# FOOD ALLERGY

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## ABSTRACT

Introduction: Any adverse effect on health resulting from repeated exposure to a substance against which the individual has been sensitized against is allergy. Food allergens are one of the many common causes of allergies. The aim of this study is to find out the common food allergens and also specify the type of food suspicious for allergy among the patients with allergic reactions. A total of 178 patients with allergic reactions were included. The test was carried out using kit with an enzyme-labelled anti-human IgE catalysing a colour reaction. The kit contains test stripes coated with 21 different common antigens. Concentration of antibody specific to certain allergen is calculated and graded into different classes. Among the patients sensitized to allergic food, mean age was 34.36 years with female to male ratio of 2.9:1. Ninty two patients (51.7%) patients were sensitized to 1 to 3 allergens, whereas, 3.9% w ere sensitized to more than 10 food allergens. Thirty three (27.9%) patients had definite antibody detection, 11(9.3%) patients had strong antibody titre and 4 (3.3%) patients had very high antibody titre. Most common food allergen was crab (20.1%) followed by potato (25.8%). Cross reactivity was seen in various food allergens. Cereals and rice showed significant reactivity (P <0.001). Other food like soybean with mustard, peanut with coconut and apple with grape also showed significant correlation (P<0.001). The most common food allergens were crab, potato, spinach, peanut, coconut, soybean, mustard, wheat, rice, shrimp/prawn, cucumber and onion. While determining the specific allergen, we should be aware of potential cross-reactivity against one or more food allergens.

## KEYWORDS

Allergens, cross-reactivity, hypersensitivity reaction, IgE, sensitized

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## INTRODCUTION

Allergy is any adverse effect on the health of an individual resulting from repeated exposure to a substance against which sensitization has occurred. It is an immediate hypersensitivity reaction and is usually IgE mediate reaction. When an individual is exposed to a specific allergen, the reaction can range from mild form with urticarial rashes to a severe form of anaphylaxis leading to even death of the individual. The response to the allegen can be rapid to delayed, which depends upon type and dose of allergen, immune status of the individual and comorbidities.[1]

Allergens can be of various types. Dust allergens and food allergens are the most common ones.[1] An adverse health effect arises due to specific immune response of one's body after initial exposure to a given food.[2] Like other allergic reactions, food allergy may be either IgE mediated or non-IgE mediated. Diagnosis of IgE-mediated food allergy needs sensitization and formation of allergen specific IgE bound to mast cells. Non-IgE mediated food allergies are characterized by delayed gastrointestinal reactions to foods, such as food protein induced enterocolitis syndrome or proctocolitis. Eosinophilic gastrointestinal disorders are also commonly triggered by foods.[1]

Any food may be the cause for allergic condition. But "priority food allergens" are responsible for over 90% of all food related allergic reactions. These priority food allergens include cow's milk and other dairy products, egg, peanuts, nuts, sesame, soybeans, mustard, fish, crustaceans, shellfish and gluten containing cereals like wheat, rye, barley.[3-7] Even fruits like kiwi, apple grape and other vegetables may cause allergic reactions, though not much common.[8]

Priority food allergens are not same in all the countries and varies a lot.[8,12,13] The reason may be the food habit, different environment and varying genetic predisposition. Food allergies are prevalent in many part of the world. In USA, it is estimated that allegy is prevalent among 3.5-4% population,[9,10] where only peanuts and tree nut allergy is seen in 1% of population.[11]

There are various methods of detection of food allergies, which includes polymerase chain reaction, skin prick test, antigen specific antibody detection and self-declaration methods.

Unfortunately, no nation-wise data is available regarding prevalence of allergies in developing countries like Nepal, except few from China and India.[12,13] In this study, we are trying to find out the prevalence of food allergens and also specify the type of food suspicious for allergy.

## MATERIALS AND METHODS

This is a record based study conducted in Kathmandu Pathlab & Diagnostic Center Pvt. Ltd. Data from March 2017 to February 2018 were collected from medical archive. Demographic data along with all the findings were entered in Microsoft Excel. Patient with signs and symptoms suggestive of allergic reactions that were sent for the investigation were included in the study.

The test was carried out using kit with an enzyme-labelled anti-human IgE (Enzyme conjugated) catalysing a colour reaction. The kit contains test stripes coated with 21 different common antigens. These antigens are cow's milk, milk powder, egg yolk, wheat flour, rice, soybean, peanut, coconut, apple, grape, potato, spinach, onion, cucumber, chicken, mustard, coffee, ginger, crab, shrimp/prawn, kiwi fruit and apricot. If samples contain specific antibodies of class IgE, they will bind to the allergens coated on the stripe. Concentration of antibody specific to certain allergen is calculated and graded into different classes (Table 1). The data were transferred in SPSS-21 and were analysed for mean, correlation of co-efficient and P-value among similar foods. P-value less than <0.05 was considered as significant.

