Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Suppl 3, 2012

Research Article

# CD23, TOTAL IGE AND TH1/TH2 CYTOKINES IN ASTHMA PATIENTS

**[1]VIJAYENDRA CHARY A, HEMALATHA R, NARENDRA BABU K, RAMESH KUMAR R, [2]SATHAVAHANA CHOWDARY, [3]DINESH KUMAR B.**

**Microbiology and Immunology Division, National Institute of Nutrition (NIN), Jamai Osmania, Hyderabad 500604, India, [2]FDTRC, National Institute of Nutrition (NIN), Jamai-Osmania, Hyderabad 500604, India, [3]Apollo Hospital, Hyderabad, India. Email: rhemalathanin@yahoo.com**

*Received: 15 Dec 2011, Revised and Accepted: 16 Feb 2012*

**ABSTRACT**

CD23 (FcεRII), is a low affinity receptor for IgE, likely to influence IgE production and inflammation in allergic diseases like asthma, rhinitis and food allergy. Serum CD23, total histamine release, total IgE and Th1,Th2 cytokines were determined in blood samples of patients with asthma(50) and age and sex matched controls (n =20). Serum sCD23 was significantly increased ($p<0.05$) in asthma (581.16 pg/mL), when compared to controls (429.49pg/mL). Similarly serum mean±SE of IgE (154.03 ± 33.24) and blood histamine (46.7 ± 7.23) levels were increased significantly ($P<0.01$) in patients with asthma; while IFN-γ, a Th1 cytokine, was significantly lower ($P<0.05$) in asthma (3.28 ± 0.65) than in controls(9.45 ± 1.58). Serum IL-4 and CD23 either were below detectable levels in buccal mucosa or stool samples. Our observations provide evidence on CD23 expression in asthma and a preferential activation of Th2 (IL-5) and suppression of Th1 (IFN- γ) response in adults with asthma.

**Keywords:** CD23, Allergy, Cytokines, IgE, Histamine, Asthma,

## INTRODUCTION

Asthma is a chronic inflammatory disorder of the airway in which many cells play a role, in particular mast cells, eosinophils, and activated T lymphocytes. The inflammation also causes an associated increase in airway responsiveness to a variety of stimuli. Asthma can occur at any age but recurrent episodes of wheezing and airway obstruction manifest before the age of 6 years in most patients [1]. The prevalence of allergic diseases has increased consistantly over past 10 years.

IgE levels are recognised as a risk factor for a variety of respiratory symptoms (2), from both clinical and expermental evidence(3,4). Asthma viewed as an inflammatory airway disease involving lymphocyte activation and releasing of proinflammatory cytokines.The low-affinity IgE receptor Fc eRII (CD23) expressed on B cells and T cells, Langerhans cells, macrophages, monocytes, eosinophils, and platelets(5,6). The expression of CD23 is upregulated by IgE and IL-4(7,8). CD23 plays a central role in the allergic reaction that is responsible for the rapid transepithelial transport of IgE/allergen complexes and subsequent delivery of intact Ags to mast cells in the subepithelial compartment (9, 10). CD23 can be shed from the membrane into a soluble form (sCD23) by endogenous proteases and exogenous proteases, CD23 activation mediates IgE regulation and stabilisation of cell-surface CD23 is known to decrease IgE synthesis[11], differentiation of B cells, activation of monocytes, and antigen presentation[12]. Increased expression of membrane-bound CD23 on B cells and resultant increase in soluble CD23 is seen in patients with allergic disorders. Asthma is associated with a predominant Th2 immune response[13,14,15], CD4+ T cells produce Th2 cytokines, including IL-4, IL-5, IL-9 and IL-13 which up regulate IgE production, play a pivotal role in the pathogenesis of the disease [16]. IL-4 which is a primary product of Th2 cells is a most potent up-regulator of CD23 antigen.

Since CD23 and other allergic mediators plays a crucial role in allergic diseases, we investigated the expression of CD23, total IgE, Th1/Th2 cytokines and histamine levels in asthma patients.

