

The effect of some Variables and Antibodies Against Inhalation and Food Allergens on Asthmatic Mail Patients Compared with Control Group

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Abstract

This research included the detection of some variables levels(histamine, serotonin, LOX5 and LTA4H), the effective level of these variables on asthmatic group. also the effect antibodies of against inhalation and food allergens which leads effective on asthmatic disease. The level of these variables increases in more asthmatic group than control group also some inhalation and food allergens increase in asthmatic group when compared with control group .

Key world: asthma, histamine, serotonin, Lipoxigenase-5 , Leukotriene A4 Hydrolase and food allergens

الخلاصة

يتضمن تحديد مستوى بعض المتغيرات (الهستامين، السيروتونين، 5-لايبوكسينجيز، الليكوترين) وتأثير مستوى هذه المتغيرات على مجموعة الربو . وكذلك تأثير الاجسام المضادة ضد استنشاق المواد المسببة للحساسية في المواد الغذائية التي تؤثر على مرض الربو. حيث ظهر ارتفاع في مستوى المتغيرات على مجموعة الربو اكثر من مجموعة الاصحاء، وكذلك ارتفاع تأثير الاجسام المضادة ضد استنشاق المواد المسببة للحساسية في المواد الغذائية على مجموعة الربو عند مقارنتها مع مجموعة الاصحاء .

الكلمات المفتاحية: الربو، الهستامين، السيروتونين، 5-لايبوكسينجيز، الليكوترين، المواد المسببة للحساسية في المواد الغذائية.

Introduction

Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and in the early morning. The etiology of asthma is likely multi factoria (Scirica *et al* 2007). Inhalant allargen classified into (indoor such as mites, insects , pets and plant) and (outdoor such as pollens and molds) .Outdoor allergens appear as a greater risk for seasonal rhinitis and asthma than indoor (Braun *et al* 1997).

House dust mites are allergens belong to the Arthropods. Mite and cockroach antigens are common, and exposure and sensitization has been shown to increase asthma morbidity (Spieksma *et al* 1997).but the pollen grains can be carried by the wind and represents a major danger as they are emitted in large quantities, it has ability to travel long distances (hundreds of km) and consequently can affect individuals who are far from the pollen source, therefore patients who are nearest to the source of the pollen generally reveal most severe symptoms (Jimenez *et al* 1994), (Goldberg *et al* 1998).

Allergens derived from animals such as cats ,dogs, horses, rabbits and other rodents such as guinea pigs, hamsters, rats , mice and gerbils can be triggers asthma (Heederik *et al* 1998).when see Molds and yeast are plants which do not possess chlorophyll but which contain large quantities of allergenic spores environments. Mold spores represent an allergen source which very important that related to an

increase asthma (Tariq *et al* 1996).also food allergy has a significant socio-economic impact. Patients presenting with symptoms linked to food should undergo a diagnostic work-up to identify the offending food and clarify a complex spectrum of disease the epidemiology of food allergy is influenced by genetic, cultural and geographical dietary influences. Severe and fatal reactions can occur at any age but those at greatest risk are adolescents and young adults with asthma a known food allergy are peanut, tree nut, fruits, milk, wine, vegetables. (Woods *et al* 2001)

The relation between asthma and some variables can reveal that Lipoxygenase-5 play an important role in the pathogenesis of asthma and the polymorphisms of the Lipoxygenase-5 promoter have also been associated with the development of asthma. The products of the lipoxygenase-5 pathway are Leukotrienes (Luo *et al* 2003). also Leukotrienes are very important agents in the inflammatory response. Some such as LTB₄ have a chemotactic effect on migrating neutrophils, and as such help to bring the necessary cells to the tissue. Leukotriene A₄ Hydrolase LTA₄H also have a powerful effect in bronchoconstriction and increase vascular permeability (Gijon *et al* 2000).

While histamine which is synthesized and released by human basophiles, mast cells, neurons and lymphocytes(2-[4-imodazole]-ethylamine) was discovered as an uterine stimulant in different extracts more than 100years ago. Its smooth muscle stimulating and vasopressor action was shown in the first experiments by Dale and Laidlaw (Dale and Laidlaw 1911). Also the Serotonin is formed by tryptophan5 hydroxyls following decarboxylation.Serotonin is a bio-amine that functions as neurotransmitter, tissue mediator and vasoactive agent which can either apparently up regulate or down regulate a given biological response. (Barnes, 2006), (Menard *et al* 2007) It has been reported that human mast cells may synthesize and release serotonin. (Kushnir *et al* 2007)

Serotonin and histamine also affect asthma that play important roles in causing severe inflammation. the reactions of histamine, serotonin release additional immunologically active mediators. histamine, serotonin have broad and complex physiological effects on several organ systems.

Methodology

The determined patient thirty five patient of asthmatic male with mean age of (65±10) years.. thirty five healthy male with mean age of (65±10) year as control group.

Antibodies against inhalation and food allergens

Patients (65±10years) were screened using. Specific IgE level was determined by test strips coated allergens. the Euroline test kit provides *in vitro* assay for human IgE antibodies to inhalation allergens in serum . from euroline test strips coated allergens that order number is dp (3117-1601E). the principle of the test provides asemi –quantitative *in vitro* assay for human IgE antibodies to inhalation in serum. the test kit contain test strip coated with parallel lines with 21 different allergen . The kit storage 2°Cto 8°C.

Other kit from Euroline that order number is dp(3712-1601E) for inhalation and food allergens. the principle of the test provides asemi –quantitative *in vitro* assay for human IgE antibodies to inhalation and food allergens in serum. the test kit contain test strip coated with parallel lines with 28 different allergen. The kit storage 2°C to 8°C.

Quantification of histamine, serotonin, Lipoxygenase-5 and Leukotriene A4 Hydrolase

In the Serum the concentrations of histamine, serotonin, Lipoxygenase-5 and Leukotriene A4 Hydrolase in the Serum were determined by using ELISA assays. ELISA kits for testing histamine ,serotonin , Lipoxygenase-5 and Leukotriene A4 Hydrolase were obtained from Elabscience Biotechnology co. Ltd.

Histamine number Product ID is (E-EL-0032) and the Package 96T The principle ELISA kit uses Competitive-ELISA as the method. And the serotonin number is Product ID is (E-EL-H2187) and Package 96T The principle ELISA kit uses Sandwich-ELISA as the method..