## RESULTS

During the study period, i.e. from March 2017 to February 2018, a total of 178 patients visited to the laboratory for allergy testing. Mean age of the patient was 35.43 years with minimum being 3 years and maximum 79 years of age. There was female preponderance, with female to male ratio of 2.56:1. Among the studied population, 60 patients (33.7%) with clinical signs and symptoms of allergy didn't shows any sensitization to allergic food reactions to the above mentioned foods (Table 1). Out of remaining 118 patients sensitized to allergic food, mean age was 34.36 years with female to male ratio of 2.9:1.

| Table 1: Classes of antibody concentration against different allergens | | |
|---|---|---|
| **Concentration (kU/L)** | **Class** | **Explanation** |
| <0.35 | 0 | No specific antibodies detection |
| 0.35-0.7 | 1 | Very weak antibody detection |
| 0.7-3.5 | 2 | Weak antibody detection |
| 3.5-17.5 | 3 | Definite antibody detection |
| 17.5-50 | 4 | Strong antibody detection |
| 50-100 | 5 | Very high antibody titer |
| >100 | 6 | Extremely high antibody titer |

| Table 2: Frequency and number of allergens sensitized among study population | | |
|---|---|---|
| Numbers of allergens | Frequency | Percent |
| 0 | 60 | 33.7 |
| 1-3 | 92 | 51.7 |
| 4-6 | 13 | 7.3 |
| 7-9 | 6 | 3.4 |
| ≥10 | 7 | 3.9 |
| **Total** | **178** | **100.0** |

These patients were sensitized to 1 or more than one food allergens. Ninty two patients (51.7%) patients were sensitized to 1 to 3 allergens, whereas, 7 patients (3.9%) were sensitized to more than 10 food allergens (Table 2). One patient was sensitized to 15 different types of food allergens.

Among the 118 patients, 70 patients (59.3%) were sensitized to some food allergens. They had either very weak or weak antibody detection. Out of 48 remaining patients, 33 (27.9%) patients had definite antibody detection, 11 (9.3%) patients had strong

| Table 3: Common food allergens tested and their grade of detection | | | | | | | |
|---|---|---|---|---|---|---|---|
| Grade | Cow's milk n (%) | Milk powder n (%) | Egg yolk n (%) | Chicken n (%) | Crab n (%) | Shrimp/ Prawn n (%) | Wheat n (%) | Rice n (%) |
| No specific antibodies detection | 173 (97.25%) | 171 (96.1%) | 174 (97.8%) | 174 (97.8%) | 128 (71.9) | 165 (92.7%) | 157 (88.2%) | 161 (90.4%) |
| Very weak antibody detection | 5 (2.8%) | 7 (3.9%) | 4 (2.2%) | 4 (2.2%) | 33 (18.5%) | 6 (3.4%) | 11 (6.2%) | 8 (4.5%) |
| Weak antibody detection | 0 | 0 | 0 | 0 | 8 (4.5%) | 4 (2.2%) | 3 (1.7) | 4 (2.2%) |
| Definite antibody detection | 0 | 0 | 0 | 0 | 4 (2.2%) | 1 (0.6%) | 6 (3.4%) | 5 (2.8%) |
| Strong antibody detection | 0 | 0 | 0 | 0 | 3 (1.7%) | 0 (0.0%) | 1 (0.6%) | 0 |
| Very high antibody titer | 0 | 0 | 0 | 0 | 2 (1.1%) | 2 (1.1%) | 0 | 0 |

