



RESEARCH ARTICLE

SCREENING FOR FOOD SPECIFIC IgE ANTIBODIES AMONG SAUDI PATIENTS WITH CLINICAL SUSPICION OF FOOD ALLERGY.

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Abstract

Background/Aim: The prevalence of food allergy is increasing all over the world and varies in different geographical locations. This study was performed to assess allergic sensitization against various food materials among Saudi patients clinically presenting with food allergy.

Patients and Methods: Data for the presence of food specific IgE antibodies were collected retrospectively from 280 Saudi patients screened between October 2012 and February 2014. These patients presented in the allergy clinic at King Khalid University Hospital, Riyadh with clinical signs and symptoms of food allergy. Out of the total 92 patients were found to have food specific IgE circulating antibodies. This group of patients comprised of 67 (72.8%) males and 25 (27.2%) females, with 78 (84.8%) children of <12 years and 14 (15.2%) adults (mean age 9.04 ± 7.71 years). Food specific IgE antibodies were quantified by radioallergosorbent test (RAST) using Pharmacia ImmunoCAP 250 analyzer.

Results: The most frequently sensitizing food allergens were milk in 57 (61.96%) patients followed by, egg white in 55 (59.78%) patients, wheat in 42 (45.65%) patients and peanut in 35 (38.04%) patients. Male children were consistently more sensitized against egg white (47.4% vs 15.3%; $p < 0.0002$), egg yolk (33.3% vs 7.6%; $p < 0.0002$), milk (47.4% vs 22.1%; $p < 0.001$), wheat (37.5% vs 12.4%; $p < 0.0006$) and peanut (37.5% vs 11%; $p < 0.0007$) compared to females. Milk sensitization was high among children whereas sensitization due to egg white was high in adults.

Conclusion: Patients were frequently sensitized against milk, egg white, wheat and peanut particularly the male children.

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Introduction:-

Food allergy is an important health concern and in United States of America alone 8% of children suffer from food allergy.^[1] Production of food specific IgE antibodies after repeated exposure to sensitizing food materials is considered a prerequisite for development of food allergy.^[2] Sensitization against various food materials can be

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detected by the presence of specific IgE antibodies however diagnosis of food allergy usually requires oral food challenge test.^[3] In the absence of clinical signs and symptoms of allergic disorders including food allergy detection of sensitizing allergens appears to be vital particularly during infancy, a period of life marked by a higher prevalence of sensitization against food allergens.^[4] Avoidance of sensitizing foods during infancy guided by the pattern of allergen sensitization has been shown to be associated with circumvention of later development of allergic disorders.^[5]

Although a wide variety of foods have been linked with food allergy the most frequently sensitizing food materials include egg, milk, fish, wheat, peanut and soy.^[6,7] Regional disparity among sensitizing food allergens is frequently observed. Egg, peanut and wheat are common sensitizing foods in Morocco^[8] whereas allergic sensitization due to peanut and pineapple is frequently observed in Ghana.^[9] Similarly, in Mexico food allergy due dairy, egg, fish, shrimp, beans and soy is common^[10] whereas fish, egg, milk, wheat, peanut and corn are frequently implicated in food allergy in Brazil.^[6] Data regarding allergen sensitization in the Kingdom of Saudi Arabia are scarce however peanut, egg and cow milk allergens have been previously identified as common food allergens in the Kingdom.^[11] Collectively these data suggest that differences observed in food sensitization could possibly be due to differences in cultural values and dietary preferences in different regions.

Currently available tools for detection of allergen sensitization comprise of in vivo skin prick testing and in vitro detection of allergen specific IgE antibodies in sera of patients.^[12] Among several prerequisites for skin prick test discontinuation of anti-histamine therapy often not possible due to disease severity and potential risk of systemic anaphylaxis are major limitations of skin prick test.^[13] In vitro assessment of specific IgE is not only devoid of the risk of anaphylaxis but the likelihood of detection of sensitization is higher than the skin prick test particularly among children.^[14] Moreover, serum concentrations of IgE against cow's milk and egg have been shown to exhibit a strong correlation with positive outcome of oral food challenge test thus obviating the need for the later test.^[15] This study was performed to assess the pattern of IgE mediated food allergen sensitization among patients clinically presenting with signs and symptoms of food allergy.

