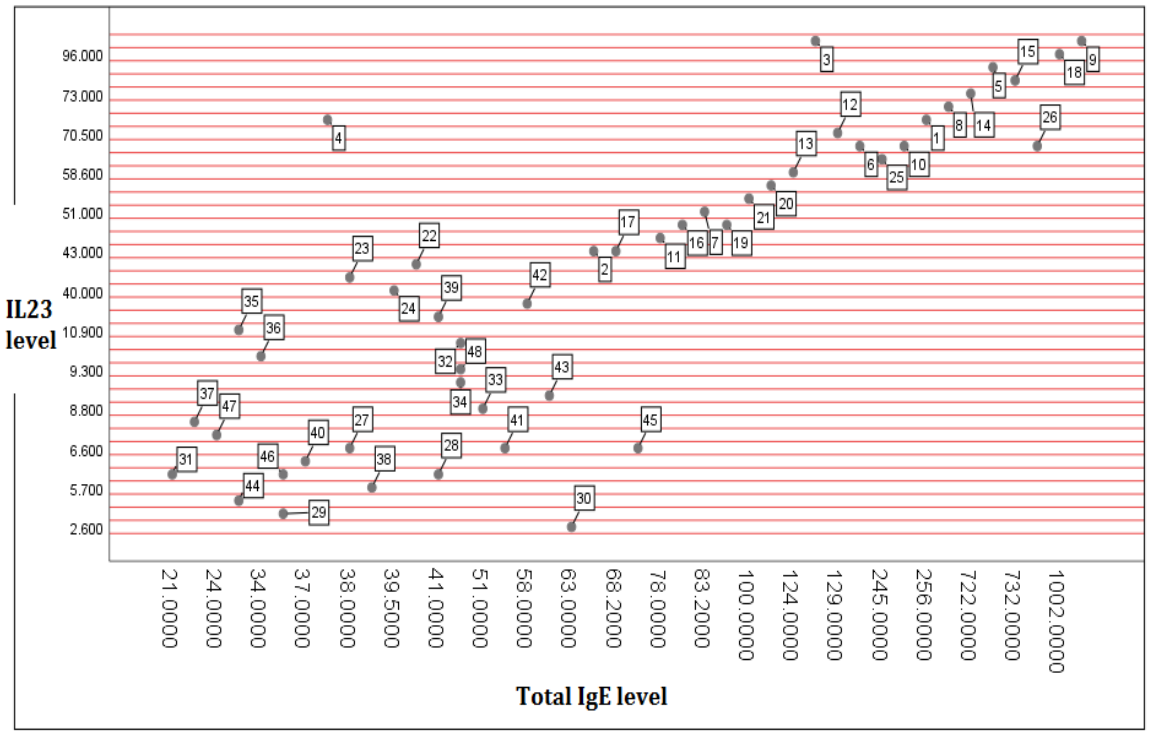

Fig. 3: Simple scatter graph representing correlation between total IgE and IL-23 levels in AR patients.

DISCUSSION

Allergic rhinitis (AR) is an atopic inflammatory disease resulting from allergen exposure in a sensitized individual, AR was defined as a process which includes 3 cardinal symptoms: (sneezing, nasal obstruction, and mucus discharge). It is a common condition that can result in substantial morbidities [17].

Atopy is defined as an inherited production of abnormal amounts of IgE in response to aeroallergens. It can be demonstrated by skin prick tests (SPT) or an increase in IgE measured as serum total IgE or specific IgE (atopic markers), however, SPT from all atopic markers has positive predictive value more than serum total IgE (which can be used for screening not the diagnosis of AR) and has the best efficacy to diagnose respiratory atopic diseases [18].

The usual normal reference range in adults and older teenagers for serum IgE is up to 100 IU/mL [19].

It is common for cases of allergic disease to have a raised circulating IgE level. Nonetheless, both a threshold for diagnosing allergic disease and a discriminator between particular disorders are lacking[20], hence it is not often possible to diagnose allergic disease on the basis of IgE level alone.

Stokes & Casale[21] reported that the utility of measuring total serum IgE or allergen specific IgE for purposes of diagnosis and management is variable. They also stated that levels of total IgE rarely provide information about IgE to specific allergens, and the existence of IgE to a specific allergen does not necessarily indicate a clinically meaningful allergic response to that substance. However, Omenaas et al [22] reported that if the total IgE level exceeded 66 IU/mL, the risk of possessing inhaled allergen-specific IgE immunoglobulins rises 37 times compared to when the level is at the bottom of the reference range.

IL-12 exerts its biological effects through binding to specific IL-12 receptors (IL-12Rs) termed IL-12Rβ1 and 12Rβ2; IL-12Rβ1 is also a component of the receptors for IL-23 [8].

IL-23 is a member of the IL-12 cytokine family and consists of IL-23 p19 and p40. Within the IL-12 family, IL-12 and IL-23 share the p40 cytokine subunit [9].

IL-12 and IL-12Rβ1/IL-23 pathway may play an important role in the pathogenesis of AR [23].

The study conducted by Wakashin et al [24] has shown that IL- 23 and Th17 cells enhance Th2 cell-mediated eosinophilic airway inflammation, suggesting that IL-23 and Th17 cells upregulate Th2 cell-mediated airway inflammation in two phases: IL-23 enhances antigen-induced activation of Th2 cells in the airways and antigen specific Th17 cells cooperate to enhance Th2 cell-mediated eosinophil recruitment into the airways. This could thus suggest that IL-23 may be implicated in Th2 cell differentiation and this machinery could be involved in part in the IL-23 mediated enhancement of allergic airway inflammation.

Moreover, **Leonardi et al** [25] reported increase in IL-23 levels among subjects with atopic diseases such as

asthma and rhinitis than children with only allergic sensitization.

In this study, there was a statistically significant positive correlation between IL-23 level (Pg/mL) and total IgE level (IU/mL) in AR patients (r = 0.768, p=0.001).

Huang **et al** [11] reported that serum level of specific IgE (sIgE) was positively relevant to the levels of IL-23, speculating that the IL-23 axis may promote the production of IgE and the chemotaxis of neutrophils resulting in AR, and IL-23 may facilitate the hypersensitivity response.

The sensitivities of sIgE were excellent for most of allergens tested. Serum specific IgE testing may be a respectable alternate to skin prick test if the latter could not be carried out [26].

Although some conflicting findings still need to be resolved, targeting Th17 cells and their related cytokines such as IL-23 may be an effective therapeutic approach for chronic inflammation and allergic air way diseases in the future [27].

CONCLUSION

Several biomarkers are found to be important in the pathogenesis of AR but correlation between these biomarkers hasn't been investigated. IL-23 is a pivotal cytokine in the pathogenesis of AR. and may become a novel target in the treatment of AR. As well as, serum total IgE levels are good indicators for AR. There was a positive correlation between serum levels of IL-23 and total IgE in AR patients.

- The authors declare that they have no financial or non financial conflicts of interest related to the work done in the manuscript.
- Each author listed in the manuscript had seen and approved the submission of this version of the manuscript and takes full responsibility for it.
- This article had not been published anywhere and is not currently under consideration by another journal or a publisher.

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