Original Article Open Access

Clinical Implications of Elevated IgE in Asthma Management among Patients

Received date: 15th August 2024
Review date: 19th September 2024
Accepted date: 6thOctober 2024

[1*]Halar Shaikh, *MBBS, FCPS*, [2]Nazeer Ahmed Memon, *MBBS, FCPS*,

[1]*Consultant, Dept. of Medicine, Jinnah Postgraduate Medical Center, Karachi*

[2] *Assistant Professor. Dept. of Medicine, Al-Tibri Medical College, Karachi*

***Corresponding Author:** Halar Shaikh (drhalarshaikh89@gmail.com)

Cite this article:
Shaikh H, Memon NA. Clinical Implications of Elevated IgE in Asthma Management Among Patients. AJMAHS. 2023; 2(3):34-39.

ABSTRACT

Background: Asthma is a complex, multifactorial disease with strong genetic predispositions and an especially high genetic relationship with high levels of Immunoglobulin E (IgE). The role of elevated IgE in the pathogenesis of asthma has been well clarified in that it plays a significant role in airway inflammation and hypersensitivity that contributes to more severe asthma and associated comorbidities such as eczema and allergic rhinitis.

Objective: This is a study whose primary purpose was to establish a correlation between highly elevated serum IgE levels and asthma severity in children, with the factor of exacerbations, hospitalizations, and concomitant atopic conditions in mind.

Methodology: A prospective study was done in 150 pediatric and adolescent patients aged 5-16 years, who presented with asthma exacerbations, in the period of January 2022 to December 2023. Total number of patients was divided into two groups: patients having raised IgE, and patients having normal IgE. Demography, clinical character, number of attacks, number of hospitalizations, and the treatment regimens were collected data. All of those were statistically analyzed by doing t-tests and chi-square tests.

Results: The mean number of asthma exacerbations was significantly higher, at 3.8±1.2, and hospitalization mean was 2.7±0.9 in the high IgE group, compared to the normal IgE group ($p=0.001$). The prevalence of atopic diseases, eczema and allergic rhinitis, were increased in the high IgE group ($p<0.05$). LABA with corticosteroids use increased in the high IgE group ($p<0.05$).

Conclusion: Increased levels of serum IgE have been associated with increased severity of asthma, exacerbations, and hospitalizations in children. A result here implies that patients with a raised IgE may benefit from more aggressive and tailored management strategy, especially anti-IgE therapy. Therefore, the long-term effects of IgE-targeted treatments have to be unraveled in this regard of asthma care.

KEYWORDS: Asthma, IgE, Allergy, Rhinitis, Clinical management.

INTRODUCTION

There is a high prevalence of asthma among the pediatric population of the world. Asthma etiology is multifactorial and complex, where genetic predisposition plays a significant role, along with environmental factors, in contributing to its underlying pathophysiology[1]. The most significant predisposing factor for the development of asthma is considered to be atopy, which is defined as a genetic predisposition to produce an immunoglobulin E (IgE)-mediated response to common environmental allergens [2]. IgE is one such subset of antibodies critically involved in the immune system[3]. It acts primarily for immunity protection and represents an important factor in type 1 hypersensitivity reactions[3,4]. Those reactions have classically defined what it means

to be an allergic response, but its role extends into airway inflammation and other more specific allergic diseases, including asthma, rhinitis, and food allergies. Despite that, though, the actual mechanisms that are operating to control IgE production and its relation in particular to asthma remain quite unclear.

Throughout all previous studies, increased IgE levels have been strongly associated with worsened asthma severity[3-7]. The same study by Siroux et al. also demonstrated a direct relationship between raised serum IgE and other severe states of the condition among children[8]. Furthermore, high IgE is also believed to have multiple direct relations with airway remodeling and hyper responsiveness[4,6]. Moreover, high IgE levels in early infancy by the age of six months are a very good prediction factor for latter asthma development[16]. Despite this, the level of serum IgE in asthma remains poorly understood within the pediatric and adolescent populations in some regions. There is an increased rate of asthma occurrence and higher mortality related to exacerbations of asthma among children[5]. Thus, there is a keen need for research on the mechanisms leading to exacerbation and resultant hospital admissions in asthma within the pediatric population. Indeed, a better understanding of IgE production and its significance in asthma will lead to new avenues for the development of targeted therapy, bringing about more personalized and effective treatment options for children with asthma.