Subjects and Methods:-

This was a retrospective study of 280 patients with clinical suspicion of food allergy who underwent radioallergosorbent testing (RAST) at King Khalid University Hospital, Riyadh between October 2012 and February 2014. Out of the total number of patients screened only 92 (32.8%) were found to have food specific IgE antibodies in their sera. This group of patients included 67 (72.8%) males and 25 (27.2%) females with male to female gender ratio of 1:2.6. There were 78 (84.8%) children and 14 (15.2%) adults with mean age of 9.04 ± 7.71 years. Patients either equal to or less than 12 years of age were considered as children whereas adults group included patients aged more than 12. Majority of the patients 58 (63%) were suffering from urticaria followed by 16 (17.3%) patients with atopic dermatitis, 11 (11.9%) with symptoms relating to gastroenterology system and 7 (7.6%) patients with airway allergy. This study was approved by the Institutional Review Board of the College of Medicine, King Saud University, Riyadh.

Radioallergosorbent test (RAST):-

Measurement of food specific IgE was performed by RAST using Pharmacia ImmunoCAP 250 analyzer (Phadia, Uppsala, Sweden) in accordance with the instructions of the manufacturers. Ten milliliter of venous blood sample from each patient was collected in a vacutainer without anticoagulant and serum was extracted by centrifugation at 3000 rpm for 5 minutes at room temperature. Serum sample was dispensed in test tubes containing allergen covalently coupled to a cellulose derivative (ImmunoCAP). Following that enzyme (alpha-galactosidase generating a fluorescent cleavage product)-labeled anti-IgE antibodies were added and the contents were allowed to react for 30 minutes at temperature of 37°C. The unbound enzyme-anti-IgE was washed and the bound complexes were incubated for 10 minutes with a developing agent (4-methylumbelliferyl-beta-D-galactoside). Finally the reaction was stopped by stop solution and the response was recorded by measuring the fluorescence of the elute. The calibration range was from 0.1 to 100 kU/L and the IgE antibody concentrations were also translated into classes. Values <0.35 kU/L were considered negative, those between 0.36 and 0.70 kU/L were interpreted as Class 1, between 0.70 and 3.5 kU/L as Class 2, between 3.5 kU/L to 17.5 kU/L as Class 3, between 17.5 to 50 kU/L as Class 4, between 50 to 100 kU/L as Class 5 and values above 100 kU/L were assigned Class 6.

