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Evaluation of Serum Immunoglobulins in Patients of Bronchial Asthma

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Abstract

The swelling and narrowing of airway which results in excessive production of mucus, cause cough, breathlessness and wheezing is called asthma. Around 5-10 % population worldwide is affected by this chronic airway disorder and become a global health problem. A complex immunological hypersensitive Ig E mediated reaction cause allergic asthma. This work is carried out with the objective to enumerate and quantify the level of Ig E in different age group and classify them into different type of asthma. Blood samples of 150 normal person and 350 asthmatic patients consisting both male and female were used in this study. The levels Ig E were estimated by ELISA kit. The level of serum Ig E is very high in comparison to other immunoglobulins and showed 2100 % increase in asthmatic patients when compared with the normal persons. There is no significant variation in serum Ig E among the different age groups. A positive correlation is found between severity of asthma and level of Ig E.

Keywords: Asthma, Immunoglobulin E, ELISA, Allergy.

Introduction

Asthma is one of the most common major non-communicable diseases. Globally, 300 million people are suffering from asthma worldwide, and it is estimated that by 2025 a further 100 million may be affected (The Global Asthma Report, 2018).The various published reports suggests that asthma is a complex heterogeneous disorder and its aetiology is attributed to the interactions between genetic susceptibility (loci on genes), host factors (obesity, nutritional factors, infections, allergic sensitization), and environmental exposures (air pollution, pollens, mold and other aeroallergens, and weather) (Pavord *et al.,* 2018).

Asthma is a clinical syndrome characterized by recurrent episode of airway obstruction. The syndrome is characterized by wheezing, tightness of chest, cough, results from bronchio-constriction, secretion of mucus, and edema, that narrow the opening of the airways (Gong, 1990). Exposure of allergen activates numerous cells of the immune system; out of them dendritic cells and T helper type 2 lymphocytes are of prime importance (Buc *et al.,* 2009). Differentiation of B cells into Ig E secreting plasma cells is a complex cascade of events in which cytokines (IL-4 and IL-13 and CCR3 and CXCR4 receptors) play a crucial role (Yssel *et al.,* 1998).

The activation of Th_2 and B lymphocytes underlies the process of sensitization to allergens in genetically predisposed individuals. Antigens processed by antigen-presenting cells (APCs) can be recognized by Th_2 cells. Interleukins released by activated Th_2 cells (e.g., IL-4 and IL-13) enhance production of IgE antibodies. These antibodies, in turn, become attached to other resident cells that possess specific receptors for IgE. A small domain (within Fcε3) of the IgE "constant"region binds to high-affinity (FcεRI) surface receptors on Mast cells or basophils or to low-affinity receptors (FcεRII, also known as CD23) on B lymphocytes and eosinophils (Presta *et al.,* 1994). Chronic inflammation eventually produces airway hyperresponsiveness. Specific Tcells also generate a memory response, which may contribute to the exacerbation of asthma symptoms on reexposure to certain stimuli (Busse *et al.,* 1995; Fahy *et al.,* 2000; Pearlman, 1994).

Rackemann, (1918) classified asthma into two major categories: extrinsic (allergic asthma, atopic asthma) and intrinsic (nonallergic asthma, idiosyncratic asthma) according to causative factors (McFadden, 2004), and which is not finding their place in both the categories is unclassified asthma. Based on the frequency and periodicity of the attack asthma also

classified into two categories of episodic and perennial (Wallace *et al.,* 2008). The family history of the disease is often related with the patients with asthma and usually found higher level of serum Ig E (Mitsunobu *et al.,* 2000). Total serum IgE was found significantly associated with the age, exposure to cigarette smoke, and raised eosinophil count in asthmatic patients (Lama *et al.,* 2009). The present study was undertaken to estimate and comparethe levels of serum immunoglobulins A, G, M, and E in control and asthmatics patients of different age group and sex and describing the relationship between serum IgE levels and severity of asthma.