The other kit Lipoxygenase-5 number is Product ID is (E-EL-H0223) and Package 96T The principle ELISA kit uses Sandwich-ELISA as the method.

The last kit Leukotriene A4 Hydrolase number is Product ID is (E-EL-H1403) and Package 96T. The principle ELISA kit uses Sandwich-ELISA as the method.

Procedure for determine WBC and RBC to asthma patients and control group by human count 5L, The Procedure first take 2-3 blood and put in EDTA tube after that make mixing 3 times from the screen choose the type patients and write all formation . put the tube in the place and choose start after 1 minutes the result show in screen .the human count 5L show positive or negative when increase or decreases on normal value also human count 5L draw the curve .

Result:

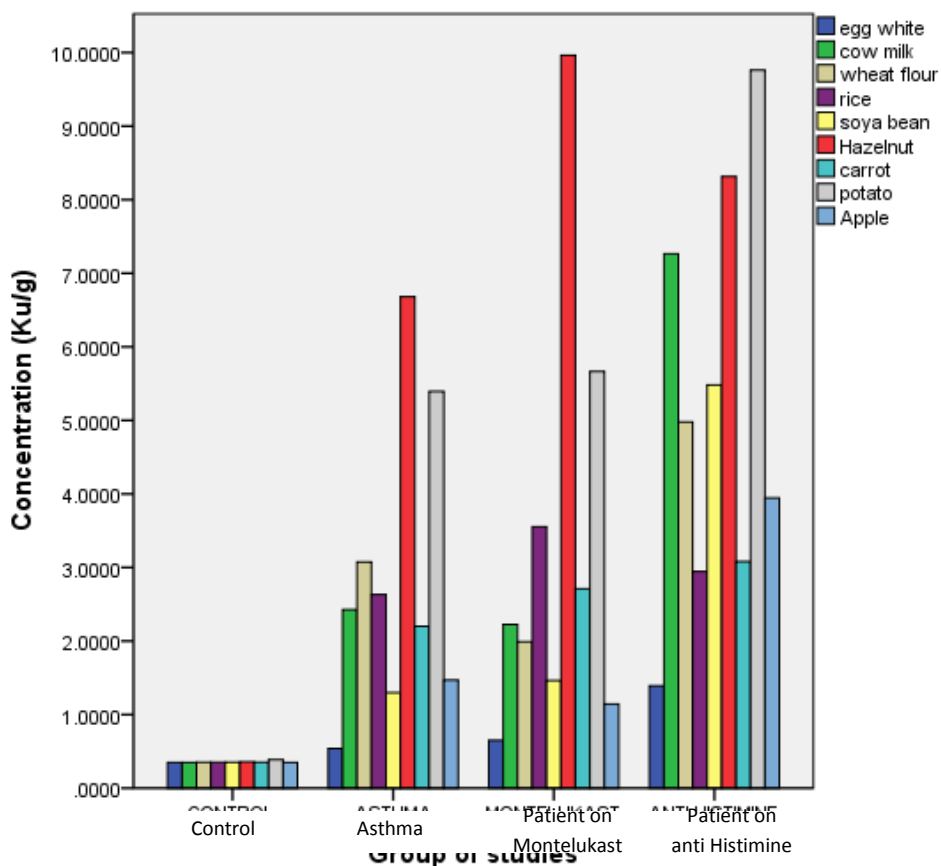


Figure (1) the effect of some food allergen on studied groups.

The above figure(1) which shows the food allergen affect on asthmatic patients more than control. that means asthmatic patients sensitive from all food allergen. But the patients take montelukast appear cow milk, wheat flour, apple decrease while egg white, rice, soybean, hazelnut, carrot, potato that increase when compared with asthmatic patients. while the patients take anti histamine when compared with asthmatic patients and the patients take montelukast all food that increases in anti histamine patients. just rice, hazelnut that is little decrease.

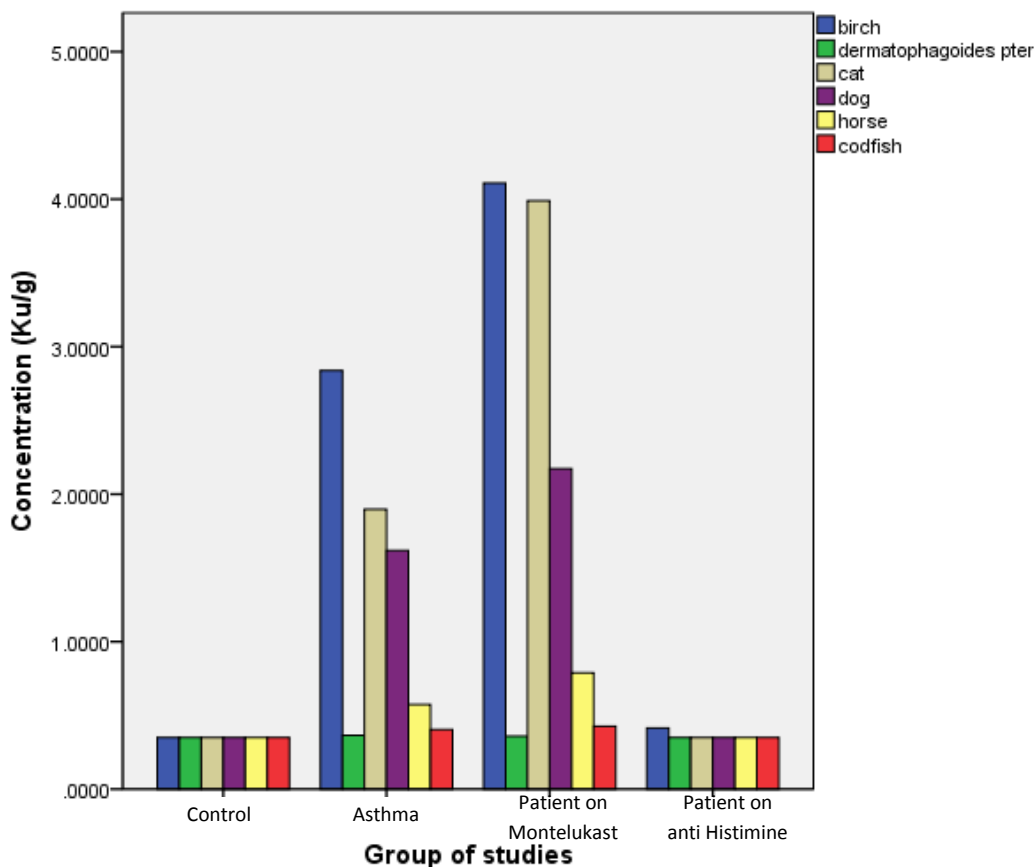


Figure (2) the effect of some animals allergen on studied groups.