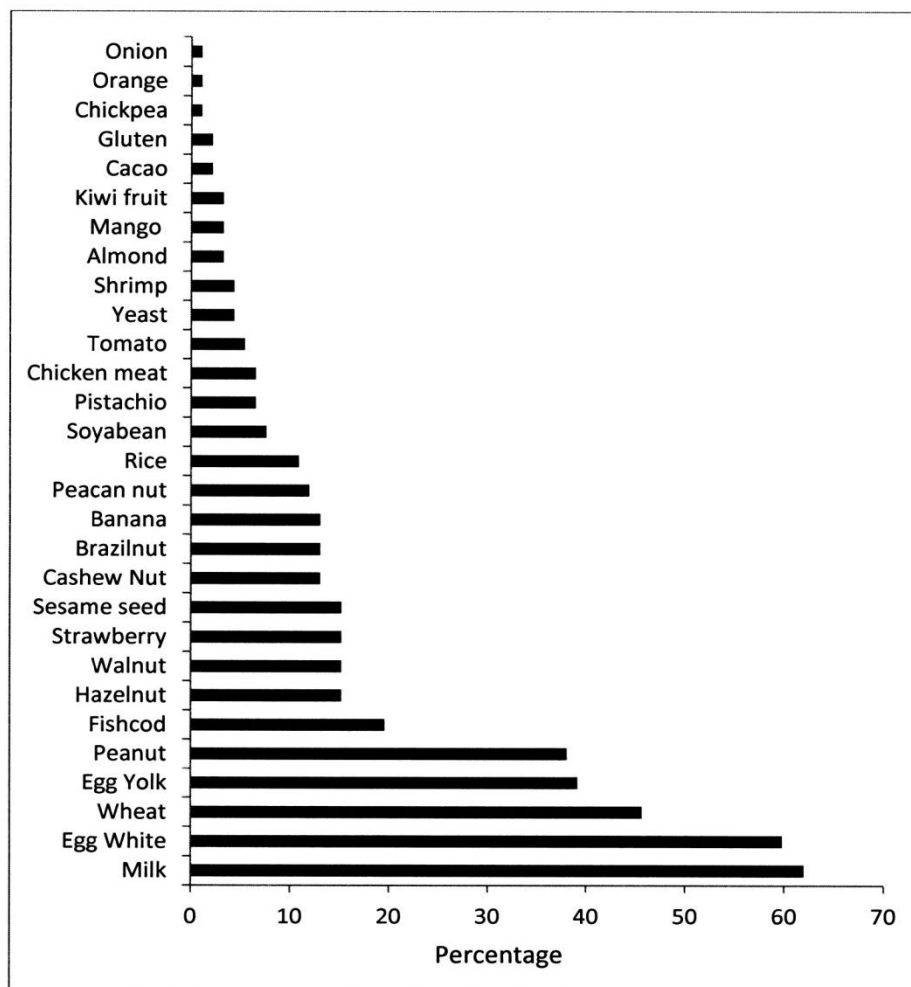


Figure 1:-Pattern of IgE mediated sensitization against food materials among patients with clinical suspicion of food allergy (n=92).

Statistical analysis:-

Data were analyzed using MedCalc Statistical Software version 11.5.0 for descriptive analysis and comparison of proportions. A $p < 0.05$ was considered statistically significant.

Results:-

Figure 1 shows data for the pattern of sensitization against different food materials. The most frequently occurring food specific IgE antibody among the patients was against milk which was present in 57 (61.96%) patients followed by egg white in 55 (59.78%) patients, wheat in 42 (45.65%), egg yolk in 36 (39.13%), peanut in 35 (38.04%) cod fish in 18 (19.75%), hazel nut in 14 (15.22%), walnut in 14 (15.22%), strawberry in 14 (15.22%), sesame seed in 14 (15.22%), cashew nut in 12 (13%) and brazil nut in 12 (13%) patients.

Comparison of sensitization for most frequently detected food specific IgE antibodies between male and female children revealed significant differences (Fig. 2). The proportions of sensitized male children were consistently higher than the females for egg white (47.4% vs 15.3%; $p < 0.0002$), egg yolk (33.3% vs 7.6%; $p < 0.0002$), milk (47.4% vs 22.1%; $p < 0.001$), wheat (37.5% vs 12.4%; $p < 0.0006$) and peanut (37.5% vs 11%; $p < 0.0007$). Analysis of the gender differences between the adult male and female patients was not performed because of the small numbers.