Methodology

The present study was carried out in the Biochemistry Department, Lala Lajpat Rai Medical (L.L.R.M.) College, Meerut. One hundred fifty (150) non allergic person comprised of the control group while 350 cases of bronchial asthma (diagnosed on the basis of American Thoracic Society, 1962) attending the allergy clinic and admitted in the medical ward of the Sardar Vallabh Bhai Patel Hospital, Meerut were taken as the study group. Asthma was classified as extrinsic, intrinsic and unclassified following the classification of Rackemann, (1918)

Blood was drawn by the venipuncture method from a vein located on the inside of the elbow and collected in heparinised test tube. A portion of this blood was centrifuged and serum obtained was used for the estimation of the serum immunoglobulins by Enzyme Linked Immunosorbent Assay (ELISA) techniquekits (Roth *et al.,* 2015). The remaining portion was used for the absolute lymphocyte count by using a Sysmex K21 Haematologyanalyzer (Sysmex Corporation, Japan). Completely randomized design (CRD) was used for this experiment.

Result and Discussion

A total number of 150 normal and 350 asthmatic study population was studied during this study. The study population comprised of different age groups as shown in fig.1 among different age groups, highest number of patient were from 21 to 30 year age followed by 31-40 year. All the asthmatics patient were showing the symptoms of wheezing (100%), sneezing (48%), cough (35.14%), rhinitis (40%), uriticaria (14%) and eczema (6%). Thirty six percent male and 20% females were having extrinsic asthma, male and female (14.29%) both were equally suffered from intrinsic asthma and 5.14% male and 10.29% females were of unclassified type. Out of the 350 asthmatic study group 52.86% were of episodic nature and 47.14% were perennial in nature as revealed by fig. 2.

The level of mean immunoflobulins in control population exhibited a decreasing pattern from Ig G to Ig E (1092.54 to 85.27 IU/ml) while in asthmatic patients the mean level of Ig G is higher than the control group (1159.89IU/ml), Ig A level is significantly decreased from 288.77IU/ml to 188.42 IU/ml, while Ig M level is significantly higher than the control group (146.11 to 179.35 IU/ml). The most important Ig E showed a significant approximately 2100 % increase from control group level to asthmatic group (85.27 to 1825.92 IU/ml) as mentioned in fig. 3. The level of serum immunoglobulin E level is always higher in asthematics in comparison to normal persons, and as the severity of asthma increased, level of Ig E also increased (Sandeep *et al.,* 2010)

Ig E is the most important immunoglobulin responsible for bronchial asthma, a comparative study was undertaken to enumerate the status of Ig E in both control and asthmatic male and females. From the fig. 4 it was evident that the level of Ig E is not significantly different among different age group in control population in both male and female. However, a significant different is observed in asthmatic population when both male and female were considered. Male possessed almost double value of Ig E than females. There is also no significant difference was observed among age groups. Significant difference between male and female Ig E level was also reported by Paula *et al.* 2014.