The result in figure(2) reveals that indicate the effect of animal allergen on asthma patients more than control, that means asthmatic patients sensitive from animal allergen .but not all that appear increase value in birch, cat, dog, horse more than control . while the patients take montelukast appear that increase in birch, cat, dog, horse more than control and asthmatic patients. While the other animal allergens reveals the have same value in all studies group,. all animal allergen that the same value in all studies group. That means the patients take anti histamine with control don't have animal allergen effect.

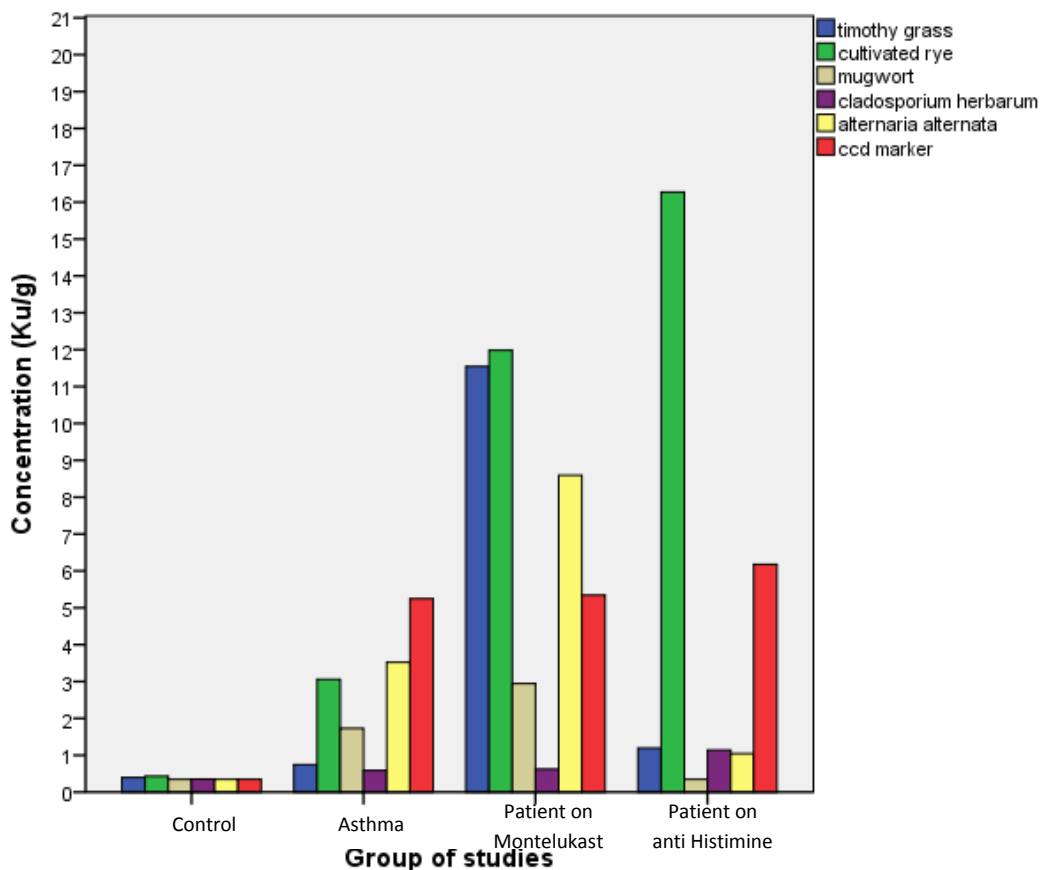


Figure (3) the effect of some plants allergen and bacteria on studied groups

The result in figure(3) shows the effect of plants allergen and bacteria on asthmatic patients is more than control. that means asthmatic patients sensitive from plants allergen and bacteria but not all that appear increase value in cultivated rye , mugwort , alternate, ccd marker more than control. while the patients take montelukast appear that increase cultivated rye , mugwort , alternate, more than control and asthmatic patients.. While patients take anti histamine when compared with asthmatic patients and the patients take montelukast all value that the same just cultivated rye and ccd marker increase than other group studied.