| | Mustard n (%) | Soybean n (%) | Peanut n (%) | Coconut n (%) | Apple n (%) | Grape n (%) | Potato n (%) | Spinach n (%) |
|---|---|---|---|---|---|---|---|---|
| No specific antibodies detection | 149 (83.7%) | 152 (85.4%) | 150 (84.3%) | 157 (88.2%) | 169 (94.9%) | 170 (95.5%) | 132 (74.2%) | 150 (84.3%) |
| Very weak antibody detection | 23 (12.9%) | 15 (8.4%) | 20 (11.2%) | 17 (9.6%) | 6 (3.4%) | 5 (2.8%) | 29 (16.3%) | 21 (11.8%) |
| Weak antibody detection | 5 (2.8%) | 7 (3.9%) | 3 (1.7%) | 3 (1.7%) | 3 (1.7%) | 3 (1.7%) | 10 (5.6%) | 4 (2.2%) |
| Definite antibody detection | 1 (0.6%) | 2 (1.1%) | 4 (2.2%) | 1 (0.6%) | 0 | 0 | 4 (2.2%) | 2 (1.1%) |
| Strong antibody detection | 0 | 2 (1.1%) | 1 (0.6%) | 0 | 0 | 0 | 3 (1.7%) | 1 (0.6%) |
| Very high antibody titer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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| | Onion n (%) | Cucumber n (%) | Coffee n (%) | Ginger n (%) | Kiwi n (%) | Apricot n (%) |
|---|---|---|---|---|---|---|
| No specific antibodies detection | 168 (94.4%) | 165 (92.7%) | 175 (98.3%) | 171 (96.1%) | 177 (99.4%) | 177 (99.4%) |
| Very weak antibody detection | 5 (2.8%) | 10 (5.6%) | 2 (1.1%) | 6 (3.4%) | 0 | 0 |
| Weak antibody detection | 4 (2.2%) | 2 (1.1%) | 1 (0.63%) | 1 (0.6%) | 1 (0.6%) | 1 (0.6%) |
| Definite antibody detection | 1 (0.6%) | 1 (0.6%) | 0 | 0 | 0 | 0 |
| Strong antibody detection | 0 | 0 | 0 | 0 | 0 | 0 |
| Very high antibody titer | 0 | 0 | 0 | 0 | 0 | 0 |

| Table 4: Frequencies of animal food allergies in the various age groups | | | | | |
|---|---|---|---|---|---|
| Age Group (years) | Number of Patients | Cow's Milk n (%) | Egg Yolk n (%) | Milk Powder n (%) | Shrimp/Prawn n (%) | Crab n (%) |
| 1-18 | 15 | 1 (6.66) | 0 | 1 (6.66) | 1 (6.66) | 5 (33.33) |
| 19-48 | 136 | 4 (2.9) | 4 (2.9) | 4 (2.9) | 11 (8.1) | 37 (27.2) |
| 48-80 | 27 | 0 | 0 | 2(7.4) | 1(3.7) | 8(29.6) |

antibody titre and 4 (3.3%) patients had very high antibody titre (Table 3).

Most common food allergen against which patients were sensitized to was crab (n=50; 20.1%) followed by potato (n=36; 25.8%) (Table 3). Least common food allergen among the study population was apricot and kiwi fruit which was observed only in 1 (0.6%) patient each. 15 out of 118 patients with food allergies were less than 18 years of age.

Different age group had prevalence of different types of food allergens. Table 4 shows prevalence of various types of animal food allergies in this age group. Crab remains the most common type of animal food in all age groups ranging from 27.2% in 19 to 48 age group category to 33.3% in pediatric age group (1-18 years). Among vegetable food allergens studied, potato and spinach were the most common allergens. In pediatric population potato and spinach both were seen in 26.8% patients with

| Table 5: Frequencies of vegetable food allergies in the various age groups | | | | | |
|---|---|---|---|---|---|
| Age Group (years) | Number of patients | Cucumber n (%) | Onion n (%) | Spinach n (%) | Potato n (%) |
| 1-18 | 15 | 3 (20) | 2 (13.4) | 4 (26.8) | 2 (26.8) |
| 19-48 | 136 | 10 (7.4) | 8 (5.9) | 21 (15.4) | 38 (27.9) |
| 48-80 | 27 | 0 | 0 | 3 (11.1) | 4 (14.8) |

| Table 6: Frequencies of food allergies against nuts, soybean and mustard in the various age groups | | | | | |
|---|---|---|---|---|---|
| Age Group (years) | Number of patients | Coconut n (%) | Peanut n (%) | Soybean n (%) | Mustard n (%) |
| 1-18 | 15 | 1 (6.66) | 2 (13.3) | 4 (26.6) | 2 (26.6) |
| 19-48 | 136 | 20 (14.7) | 26 (19.1) | 21 (15.4) | 22 (16.2) |
| 48-80 | 27 | 0 | 0 | 1 (3.7) | 3 (11.1) |

| Table 7: Sex –wise and age-wise frequency of sensitized patients to number of allergen | | | | | |
|---|---|---|---|---|---|
| **Sex** | **Age group (years)** | **No allergen** | **1 allergen** | **>1 allergens** | **Total** |
| | 1-14 | 1 | 1 | 3 | 5 |
| | 15-18 | 2 | 0 | 3 | 5 |
| **Male** | 19-48 | 14 | 6 | 16 | 36 |
| | 48-100 | 3 | 0 | 1 | 4 |
| | **Total** | **20** | 7 | **23** | **50** |
| | 1-14 | 0 | 1 | 0 | 1 |
| | 15-18 | 1 | 1 | 2 | 4 |
| **Female** | 19-48 | 29 | 29 | 42 | 100 |
| | 48-100 | 10 | 8 | 5 | 23 |
| | **Total** | **40** | **39** | **49** | **128** |