Fig. 1 Distribution of Study Population

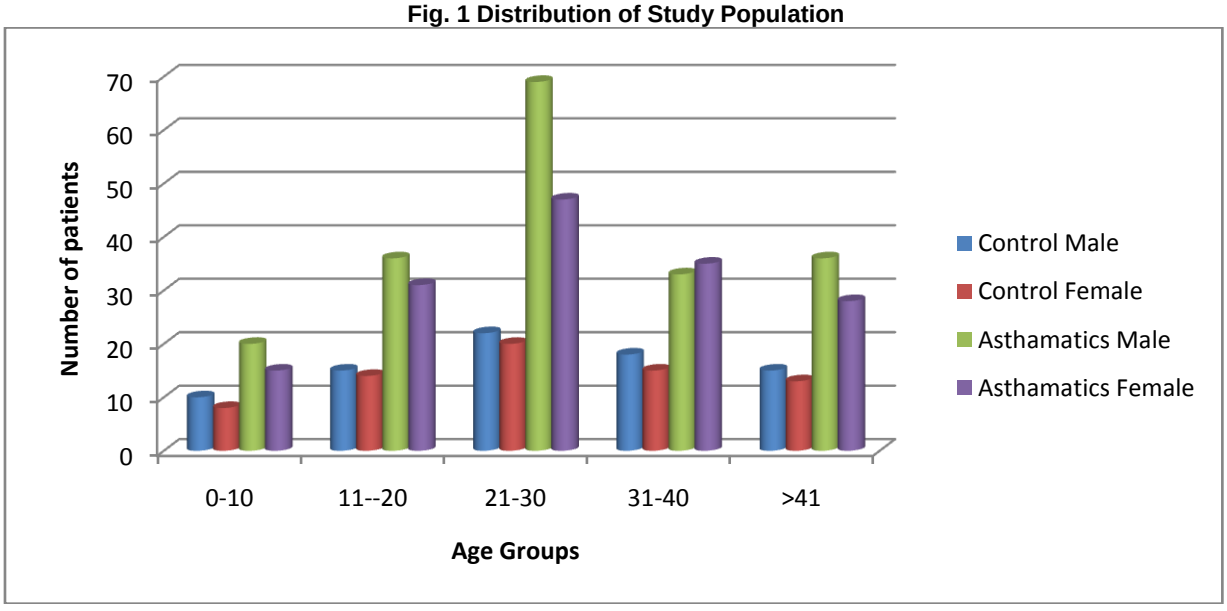


Fig. 2 Types of Asthma

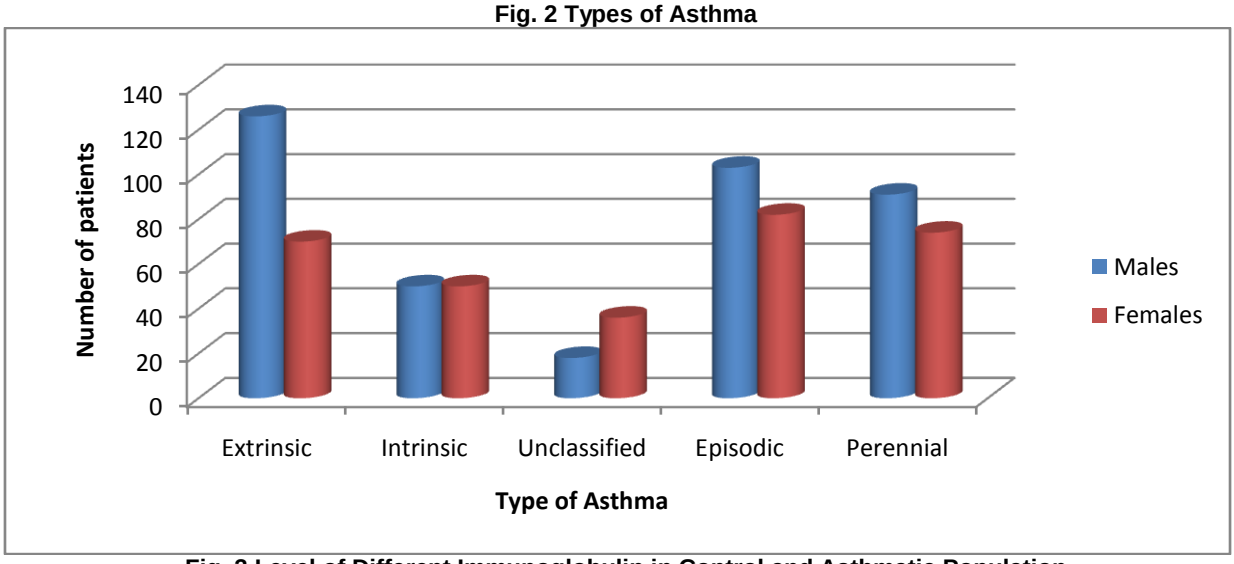