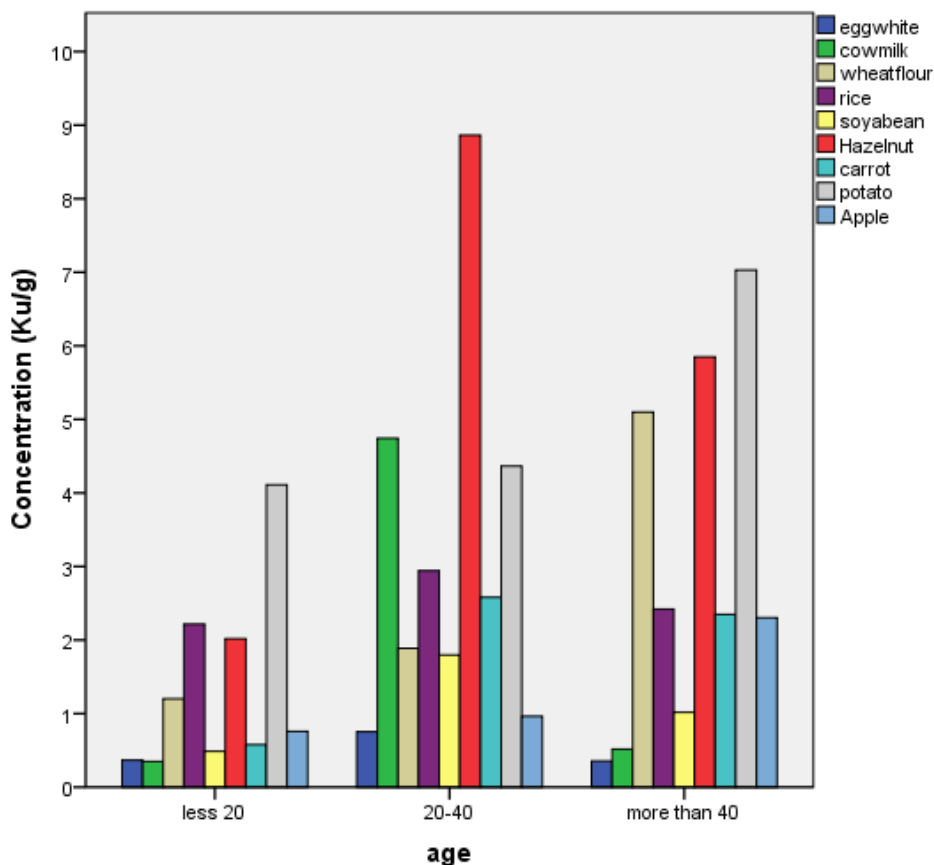


Figure (4) the effect of some food allergen on asthmatic patients age

The effect of age on food allergen which effect on asthmatic patients was shown in figure(4) . that means asthmatic patients sensitive from all food. But the patients less than 20y appear special sensitive from potato, wheat flour, rice, hazelnut. And when reveal patients that age 20y to 40y that sensitive from all food that means increase value more than less 20y. while when appear patients with age more 40y the same value or little increase with age 20y to 40y just appear hazelnut, cow milk decrease than other age.

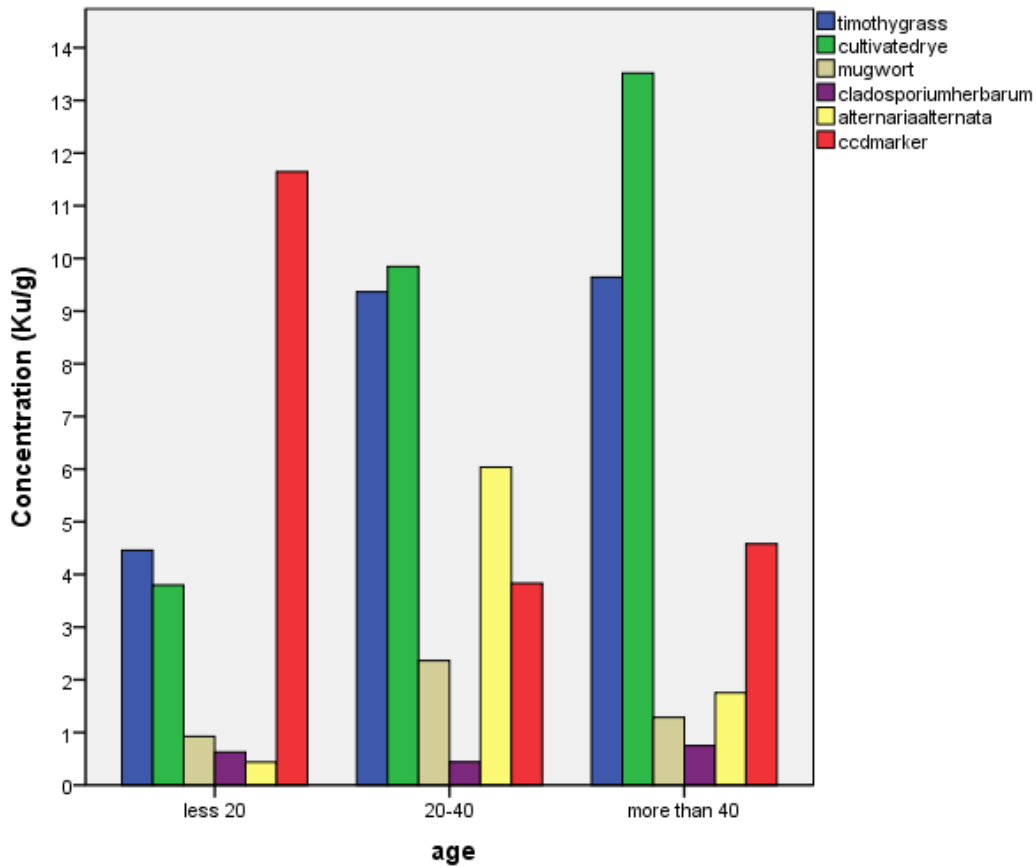


Figure (5) the relation between plant allergen and bacteria and asthmatic patients age.

The effect of age on plants allergen and bacteria which effect on asthmatic patients was shown in figure(5) . patients less than 20y appear special sensitive from cultivated rye , grass , ccd marker. While patients that age 20y to 40y sensitive from all plants allergen except ccd marker and age more than 40y the same value just cultivated rye , grass increase than other age.