| Table 8: Statistical analysis of various food allergens | | | | | |
|---|---|---|---|---|---|
| **Allergens** | **Cow's milk** | **Egg Yolk** | **Milk Powder** | **Chicken** | **Crab** | **Shrimp** |
| **Cow's milk** | | .006* | .000** | .733 | .527 | .869 |
| **Egg yolk** | .006* | | .028* | .761 | .323 | .643 |
| **Milk powder** | .000 | .028 | | .684 | .610 | .971 |
| **Chicken** | .733 | .761 | .684 | | .647 | .643 |
| **Crab** | .527 | .323 | .610 | .647 | | .000** |
| **Shrimp** | .869 | .643 | .971 | .643 | .000** | |
| **Allergens** | **Potato** | **Onion** | **Cucumber** | **Spinach** | **Ginger** | |
| **Potato** | | .000** | .000** | .000** | .003* | |
| **Onion** | .000** | | .000** | .000** | .001** | |
| **Cucumber** | .000** | .000** | | .000** | .006* | |
| **Spinach** | .000** | .000** | .000** | | .078 | |
| **Ginger** | .003* | .001** | .006* | .078 | | |

**. Correlation is significant at the 0.01 level (2-tailed).    *. Correlation is significant at the 0.05 level (2-tailed).

allergies (Table 5). In adult population (19-48 years) potato was the most common allergen seen in 37 patients (27.2%) followed by spinach in 21 (15.4%) patients. Similarly, 20% pediatric population were sensitized against wheat flour, whereas, 1.5% and 2.7% population were sensitized among the age group of 19-48 years and 49-80 years respectively. Similar findings were observed against rice with 20%, 9.6% and 3.7% sensitized among age group of 1-18 years, 19-48 years and 49-80 years respectively. Frequencies of allergic reaction against coconut, peanut, mustard and soybean is shown in table 6. Sensitization against peanut was seen in 15.7% (28/178) population. All the cases were younger than 49 years of age. Almost 27% of the study population who were sensitized to mustard and soybean were of pediatric age group. Coconut sensitization was observed in adult population (n=20, 11.2%).

Many of the study population were sensitized against more than one food allergens. Among 178 studied populations 72 patients (40.4%) were sensitized to more than one food allergens. Among these 72 patients female outnumbered the males. Almost 68.1% females were sensitized to more numbers of allergens in comparison to male patients (Table 7). However, P value was not significant (P>0.05). Age-wise individual sensitized to more number of allergens were seen in increasing age group with significant P value. (P<0.05)

Cross reactivity was observed in various food allergens. Cereals and rice showed significant reactivity (P <0.001). Other food like soybean with mustard, peanut with coconut and apple with grape also showed significant correlation (P<0.001). Statistical analyses of correlation which demonstrate possible cross-reactivity among various foods are shown in Table 8. In the study cross-reactivity among crab and shrimp is significant. Similar finding was observed among cow's milk, milk powder and egg yolk (Table 8). Among vegetables significant cross-reactivity was observed among potato, cucumber, onion and spinach along with ginger.

## DISCUSSION

Food allergy usually affects population of all ages and is one of the serious public health problems. Since sensitization and tolerance against particular food occurs in infancy and early childhood period, priority should be given to the pediatric population. There is evidence of increased prevalence of food allergy during the last 1-2 decades.[4,14] Currently, no treatment for food allergy exists. Managing the disease involves identification of specific allergen and strict dietary avoidance of the allergen along with symptomatic management. Diagnosis and management of the disease can vary between clinical practice settings. Food allergy can be of IgE-mediated and non-IgE-mediated, with former causing severe allergic reaction than the latter. Lactose intolerance; an example of non-IgE mediated food allergic conditions; is self-limiting and usually doesn't recur.