## MATERIALS AND METHODS

### Subjects and controls

Adults visiting the Allergy clinic, Hyderabad, suffering from Asthma, (total no. of patients 50) were recruited and age (18-35yrs) & sex matched adults (n=20) were taken as controls. Blood samples were obtained from all of the above patients after standard questionnaire to estimate the serum CD23, histamine release, total IgE and Th1, Th2 cytokines. CD23 was also determined from buccal mucosa and stool samples. Informed consent was obtained from the patients and control subjects. Ethical approval was taken from the hospital management for collection of the samples and to carry out the project.

### Estimation of cytokines, CD23, total IgE and Histamine levels

The cytokines such as IL-4, IL-5 and IFN-γ in the serum were measured on fluorescent-coded beads known as microspheres, which are then read in a compact analyzer (Luminex xMAP technology, Milliplex, Millipore). The sCD23 estimation in the serum was measured by Immunoassay kit (Quantikine Human CD23/ Fc€RII) which employs the quantitative sandwich enzyme immunoassay technique. Histamine release test was performed according to Immunotech EIA histamine kit instructions. Serum IgE levels were estimated by a solid phase ELISA (UBI MAGIWEL Total IgE Quantitative ELISA kit) based on the sandwich technique. Biotek multimode (micro well) detector system was used to estimate the concentration of IgE at 450nm.

### Statistical analysis

The data analysis was performed by using SPSS windows version (15.0), The ANOVA was used to assess the difference between groups of different parameters, else Kruskal-Wallis one way ANOVA was done to see the difference between groups. Results were presented as mean± Standard error of the mean (SEM). Pearson's correlation coefficient was done to see relation between the parameters.

## RESULTS

**Controls:** The serum IgE was within normal range and ranged from 75.83 to 229.22 IU/mL and with a mean of 154.03 IU/mL. The mean histamine and CD23 were 46.7 (nM/mL) and 429.49 (pg/mL) respectively in the controls. IFN-γ and IL-5 were detectable in all adults, whereas IL-4 was below detectable range in all the adults studied. The mean IL-5 and IFN-γ were 1.1 (pg/mL) and 3.28 (pg/mL) respectively (Table 1 & Figure1).

**Asthma:** the serum IgE in asthma range from 240.49 to 419.90 IU/mL and mean was 330.2 IU/mL which was significantly ($p<0.01$) higher when compared to controls.serum CD23 and histamine levels were 429.49 **(**pg/mL**)** and 46.7 (nM/mL) respectively in adults with asthma. Both Total IgE and total histamine were significantly($p<0.01$) higher when compared to controls. IFN-γ and IL-5 were significantly higher in bronchial asthma. Pearson's correlation coefficient showed a significant ($P<0.05$, $r=0.50$) association between IL-5 and total serum IgE concentration, however, IFN- γ or CD23 were not correlated with IgE(Table 1 & Figure1).

**Table 1: Total IgE, Serum CD23, Total Histamine & Cytokine profile in adults with asthma and control subjects**

| Parameters | Control (Mean±SE) | Asthma (Mean±SE) |
|---|---|---|
| Total IgE (IU/mL) | 154.03 ± 33.24 (78.83, 229.22) | 330.2 ± 43.01** (240.49, 419.9) |
| Total Histamine (nM/mL) | 46.7 ± 7.23 (29.02, 64.38) | 68.22 ± 3.61** (60.37, 76.08) |
| S.CD23 (pg/mL) | 429.49 ± 31.29 (352.92, 506.06) | 581.16 ± 35.72* (506.4, 655.93) |
| Cytokines IL5 (pg/mL) | 1.1 ± 0.26 (0.38, 1.82) | 4.08 ± 0.25* (1.55, 2.62) |
| Cytokines IFNγ (pg/mL) | 9.45 ± 1.58 (5.93, 12.97) | 3.28 ± 0.65* (1.2, 5.36) |