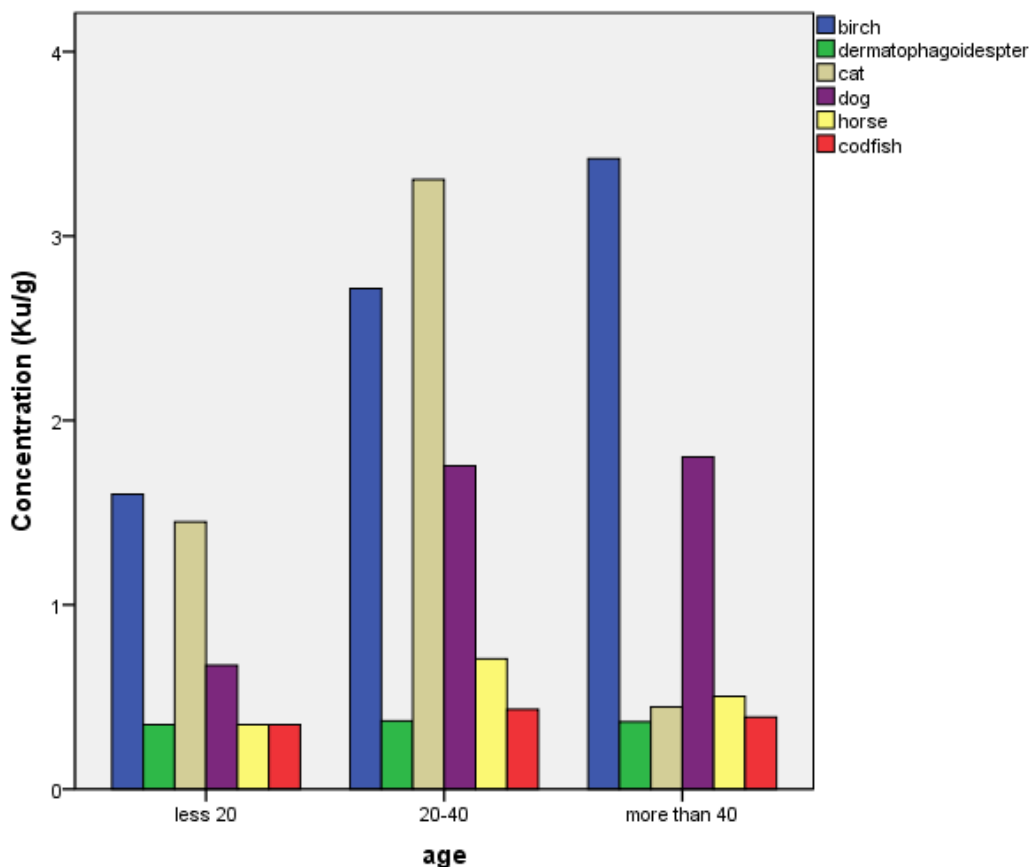


Figure (6) the relation between animal allergen and asthmatic patients age .

The effect of age on animal allergen which effect on asthmatic patients was shown in figure(6) . asthmatic patients less than 20y special sensitive from birch, cat, dog. And patients that age 20y to 40y also sensitive from birch, cat, dog and horse This value Increase than age less 20y. while patients with age more than 40y are sensitive from birch, horse more than other age but other animal allergen decrease in age more than 40y .

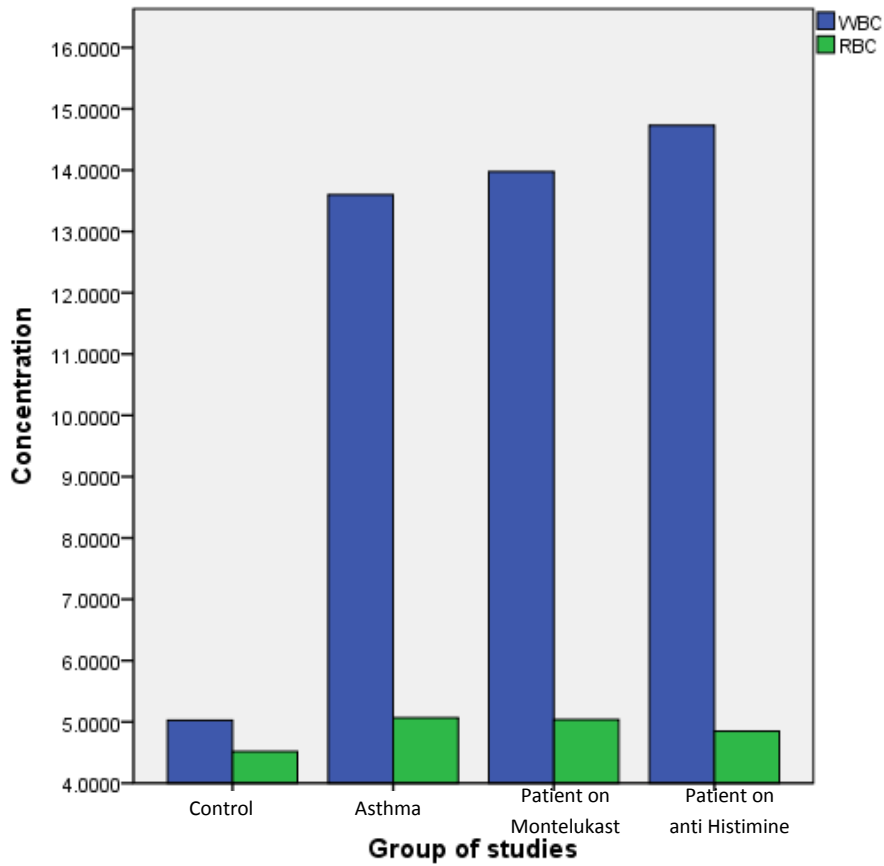


Figure (7) the effect of WBC ,RBC on control and asthmatic patients.

Figure (7) reveal that in all studies group WBC value increase more than control group. but RBC the same value in all studies group (that means no difference).

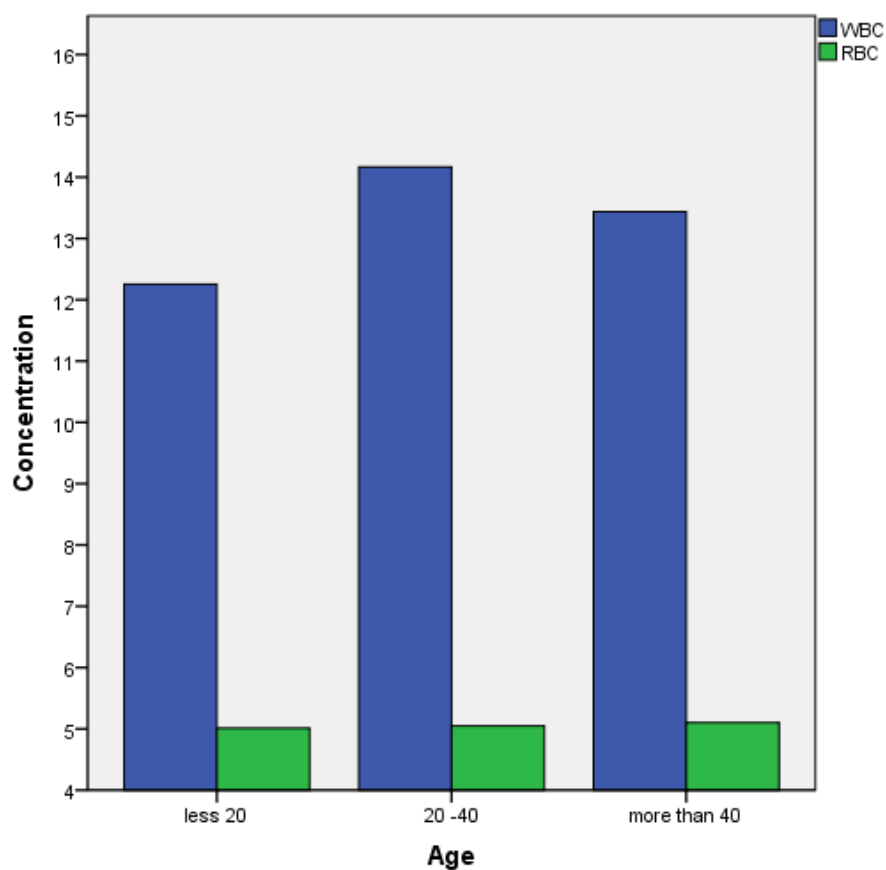


Figure (8) the effect of WBC ,RBC on asthmatic patients age.