Fig. 3 Level of Different Immunoglobulin in Control and Asthmatic Population

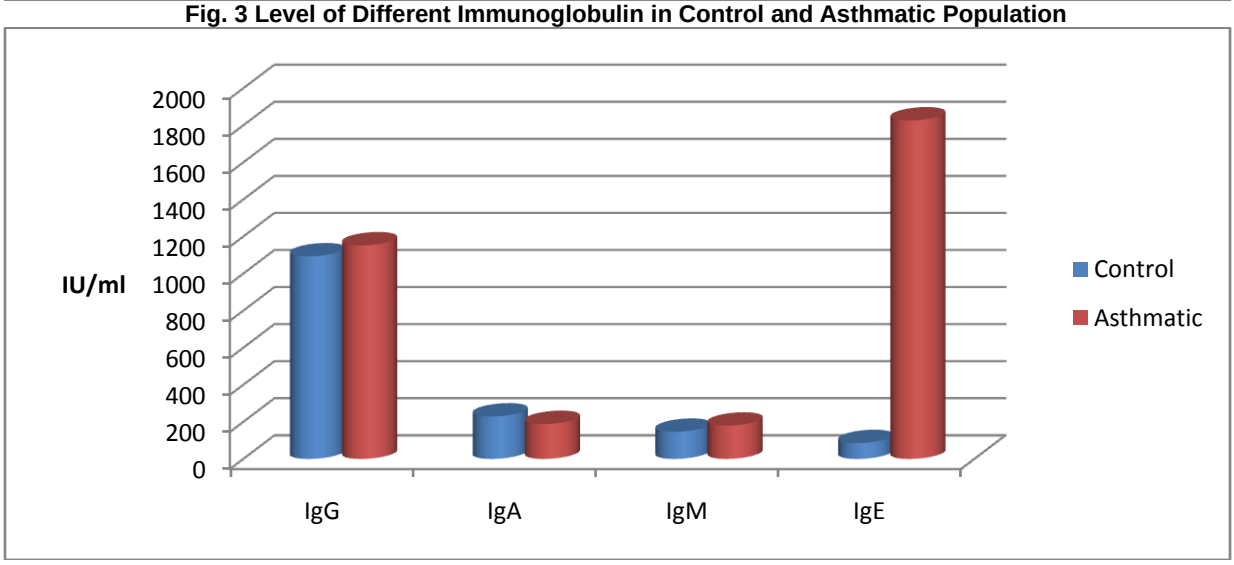


Fig. 4 Ig Level in Control and Asthmatic Study Population