** p< 0.01 Significantly different from control; * p<0.05 Significantly different from control

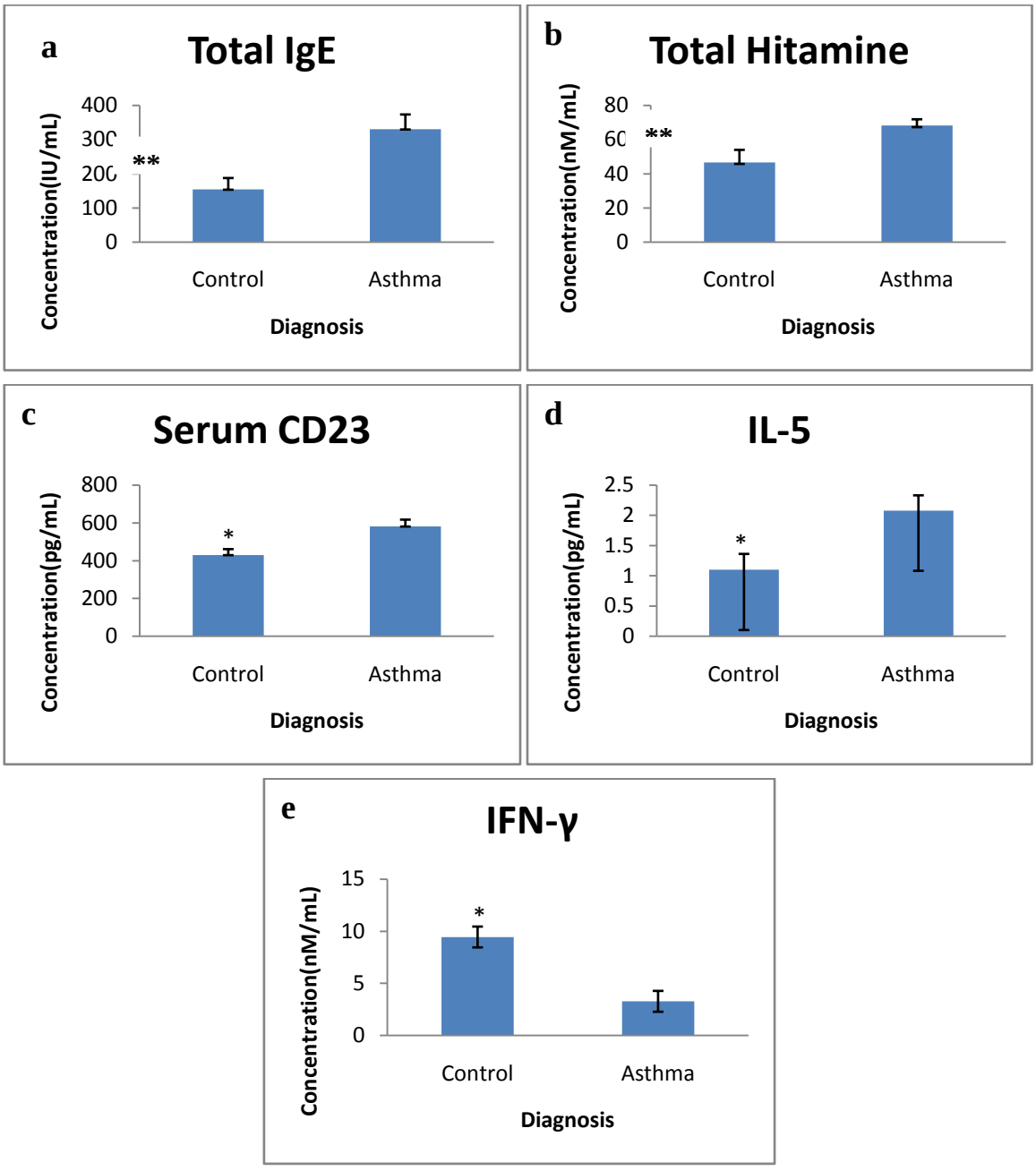


**Fig. 1: Levels of total IgE, blood histamine, serum CD23, Cytokines (IL-5 & IFN-γ)**

a) ** P < 0.01 significantly different from asthma; B) ** P < 0.01 significantly different from asthma; C) * P <0.05 Significantly different from asthma; D) ** P <0.05 Significantly different from asthma and E) ** P < 0.05 significantly different from asthma.