Figure (8) when compare between them in WBC value the same in all studied group in asthmatic patients. And RBC the same value in all studied group in asthmatic patients that mean age to asthmatic patients don't have effect.

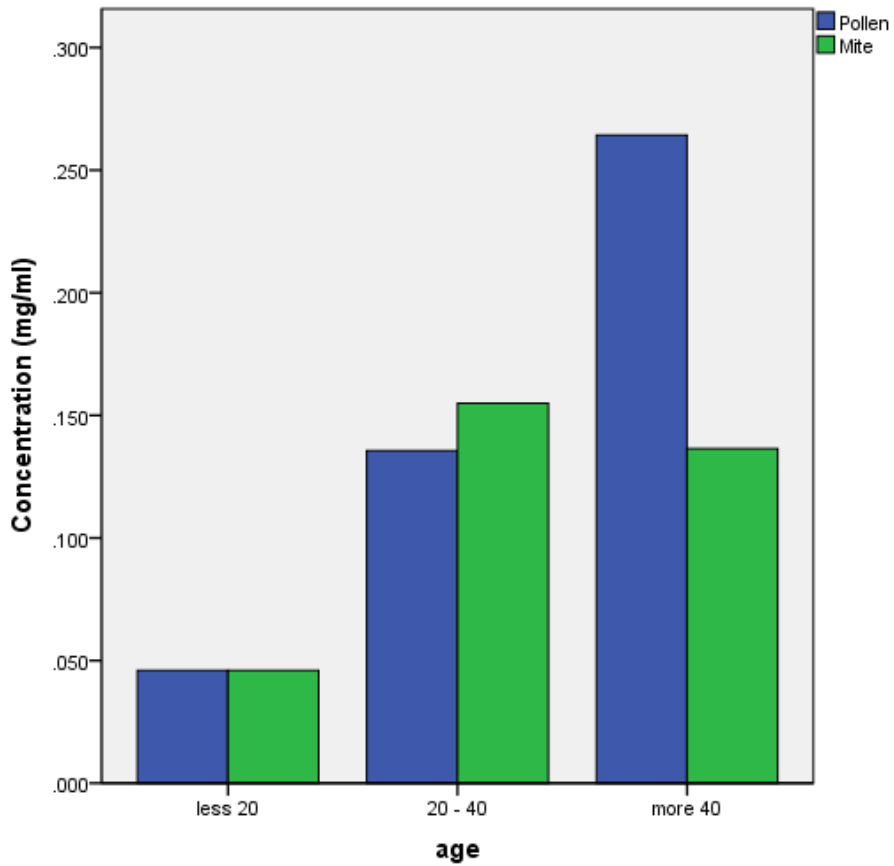


Figure (9) the relation of pollen ,mite and studied groups age.

The effect of age on pollen ,mite on asthmatic patients which effect on asthmatic patients was shown in figure(9) in pollen value increase with increase age . while in mite from age more 40y little decrease than age 20y to 40y and age less 20y.

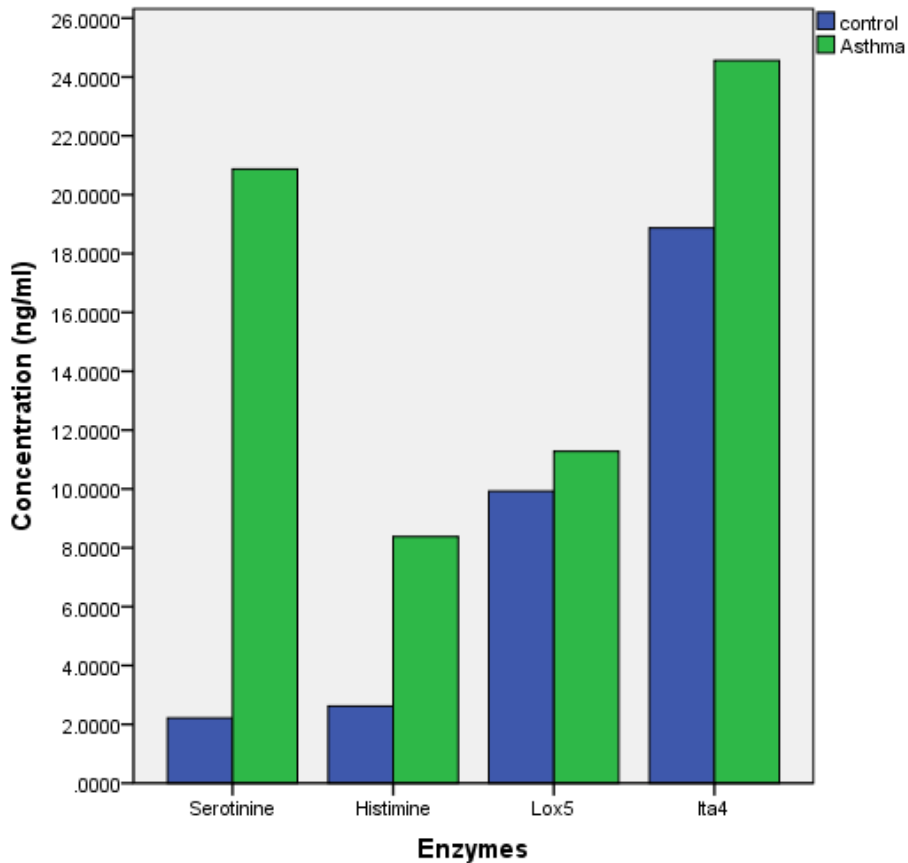


Figure (10) the effect of some variables (histamine, serotonin, LOX5 and LTA4H) on control and asthmatic patients.