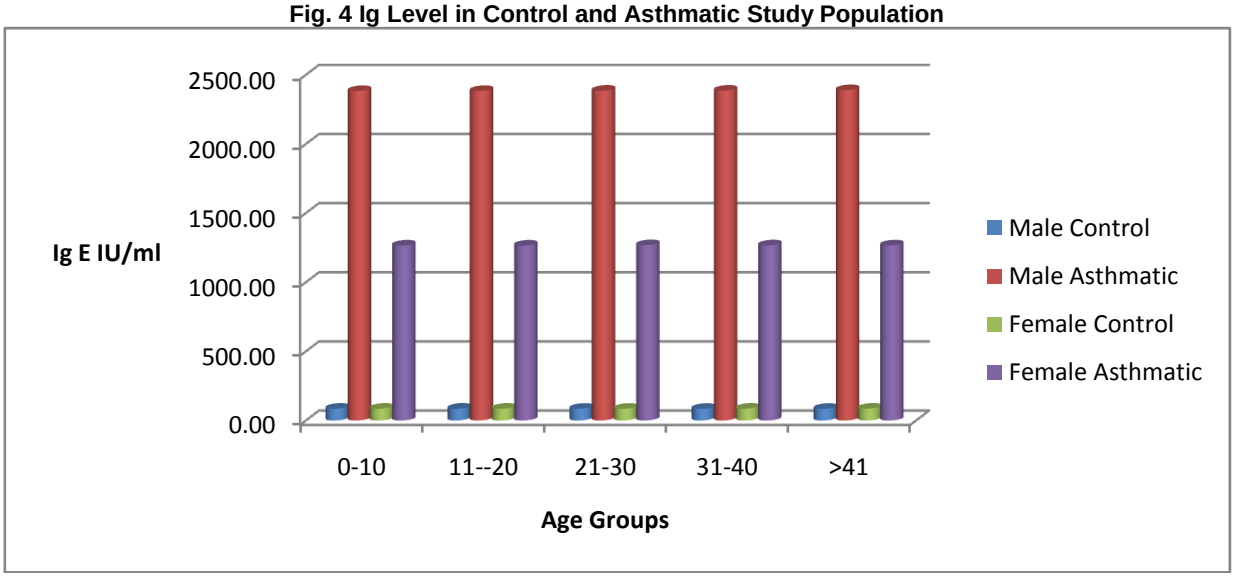
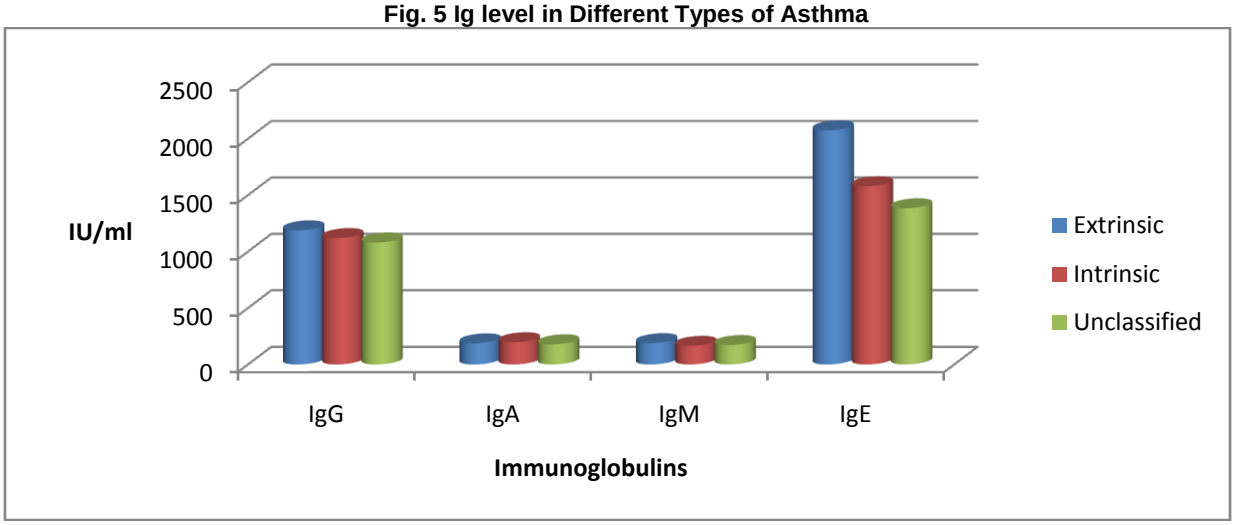


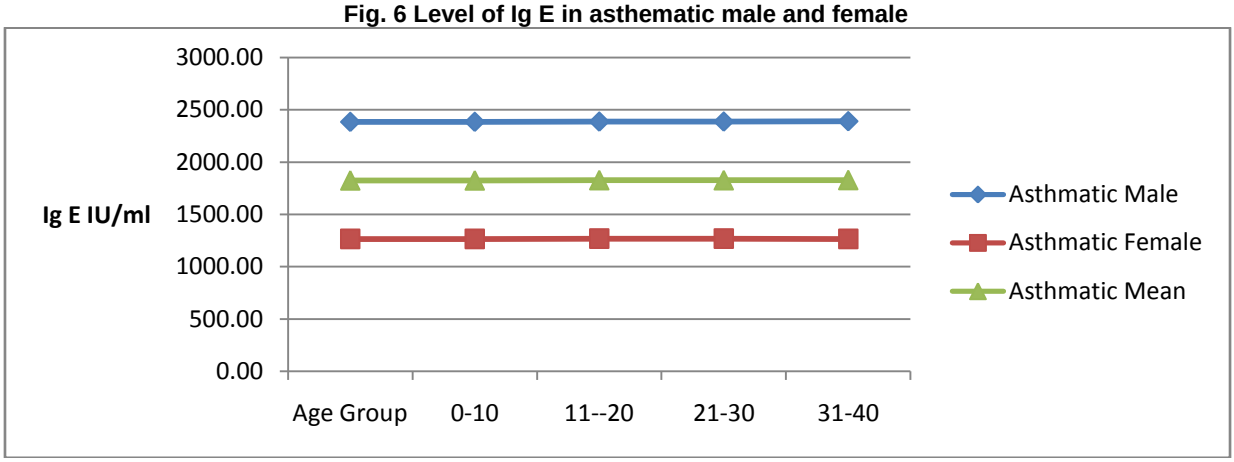
Fig. 5 Ig level in Different Types of Asthma