**DISCUSSION**

Allergic diseases are complex disorders in which inflammatory and immunological mechanisms are involved [17]. The activity of IgE is associated with a network of proteins; prominent among these are its two principal receptors, FcεRI (high-affinity Fc receptor for IgE) and CD23 or FcεRII [18,16]. Elevated levels of CD23 expression has been observed in humans with asthma, non allergic asthma and rhinitis [17]. We found enhanced response of serum CD23 in bronchial asthma than in controls (Fig. 1c), where as CD23 was not secreted in stool or expressed on buccal mucosal cells. Though CD23 has been suggested as a marker to identify allergic condition.

It was earlier anticipated that reduced microbial exposure in early life is responsible for a shift of the Th1/Th2 balance in the immune system towards the pro-allergenic Th2 response, This Th1/Th2 imbalance results in the clinical expression of allergy and/or asthma. Studies on mice and humans have shown Th2 cytokines [IL-4, IL-13, and IL-5] as major contributors to allergy and asthma [18]. In our study serum IL-4 was below detectable level in all the subjects, nevertheless IL-5 was associated with bronchial asthma (Fig. 1d).

We found a strong association of IL-5 with serum IgE in Bronchial Asthma. However, In normal adults IFN-γ appears to down regulate the production of IL-5 and IgE but in bronchial asthma IL-5 contributes to increased IgE production.

From a number of studies it seems that IFN-γ might be one of the appropriate candidate marker of the prediction of bronchial asthma and allergy. Production of IFN-γ has been used as potential for the post natal immune maturation processes that are associated with the subsequent risk for the development of bronchial asthma or allergic diseases [19]. Previous studies have found lower IFN-γ production in bronchiolitis to be linked with abnormal pulmonary function and development of asthma at later life [20,21,22].

The plasma histamine levels of acute asthmatics are raised when compared with normal subjects, by contrast, whole blood levels are unchanged and urinary levels are slightly, but not significantly reduced [23]. But in our study whole blood histamine levels were raised in adults with asthma when compared to controls. Histamine affects the maturation of dendritic cells and specifically regulates the development of Th1 and Th2 T cells [24,25,26]. CD23 had been shown to be increased in infants aged 7 to 12 months but not in older age groups, in contrast, we found up regulation of CD23 in older age group.

**CONCLUSION**

Our observations provide evidence on CD23 expression in adults with and without asthma and a preferential activation of Th2 (IL-5) and suppression of Th1 (IFN- $\gamma$ ) in adults with asthma. Absence of CD23 in stool samples suggests lack of food sensitivity in the study subjects.

**ACKNOWLEDGEMEN**

The authors are indebted to those who were helped during this study. We would like to thank CSIR-HRDG and National Institute of Nutrition(ICMR) for financial support and carry out this work.