Figure (10) show the comparative between asthmatic patients and control group that appear all variables(histamine, serotonin, LOX5 and LTA4H) increase value in asthmatic patients more than control group. While the serotonin , LTA4H is very high value when compared with control. while histamine. Lox5 is high value when compare with control.

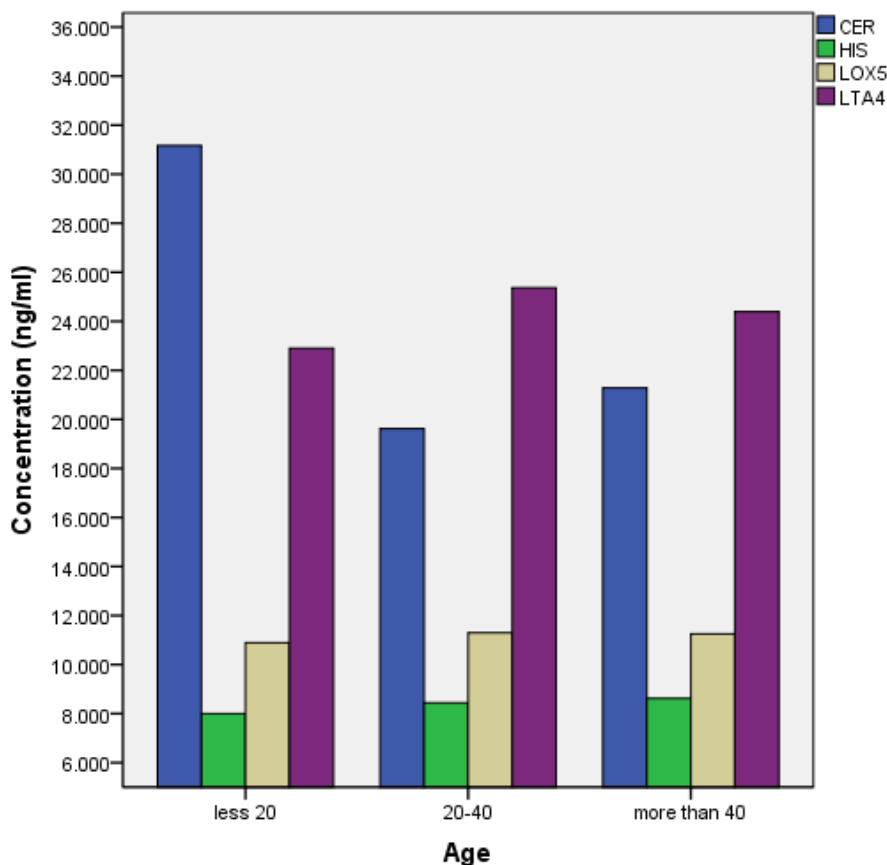


Figure (11) the effect of histamine, serotonin, LOX5 and LTA4H on asthmatic patients age .

Figure (11) show the comparative between asthmatic patients age that appear in histamine and Lox5 is the same value in all age. While in the serotonin is the high value in the age less 20y. while LTA4H enzyme is little different between age .

Discussion

Food allergy is defined as a condition caused by an IgE-mediated reaction to a food material. The results revealed asthmatic patients and patients taking pharmacological drugs such as montelukast and anti histamine were highly sensitive to some food allergy. In addition, patients who develop an allergy to one food are at greater risk of developing allergy to other foods and/or inhalants. Allergy reaction may be directed to a variety of potential allergenic proteins in foods (eg, white proteins in hen's eggs, casein and when proteins in cow's milk, egg and parvalbumin in finned fish (Bellioni *et al* 1999).

Histamine can present naturally in foods such as tomatoes, spinach, strawberries and other food (Feldman *et al* 1983). The ingestion or inhalation of foods with high histamine content may lead to immediate anaphylactoid reactions (Macan *et al* 2000).

Like other diseases, both genetic susceptibility and environmental factors influence the effect of the phenotypic expression of food allergy. However, genetics studies of food allergy are few. For peanut allergy, the influence of HLA class II genes has been demonstrated (Howell *et al* 1998). However, there was another effect in the increased sensitivity to food allergic incidence that cannot be attributed to genetic factors only three major environmental factors are alterations in exposure

to infectious diseases during early childhood, pollution and dietary changes(Charles *et al* 2001).

There was no evidence about the relation between the age and increases of food allergy but revealed association with increased rate of sensitization to food in children and the Cow's milk allergy is a common disease of infancy and childhood. (Macan *et al* 2000) However, there search result appeared increased allergy to food allergens among age group (20-40) years while other studies showed allergy to foods is much more in the early neonatal period and also in elderly (Sampson *et al* 1991).

The effect of food on asthma patient revealed more than control that asthma patients sensitive from all food. Some studies showed the patients with families' history with asthma was approximately 4-fold higher than expected when compared to normal population(Strobel *et al* 1998).

The most sensitive individuals may reveal greatly exposure to animal dander such as cat dander dog, pet and horse cat and dogs are a major source of allergens in the home environmental. Asthma patient showed highly sensitive to animal dander also the patients taken the medication such as montelukast due the effect of this allergen on the susceptibility to increase the sensitivity to such allergens(Zeiger and Heller , 1995). Also the house dust mites and pollen grains are produce the major allergens associated with asthma; exposure of patients with asthma who are allergic to high levels of dust mite allergen has been shown to increase the reaction to this allergen as shown in this results (Simpson and Custovic 2005).

White blood cells play a very important role in coordinating the inflammatory response in asthma; T- lymphocytes have ability to release specific patterns of cytokines, resulting in the recruitment and survival of eosinophils and in the maintenance of mast cells in the airways. As part of the response to the allergen, in the fight against the foreign invader, that leads increased level of these cells associated with asthma. Many studies have shown increased level of WBC in patients with asthma (Sur *et al* 1993) (Martel *et al* 2003).