IgE-mediated food allergy is the classical example of immediate type of hypersensitivity reaction. The most severe clinical form of manifestation is anaphylaxis. It is a systemic manifestation of allergic reaction and usually involves multiple organs. It is triggered by allergen cross-linking ofIgE bound to the surface of mast cells or basophils,[15] Mast cells and basophils are the the major source of chemical mediators responsible for the clinical features of anaphylaxis. Other cells, namely neutrophils and macrophages along with IgG have been described to contribute to anaphylaxis.[16-18]

Out of 178 patients with clinical feature of allergic reaction, who visited to the laboratory for allergy testing, 118 patients (66.3%) were sensitized against one or more food allergens. A study done in South India had prevalence rate of 26.5% individuals sensitized to food allergens.[19] However, this study was done as a screening test in the community and our study was done among the patients with clinical features of allergy. High level of allergic patients sensitized to food allergens was observed in a study done in Singapore. Chiang et al found 40% among studied 227 children were sensitized against egg.[20] Allergic reactions are more common in females than in males. In the present study, pediatric population has male predominance whereas in adult prevalence rate of food allergy was much higher in females than in males (71% vs.19.4%). Similar findings were observed in other studies.[21-23] In their study, they observed that male predominance before puberty and slow and steady rise in adulthood and ultimately female preponderance in adulthood. This interesting fact may be associated with immune system of the female. As we know that most of the autoimmune diseases are more prevalent in females and that peak of these diseases are seen in adulthood.

Theoretically, any food containing a protein could elicit an allergic reaction. More than 90% of food allergies are triggered by the following 11 food types: cow's milk, egg, wheat, soy, fish, shellfish, peanut, tree nuts (cashew, walnut, hazelnut, etc.), sesame, celery, and mustard seed.[24] In our study, among animal protein, crab was the most common food our patients were sensitized against, followed by shrimp/prawn. Forty four percent of patients who were allergic to food allergens were allergic to crab and 11% were allergic to shrimp/prawn. Similarly, 3.38% of patients were sensitized against hen egg and cow's milk. In North America, it is estimated to be 1.5% and 2.5% respectively.[25] Milk allergy affects up to 2.5% of infants, with approximately 1% of all children developing IgE-mediated milk allergy and approximately 1.5% of children developing non-IgE-mediated milk allergy.[26]

Potato and spinach were the most common vegetable food against which our patients were sensitized against with prevalence rate of 37.2 % and 23.7 % respectively. Other foods like cucumber and onion were also common food against which patients were sensitized (11.0% and 8.4% respectively). Significant numbers of patients in our study were also sensitized against peanut (23.7%) and coconut (17.7%). Among celery, 14.4% of total 118 patients sensitized to food allergens had IgE antibody against rice and 17.7% patients had IgE antibody against wheat. Similarly 21.7% patients were sensitized against soybean and 20.3% against mustard. Hence, in our study most common food allergens were crab, potato, spinach, peanut, coconut, soybean, mustard, wheat, rice, shrimp/prawn, cucumber and onion in descending order. All of these food allergens were observed in more than 10% of allergic patients. In China,[27] Thailand,[28] Korea,[29] Singapore,[30] similar foods were more prevalent to cause allergy. Though less prevalent; patients were sensitized against fruits like chicken, milk, coffee, apple, grapes and even kiwi fruit and apricot.

Cross-reactivity is a common phenomenon in allergic reactions and occurs when immune mechanism directed against specific antigen causes reactivity to other antigens. The classical example is molecular mimicry in rheumatic heart disease. It is well-known that certain component cross-reacts with others. Ara h 8, present in peanut, frequently cross-reacts with birch pollen allergens.[30] In our study, there is significant correlation among various food allergens (Table 8). It is well known that animal proteins, frequently cross-react to each other. Since a group of food that we consume originate and comprise of similar allergen, cross-reactivity is quite frequent.[30] Another drawback may be the diagnostic procedure used. IgE levels against whole food containing different antigen (allergens) would not discriminate between IgE to the two allergens with differing potential to cross-react.[30] Polymerase chain reaction is highly specific, however, sensitivity is low and isn't always helpful to the treating physician. Skin prick test, is one of the reliable and time tested method of identifying the specific allergen. However, it may also have some serious complications in few patients. Serum antibody detection is less invasive and cost-effective method of detection but with limited specificity. Cross reactivity is quite common and false positive is one of the common hurdles in this method of detection. Thus, a laboratory investigation along with self-declaration method is the only solution for the optimal management of the patient.

In Conclusion, food allergy is a complex, multifactorial disease with increasing prevalence worldwide. Various countries have different common food allergens. In this study, the most common food against which patients were sensitized against were; were crab, potato, spinach, peanut, coconut, soybean, mustard, wheat, rice, shrimp/prawn, cucumber and onion. While determining the specific allergen, we should be aware of potential cross-reactivity against one or more food allergens. Proper study regarding, identification of allergens prevalent in our community is mandatory so as to minimize potential health hazard, as the only management is to suggest the patient to remain distant from the specific allergen.

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