IgG differ significantly from unclassified and intrinsic to extrinsic type of asthma while there is no significant difference between extrinsic to unclassified. In case of both Ig A and Ig M, there is no significant difference among the asthmatic types. However both extrinsic and intrinsic type of asthma differs significantly from unclassified asthma when values of Ig E were observed. It was also observed that the level of Ig E in asthematic male is significantly different from asthematic female. But there was no significant difference between different age groups in both male and females.The results of the present study showed that serum Ig E level was highly significantly higher in the asthma group compared with the control group. Our study is in agreement with the study by Sandeep *et al.* (2010), who investigated serum IgE level in 60 asthmatic patients between 18 and 60 years of age, (31 male and 29 female), and 13 healthy controls between 18 and 60 years of age. They attributed this to the fact that there is a link between total IgE and asthma, which appears to be independent of allergen sensitization.

Bronchial asthma may be attributed to various other factors involved, because other cells in affected bronchi can also produce the mediators; this is inclusive of vascular endothelium, airway epithelium, and inflammatory cells already present in asthmatic patients suffering arecurrent attack (Sherrill *et al.,* 1999). It may be proposed that the levels of IgE are quite high locally at the site of inflammation and the serum levels do not necessarily reflect the levels in lungs and bronchus. It is also known that IgE is bound to mast cells with rather high affinity (Kindt *et al.,* 2007) and hence the circulating IgE may not give a conclusive evidence of the severity of inflammation.

Fig. 6 Level of Ig E in asthematic male and female



Conclusions

The above mentioned study summarized that the study population comprises both male and female patients were suffering from severe bronchial asthma. The level of immunoglobulin E is higher in male patients in comparison to females. The extrinsic type of asthma showed highest level of Ig E followed by intrinsic and unclassified type. From this study it is evident that serum Immunoglobulin E level is found significantly high in asthmatics when compared to normal patients. The IgE levels increased as the severity of asthma increased, and a positive correlation is established between severity of asthma and Ig E level.

The findings outlined here strongly suggest that the severity of asthma is mediated primarily by IgE. However, findings derived from studies of allergen avoidance or bronchial provocation cannot define whether the inflammatory responses can be traced to IgE activation of mast cells or to effector T cells. The default immune response is a modified Th_2 response rather than a Th_1 response and it appears

not to be related to asthma. Although IgE is just one player in a highly complex immune response orchestrated by Th2 cells, it is undoubtedly of central importance in both immediate hypersensitivity and the late-phase responses characteristic of allergy and asthma. The evidence for a role of allergens in asthma provides a compelling rationale for several forms of treatment. These include allergen avoidance, immunotherapy, and the new approach of directly neutralizing Ig E antibodies.

The present study is basic investigation of levels of immunoglobulins and has certain limitations but it has very high potential for further investigation of various factors or allergens and their relation with Ig E.

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Table 1 Distribution of Control and Asthematicstudy Population

	Control			Asthamatics		
Age Group	Male	Female	Total	Male	Female	Total
0-10	10	8	18	20	15	35
11-20	15	14	29	36	31	67
21-30	22	20	42	69	47	116
31-40	18	15	33	33	35	68
>41	15	13	28	36	28	64
	80	70	150	194	156	350

Table 2 Classification of Study Population in Different Types of Asthma

Type	Males (%)	Females (%)	Total (%)
Extrinsic	126 (36.00)	70 (20.00)	196 (56.00)
Intrinsic	50 (14.29)	50 (14.29)	100 (28.57)
Unclassified	18 (05.14)	36 (10.29)	54 (15.43)
Episodic	103 (29.43)	82 (23.43)	185 (52.86)
Perennial	91 (26.00)	74 (21.14)	165 (47.14)
Total	194	156	350

Table 3 Asthematic Patients eith Different Symptoms

Symptoms	Wheezing	Sneezing	Cough	Rhinitis	Uriticaria	Eczema
No	350	168	123	140	49	21
Percentage %	100	48	35.14286	40	14	6