Red blood cells show increased levels in person with asthma because of decreased air flow y narrowed and inflamed airways, that leads to less amount of oxygen to reach the lungs. Asthma limits the sufficient amount of oxygen-carry by red blood cells, so the body compensates by producing more red blood cells in an effort to transport oxygen to the lungs; hence elevating red blood cell levels.

Many studies had proved the relation of some substance such as histamine, serotonin, leukotrine and lipoxigenase with exacerbation of asthma, the role of leukotrienes (LTs) in asthma through stimulation and their effects on neutrophil adherence to vascular endothelium and increase vascular permeability²⁴, histamine caused bronchoconstriction in patients with asthma(Ekici , 2006)

Refrence

- Barnes PJ. (2006) Histamine and serotonin. *Pulm Pharmacol Ther*;14(5):329-39.
- Bellioni-Businco B, Paganelli R, Lucenti P, Giampietro PG, Perborn H, (1999) Businco L. Allergenicity of goat's milk in children with cow's milk allergy. *J Allergy Clin Immunol.*;103(6): 1191-4. (Ib).
- Braun-Fahrlander C, Wuthrich B, Gassner M, Grize L, Sennhauser FH, Varonier HS, et al. (1997), Validation of a rhinitis symptom questionnaire (ISAAC core questions) in a population of Swiss school children visiting the school health services. SCARPOL-team. Swiss Study on Childhood Allergy and Respiratory Symptom with respect to Air Pollution and Climate. *International Study of Asthma and Allergies in Childhood. Pediatr Allergy Immunol.*;8(2):75-82.

- Charles J.; Travers P; Walport M.; Shlomchik M. (2001).*Immunobiology; Fifth Edition*. New York and London: Garland Science. pp. e-book. ISBN 978-0-8153-4101-7.
- Dale HH, Laidlaw PP. (1911) Further observations on the action of b-imidazolylethylamine. *J Physiol*; 43:182-95.
- Ekici M. (2006). Perception of dyspnea during exacerbation and histamine-related bronchoconstriction in patients with asthma. *Ann Allergy Asthma Immunol*, 96: 707-712
- Feldman JM. (1983) Histaminuria from histamine-rich foods. *Arch Intern Med*;143:2099–2102.
- Gijon MA spener , DM, siddqi. AR. Bonvetre SR and Lestie (2000) cytosolic phospholipase A2is required for macrophage archidonic acid release by agonists that do and do not moillze calcium novel role of nitrogen activated protein kinase pathway in caytocolic phosplipase A2 reguliazation 6.io.Chem.275 201140-20156.
- Goldberg A, Confino-Cohen R, Waisel Y. (1998).; Allergic responses to pollen of ornamental plants: high incidence in the general atopic population and especially among flower growers. *J Allergy Clin Immunol.*;102(2):210-4.
- Heederik D, Venables KM, Malmberg P, Hollander A, Karlsson AS, Renstrom A, et al(1998). Exposure-response relationships for work-related sensitization in workers exposed to rat urinary allergens: results from a pooled study. *J Allergy Clin Immunol*. 103(4):678-84.
- Howell WM, Turner SJ, Hourihare JD, et al(1998). HLA Class II DRBI, DQBI and DPBI genotypic associations with peanutallergy, evidence from a family-based and case-control study. *Clin Exp Allergy*.;28:156–162. (IIa).
- Jimenez A, Moreno C, Martinez J, Martinez A, Bartolome B, Guerra F; et al. , (1994) Sensitization to sunflower pollen: only an occupational allergy? *Int Arch Allergy Immunol*. 105(3):297-307
- Kushnir-Sukhov NM, Brown JM, Wu Y, Kirshenbaum A, Metcalfe D. (2007) Human mast cells are capable of serotonin synthesis and release. *J Allergy Clin Immunol*; 119(2):498-9.
- Luo M, Jones SM, Peters-Golden M, Brock TG. (2003); Nuclearlocalization of 5-lipoxygenase as a determinant of leukotrieneB4 synthetic capacity. *Proc Natl Acad Sci USA*100(21):12165-12170.
- Macan J, Vucemilovic A, Turk R, (2000) et al. Occupational histamine poisoning by fish flour: a case report. *Occup Med*.;50:22–24.
- Martel-Pelletier, J.; Lajeunesse, D.; Reboul, P. and Pelletier, J.P. (2003). Therapeutic Role of Dual Inhibitors of 5-LOX and COX, Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs. *Annals of the Rheumatic Diseases* , 62: 501–509.
- Menard G, Turmel V, Bissonnette EY. (2007) Serotonin modulates the cytokine network in the lung. *Clin Exp Immunol*; 150(2):340-8.
- Sampson HA, Bernhisel-Broadbent J, Yang E, (1991) Scanlon SM. Safety of casein hydrolysate formula in children with cow milk allergy. *J Pediatr*.;118:520–525 (Ia) .
- Scirica CV, Celedon JC. (2007), Genetics of asthma: potential implications for reducing asthma disparities. *Chest*.; 132 (5): 770S-781S.
- Simpson A, Custovic A. (2005)Pets and the development of allergic sensitization. *Curr Allergy Asthma Rep*.;5:212–20.

- Spieksma FT. (1997), Domestic mites from an acarologic perspective. *Allergy*;52(4):360-8.
- Strobel S, Mowat AM. (1998) Immune responses to dietary antigens: oral tolerance. *Immunol Today*;19:173–181. (LB).
- Sur S, Crotty TB, Kephart GM, et al. (1993) Sudden onset fatal asthma: a distinct entity with few eosinophils and relatively more neutrophils in the airway submucosa. *Am Rev Respir Dis*; 148: 713–719.
- Tariq SM, Matthews SM, Stevens M, Hakim EA. (1996) Sensitization to *Alternaria* and *Cladosporium* by the age of 4 years. *Clin Exp Allergy*;26(7):794-8.
- Woods RK, Abramson M, Bailey M, Walters EH (2001).International prevalence of reported food allergies and intolerances: comparisons arising from the European Community Respiratory Health Survey (ECRHS) 1991-1994. *Eur J Clin Nutr*;55:298-304.
- Zeiger RS, Heller S. (1995) The development and prediction of atopy in high-risk children: follow-up at age seven years in a prospective randomized study of combined maternal and infant food allergen avoidance. *J Allergy Clin Immunol*;95: 1179–1190. (Ib)