Another clinical value of studying serum IgE levels in relation to asthma severity is that it could offer a broader insight into the disease. This is a multidimensional disease influenced by the contribution of both genetic, environmental, and immunological factors. This study aims to carry out an elaborate comparison of the clinical results in patients with raised IgE levels versus normal ones. In this study, we provide clear correlation between IgE levels and asthma severity by analyzing the relationship of high levels of IgE with exacerbations of asthma, hospitalizations, and markers of disease severity like pulmonary function, as well as quality-of-life measures.

MATERIALS AND METHODS

A prospective study was conducted at a tertiary care hospital between January 2022 and December 2023. Children and adolescents aged between 5 and 16 were admitted due to exacerbations of asthma. They received their first ever measurement of serum immunoglobulin E (IgE) as part of the hospital admission process. Patients were categorized into two based on their serum IgE levels. Those within the normal limits of IgE were grouped in the Normal IgE group, whereas patients having values above the defined upper limit were classified in the High IgE group. IgE levels were determined using Siemens Advia Centaur total IgE kit. All participants' demographics and clinical characteristics were recorded, including age at time of presentation, gender distribution, body mass index (BMI), age of onset, family history of asthma (including parents and siblings), other diseases, such as eczema, allergic rhinitis, and allergic conjunctivitis. The two groups were compared also based on the use of asthma control medication in the six months preceding their first exacerbation. It included use of inhaled corticosteroids administered through an inhaler or nebulizer, combined inhaled corticosteroids with LABA, and oral Montelukast therapy. A one-year follow-up of study participants was conducted in the number of exacerbations that required urgent care, mean LOS, and number of hospitalizations.

Patients who fell under the High IgE group had serology tests ordered to detect specific environmental and food allergens. The IgE class level, reflecting the magnitude of reactivity to specific allergen(s), was recorded. A value of Class II and above was considered clinically significant. Diagnosis for asthma followed the Global Initiative for Asthma (GINA) guidelines that include identification of typical respiratory symptoms such as wheezing, shortness of breath, chest tightness, and coughing in addition to evidence of fluctuating airflow limitation[20]. A bronchodilator response that followed an FEV1 increase of more than 12% after administration of salbutamol confirmed asthma[20]. Those patients diagnosed with conditions including bronchopneumonia, bronchiolitis, upper airway obstruction, chronic lung disease, cystic fibrosis, tuberculosis, congenital heart disease, or immune deficiency syndromes were excluded in the study. The ATS and ERS guidelines defined asthma exacerbation. They employed the definition of a course of two or more days over a

prolongation of a worsening of symptoms and/or lung function, or an increased reliance on rescue bronchodilators. Moderate exacerbation did not include ED visits and hospitalizations. Severe exacerbations included ED visits or hospitalizations and oral corticosteroids for at least three days[19].

The IBM SPSS, Version 24.0 was used in analyzing the data. The means with corresponding standard deviations have been used to denote continuous variables. Data considered to be categorical in nature have been presented as frequencies and percentages. Differences in means between groups have been analyzed using the t-test while analysis for categorical data has been performed using the Chi-square test. Any p-value ≤ 0.05 was construed to be statistically significant.

RESULTS

150 patients were enrolled in the study, with 72 (48%) in the category of having high IgE level and 78 (52%) in the category of having normal IgE level.
The patients in the high IgE category had a significantly higher prevalence of eczema and allergic rhinitis than the patients in the normal IgE category but the frequency of allergic conjunctivitis was not so amazingly different (p=0.06). Increased familial history of asthma was higher in the high IgE group (p <0.05). While the use of controller medication was not different between the two groups, the use of inhaled LABA in combination with inhaled steroids was significantly higher in the high IgE group (p <0.05). Clinical and demographic characteristics are listed in Table 1.

The mean number of asthma attacks requiring ER visits was markedly higher in the high IgE group at 3.8±1.2 than that of the normal IgE group at 2.6±1.1 (p=0.001). In addition, hospitalization was also significantly increased in the high IgE group at 2.7±0.9 compared with the normal IgE group at 1.9±0.8 (p=0.001). On the other hand, mean LOS did not show a difference between both groups with p-value being 0.85. Summary of findings is given in table 2.