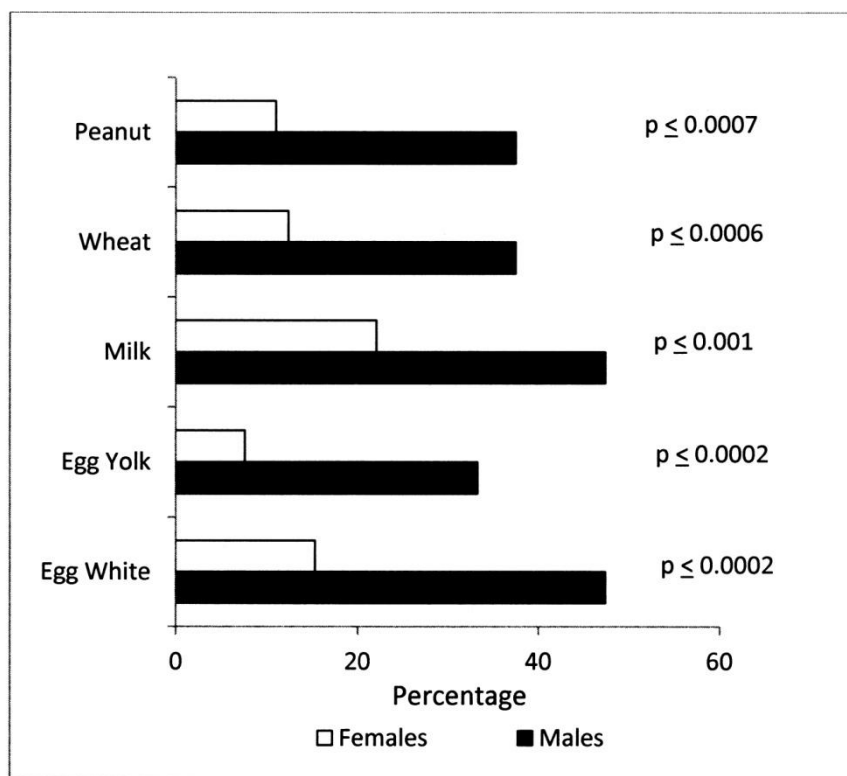


Figure 2:-Pattern of IgE mediated sensitization among males and females in the study population. (Males=67, Females=25)

Figure 3 shows data comparing proportions of children and adults harboring frequently detected food specific IgE. Higher proportions of children were found to have food specific IgE antibodies against milk, egg white, egg yolk, wheat and peanut allergens compared to adults. Among the adults egg white specific IgE were present in majority (50%) followed by peanut (42.8%) and wheat 35.7%). None of the adults was found have circulating food specific IgE against hazelnut, walnut and brazilnut compared to the children. Statistically significant difference was however detected only for milk specific IgE with a higher proportion of children harboring these antibodies.

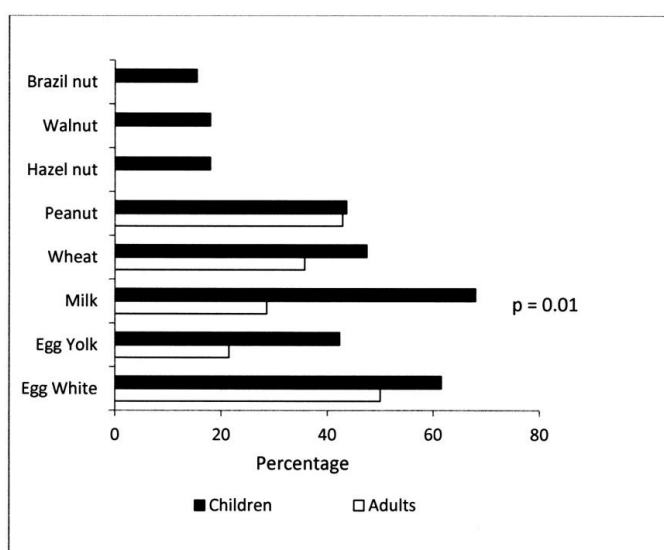


Figure 3:-Comparison of IgE mediated food sensitization among the adults and children. (Adults=14, Pediatrics=78)