**REFERENCES**

1. Gern JE, Robert F, Lemanske Jr and William W Busse. Early life origins of asthma. The journal of clinical investigation 1999; 104:837-843.
2. Dolovich J, Zimmerman B, Hargreave FE. Allergy in asthma. In: Clark TJH, Godfrey S, eels. Asthma, 2nd ed. London: Chapman & Hall, 1983; 132- 159.
3. Monteseirin J, Guardia P, Delgrado J, et aL Peripheral blood T lymphocytes in season bronchial asthma. Allergy 1993; 50." 152-156.
4. Vidhcow JC, Olehling A, Boer L, et al. Pulmonary function, activated T cells, peripheral blood eosinophilia, and serum activity for eosinophil survival in vitro. A longitudinal study in bronchial asthma. J Allergy Clin Immuno11994; 94: 240-249.
5. Conrad D.H. FcεRII/CD23: the low affinity receptor for IgE. Annu. Rev. Immunol 1990; 8:623–645.
6. Jagadeeshwar K, Sangram, Venumadhav et al. a study on serum ige levels, peripheral eosinophils and individual symptoms in patients with non-infective rhinitis and asthma and related conditions. Int J Pharm Pharm Sci 2012; 4(1): 88-92.
7. Lorenzo G. Di. Serum levels of total IgE and soluble CD23 in bronchial asthma. Mediators Inflamm 1996; 5(1): 43–46.
8. Corrigan CJ, Kay AB CD4 lymphocyte activation in acute severe asthma. Relationship to disease severity and atopic status. Am Rev Respir Dis 1990;141: 970-977.
9. Yu, L. C., G. Montagnac, P. C. Yang, D. H. Conrad, A. Benmerah, and M. H. Perdue. Intestinal epithelial CD23 mediates enhanced antigen transport in allergy: evidence for novel splice forms. Am. J. Physiol 2003; 285:223.
10. Bevilacqua, C., G. Montagnac, A. Benmerah, C. Candalh, N. Cerf-Bensussan, M. H. Perdue, and M. Heyman. Food allergens are protected from degradation during CD23-mediated transepithelial transport. Int. Arch. Allergy Immunol. 2004;135:108.
11. Delespesse, G. et al. IgE receptors on human lymphocytes. Detection of cells bearing IgE receptors in unstimulated mononuclear cells by means of a monoclonal antibody. Eur. J. Immunol 1986;16: 1043-1047.
12. Tsicopoulos A, Joseph M. The role of CD23 in allergic disease clin Exp Allergy 2000;30:602-605.
13. Di Lorenzo G, Mansueto P, Melluso M, et al. Serum levels of soluble IL-2R, CD4 and CD8 in bronchial asthma. Mediators of Inflamm 1995; 4: 270-272.
14. Ishizaka K, Ishizaka T, Hornbrook MM Physico-chemical properties of human reaginic antibody IV. Presence of a unique immunoglobulin as a carrier of reaginic activity. J Immunol 1966;97:75-85.
15. Monteseirin J, et al Peripheral blood T lymphocytes in season bronchial asthma. Aller 1993;50: 152-156.
16. Omenaas E, Bakke P, Elsayed S, Hanoa R, Gulsvik A Total and specific serum IgE levels in adults: relationship to sex, age and environmental factors. Clin Exp Allergy 1994;24:530-539.
17. Sergio Romagnani , Lymphokine Production by Human T Cells in Disease States, Annual Review of Immunology 1994;12: 227-257.
18. Gould, H. J. et alThe biology of IgE and the basis of allergic disease. Annu. Rev. Immunol 2003;21:579–628.
19. Sheng-Chin Liao IL-19 Induced Th2 Cytokines and Was Up-Regulated in Asthma Patients. The J Immunol 2004;173: 6712-6718.
20. Hugo PS Van Bever Determinants in early life for asthma development Allergy. Asthma & Clinical Immunology 2009;5:6.
21. Caron, G et al Histamine polarizes human dendritic cells into Th2 cell-promoting effector dendritic cells. J.Immunol 2001;167: 3682–3686.
22. Jutel M, Blaser K, Akdis CA The role of histamine in regulation of immune responses. Chem Immunol Allergy 2006;91:174-87.
23. Hannah J. Gould and Brian J. Sutton IgE in aller and Asth tod nat rev 2008; 8: 205-215
24. Sánchez-Guerrero et al Soluble CD23 (sCD23) serum levels and lymphocyte subpopulations in peripheral blood in rhinitis and extrinsic and intrinsic asthma. Clin Exp Allergy 1994;49(8): 87–592.
25. Soniya Scaria, Emmanuel James, Dharmaratnam A.D. Epidemiology and treatment pattern of atopic dermatitis in patients attending a tertiary care teaching hospital. Int. J. Res. Pharm. Sci 2011; 2(1):38-44.
26. LY.P Ngoc et al Cytokines, allergy, and asthma. Curr Opin Allergy Clin immunol 2005;5:161–166.