Table 5: Clinical and Demographic Characteristics (n=150)

Parameter	High IgE Group (n=72)	Normal IgE Group (n=78)	p-value
Age (in years)	11.7±0.6	10.9±0.9	0.07
Male: Female Ratio	1.3:1	1.4:1	0.12
BMI (kg/m^2)	14.5±0.8	13.4±1.0	0.15
Age at asthma onset (in years)	3.7±0.8	6.1±0.9	0.06
Eczema	22 (30.5%)	12 (15.4%)	.<0.001
Allergic Rhinitis	61 (84.7%	36 (46.2%)	<0.001
Allergic Conjunctivitis	12 (16.7%)	8 (10.3%)	0.06
Family History of Asthma,	45 (62.5%)	28 (35.9%)	<0.001
Inhaled Steroid Use	34 (47.2%)	29 (37.2%)	0.28
Inhaled LABA with Steroid Use	32 (44%)	23 (29.5%)	<0.001
Montelukast Use	68 (94.4%)	62 (79.5%)	0.38

Parameter	High IgE Group (n=72)	Normal IgE Group (n=78)	p-value
ER Admission for Asthma Exacerbations	3.8±1.2	2.6±1.1	0.001

Number of hospitalization (mean)	2.7±0.9	1.9±0.8	0.001
Length of Stay (mean days)	3.3±1.1	3.2±1.3	0.85

DISCUSSION

Our findings present a strongly significant association of higher sera IgE in the asthma-afflicted children with higher rates of exacerbations and hospitalizations. At 3.8±1.2, the high IgE group showed a significantly increased rate of exacerbations that is larger than the normal IgE group, which was at 2.6±1.1, (p=0.001). In addition, annual hospitalizations were also found to be increased in the high IgE group with 2.7±0.9 compared to the normal IgE group with 1.9±0.8, p = 0.001. Common comorbidities in the pediatric population include atopic conditions: asthma, allergic rhinitis, food allergies, and eczema. Being diagnosed with one has been known to increase the chance for another so that many describe the "atopic march"[15]. Our study demonstrated significantly higher prevalence in the high IgE group for eczema and allergic rhinitis, consistent with previous studies. For example, Havnen et al. found that 47% of asthmatic children had elevated IgE levels, the incidence of which was found to increase to 58% when other hypersensitivity conditions, such as atopic dermatitis, were present[10,11].

Interestingly, we found a significant correlation between the elevated IgE level and a family history of asthma (p<0.05). That is at variance with some previous reports that did not make mention of any such association of high IgE levels with the family history of asthma or allergic diseases [12,13]. Though our study did not reveal a clinically relevant difference in the two groups concerning the incidence of allergic conjunctivitis. We also saw a very high relationship between IgE elevation and food and environmental allergies. Percentages of the high IgE group who tested positive to the environment allergen were 73.7%, and to the food allergen were 29.3%. These are in agreement with other related studies, such as Foong et al, who published a study wherein the risk of exacerbating an asthma attack is significantly higher in patients affected by IgE-mediated allergies[17]. The most common allergens were dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae) affecting 82.5% and 78.3% of patients, respectively, which puts much importance on dust mites when one is in the control measures concerning asthma.

We also noted an important difference in the use of inhaled LABA with corticosteroids; this was more common in the high IgE group than in the rest (p<0.05). It thus seems that a higher level of IgE is associated with a more severe form of asthma and, hence, a more aggressive treatment approach[15,18]. These observations highlight a need for more aggressive treatment in patients with high IgE, including LABA and inhaled steroids. Our study findings show that anti-IgE therapy could provide an alternative good form of treatment in the management of asthma. IgE represents a very critical mediator in the hypersensitivity response leading to inflammation and airway remodeling in asthma. In this connection, Omalizumab among other anti-IgE therapies has been shown to successfully reduce the use of corticosteroids and lower the rate of asthma exacerbations, while quality of life among patients suffering allergic asthma improves[14,15]. Further studies are required to assess the benefits of such interventions in patients with high IgE levels. Our study further underscores the utility of serum IgE levels for the purposes of diagnosis and prognosis in distinguishing between allergic and non-allergic asthma, and for the prognosis of risks of exacerbations[19]. Early detection of increased IgE levels may make it possible for health care providers to institute more specific, individualized management strategies that will result in better outcomes for asthma patients in the long run. The incidence of deaths from asthma is increasing, so further studies on the relationship between increased IgE levels and more severe asthma attacks merit consideration.

Non-asthmatic control group for comparing the levels of IgE cannot be done; therefore long term follow up to determine the outcome of patients in the long run cannot be determined. The serum IgE levels also could not be ascertained for seasonal variations if any. In regard to this, there should be a consideration of prospective design along with lung function estimation between

patients with high IgE compared to normal IgE levels to derive its relation with lung function.