Discussion:-

The most common sensitizing food allergens in this study were milk, egg, wheat, peanut and fish. These foods have been implicated in food allergy in young children all over the world although the pattern may vary in different regions with regards to the relative frequency of each allergen.^[16] Whereas egg allergy in Oceania and Asia^[17,18] appears to be more common than milk allergy, in the Americas and the Middle East milk allergy is more frequently observed than egg allergy.^[19-21] The later observation is in keeping with the findings of the present study indicating that the pattern of food sensitization appears to be concordant with the clinical diagnosis of food allergy at least in this instance. In addition, diagnosis of allergy due to egg, milk, peanut and fish can be predicted on the basis of previously established predictive decision points by quantifying serum levels of specific IgE antibodies against these foods.^[22]

Among several factors contributing to the variation in sensitization to food allergens in different locations local dietary habits appears to be a major determinant. A similar study performed over sixteen years from King Khalid University Hospital, Riyadh reported 17.2% patients harboring food specific IgE antibodies and peanut was the most frequent sensitizing allergen with milk as the third most common sensitizing allergen.^[23] In the present study food specific antibodies were detected in 32.8% patients and milk specific IgE antibodies were detected in the majority of the patients. These observations indicate that over the last one and a half decade not only the percentage of patients harboring food specific IgE antibodies has almost doubled but also reflect a change in the eating preferences of the patient population attending King Khalid University Hospital, Riyadh. Contrary to the findings of the present study wheat was recently reported to be the most frequent sensitizing food in a subset of patients suffering from food allergy in Riyadh.^[24] Discrepancy between the two studies from Riyadh may possibly be due to differences in study populations. Because of the insufficient existing data for food allergen sensitization in the Kingdom and being a single center study the findings of the present study may not reflect the pattern of food sensitization in general population.

Children comprised of 84.8% of the study group in this study where the proportion of sensitized male children was significantly higher than the female children. This observation was consistent with the previous meta-analysis of 591 published reports documenting a higher prevalence of food allergy among male children.^[25] Little is known about pre-pubertal male predisposition to allergy however as an X-linked recessive trait associated with allergy it is more likely to be expressed in male children predisposing them food allergy at a very young age.^[25] In addition the presence of higher concentrations of total IgE antibodies in the cord blood of male infants compared to the female not only indicates the tendency for having allergic disorders but also points to the genetic basis of male predisposition.^[26] The preponderance of allergy among adult females has been attributed to female hormones. Estrogen is believed to exert a stimulating effect on B cell differentiation resulting in production of higher amounts of immunoglobulins.^[27] Moreover, estrogen and progesterone have been shown to skew immune response towards Th2 type thus promoting antibody mediated immune reactions.^[28] Small numbers prevented the comparison for food sensitization between the adult male and female populations in the present study thus making it difficult to interpret the data.

Whereas the milk was the most frequent sensitizing allergen among the children egg while was the most common sensitizing allergen among the adults in the present study. Similar findings have been reported previously where adults were reported to frequently exhibit food sensitization against sea foods, fruits and vegetable and the most common food allergen sensitization among children was due to egg and milk allergens.^[29] Although higher sensitization against milk protein among children may be due increased exposure to milk protein as it is a major dietary component among children the role of other allergen related factors may also be critical in induction of food allergy. Juvenile rats exhibit a higher Ovalbumin sensitization rate compared to adult rats possibly by increasing permeability of intestinal tight junctions.^[30] It is highly likely that the differences in food allergen sensitization between the adults and the children could be due to allergens related factors capable of interfering with tight junction permeability in the gut. Age-related intestinal barrier dysfunction observed in rats is characterized by mucosal atrophy, tight junction damage with decreased epithelial tight junction protein and increased intestine bacteria counts may also be an important factor in determining allergen sensitization among children and adults.^[31]

In conclusion the most frequent sensitizing food materials detected in the present study were milk, egg, wheat, peanut and fish. The pattern of allergen sensitization was similar to already reported pattern of food sensitization. Gender differences were observed, sensitization against milk allergen was common among children whereas the majority of adults were sensitized against egg white. This being a retrospective study was limited by being a single

center study, small numbers and lacking skin prick data. Large scale studies across the Kingdom are recommended to gain a better understanding of the food allergen sensitization in the local population.

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