CONCLUSION

This study represents the best evidence yet that increased IgE levels are associated with a higher rate of asthma exacerbations and hospitalization in children, suggesting that asthma-related high IgE necessitates tailored management strategies. The study suggests the crucial need to consider anti-IgE therapy as an option for these patients. Given the pivotal role of IgE in asthma pathophysiology, it will be highly worthwhile to determine whether anti-IgE could diminish exacerbations and hospitalizations while also improving the overall management of the disease and the quality of life in patients. However, a careful consideration of broader perspectives is required for anti-IgE therapy. Its utility regarding the resolution of acute symptoms is promising, but its impact on long-term disease progression as well as the preservation of health of the immune system needs careful consideration. Further research in such areas should explore the ways through which IgE-targeted treatments could be integrated into asthma treatment plans further to personalize asthma care. This would actually encompass a better approach to symptom relief and attenuation at the immune process level that defines a larger portion of the severity in asthma. Studies of the activity of this anti-IgE therapy in different populations, age groups, as well as in genetic and environmental conditions will provide valuable information regarding its broader application in various patient populations.

REFERENCES

1. Dharmage SC, Perret JL, Custovic A. Epidemiology of Asthma in Children and Adults. Front Pediatr. 2019;7:246.

2. Asthma NAE and PP Third Expert Panel on the Diagnosis and Management of. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung, and Blood Institute (US); 2007.

3. Naqvi M, Choudhry S, Tsai HJ, Thyne S, Navarro D, Nazario S *et al.* Association between IgE levels and asthma severity among African American, Mexican, and Puerto Rican patients with asthma. J Allergy Clin Immunol. 2007;120(1):137–43.

4. Samitas K, Delimpoura V, Zervas E, Gaga M. Anti-IgE treatment, airway inflammation and remodeling in severe allergic asthma: current knowledge and future perspectives. Eur Respir Rev. 2015;24(138):594–601.

5. Serebrisky D, Wiznia A. Pediatric Asthma: A Global Epidemic. Ann Glob Health. 2019;85(1):6.2

6. Sunyer J, Antó JM, Sabrià J, Roca J, Morell F, Rodríguez-Roisin R *et al*. Relationship between serum IgE and airway responsiveness in adults with asthma. J Allergy Clin Immunol. 1995;95(3):699–706.

7Borish L, Chipps B, Deniz Y, Gujrathi S, Zheng B, Dolan CM. Total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma. Ann Allergy Asthma Immunol 2005;95(3):247–53

8. . Siroux V, Oryszczyn MP, Paty E, Kauffmann F, Pison C, Vervloet D *et al*. Relationships of allergic sensitization, total immunoglobulin E and blood eosinophils to asthma severity in children of the EGEA Study. Clin Exp Allergy. 2003;33(6):746– 51.

9. Unal D, Gelincik A, Elitok A, Demir S, Olgac M, Coskun R *et al*. Impact of high serum Immunoglobulin E levels on the risk of atherosclerosis in humans. Asia Pac Allergy 2017;7(2):74–81.

10. Havnen J, Amlie PA, Hvatum M, Oseid S, Veggan T, Aas K. IgE concentrations in allergic asthma in children. Arch Dis Child. 1973;48(11):850–5.

11. Ng C, Hon KL, Kung JS, Pong NH, Leung TF, Wong CK. Hyper IgE in Childhood Eczema and Risk of Asthma in Chinese Children. Molecules. 2016;21(6):753.

12. Lama M, Chatterjee M, Chaudhuri TK. Total serum immunoglobulin e in children with asthma. Indian J Clin Biochem. 2013;28(2):197–200.

13. Satwani H, Rehman A, Ashraf S, Hassan A. Is serum total IgE levels a good predictor of allergies in children? J Pak Med Assoc. 2009;59(10):698–702.

14. D'Amato G, Liccardi G, Noschese P, Salzillo A, D'Amato M, Cazzola M. Anti-IgE monoclonal antibody (omalizumab) in the treatment of atopic asthma and allergic respiratory diseases. Curr Drug Targets Inflamm Allergy. 2004;3(3):227–9.

15. Milgrom H, Berger W, Nayak A, Gupta N, Pollard S, McAlary M ***et al***. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). Pediatrics. 2001;108(2):E36.

16. Mrazek DA, Klinnert M, Mrazek PJ, Brower A, McCormick D, Rubin B ***et al***. Prediction of early-onset asthma in genetically at risk children. Pediatr Pulmonol. 1999;27(2):85–94.

17. Foong RX, du Toit G, Fox AT. Asthma, Food Allergy, and How They Relate to Each Other. Front Pediatr. 2017;5:89.

18. Chabra R, Gupta M. Allergic and Environmentally Induced Asthma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Aug 16]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK526018/

19. Forno E, Celedón JC. Predicting asthma exacerbations in children. Curr Opin Pulm Med. 2012;18(1):63–9.