ORIGINAL RESEARCH ARTICLE

Food-specific IgG Antibody Levels in Indian Subjects: A Retrospective Analytical Study

Shailesh Desai[1], Moumita Misra[2], Raj Jatale[3], Alap Christy[4], Shibani Ramchandran[5]

Received on: 28 February 2024; *Accepted on:* 04 June 2024; *Published on:* 19 August 2024

Abstract

Background: Many adverse food reactions have shown association with the presence of food-specific IgG antibodies in human serum. However, testing for such antibodies for diagnosis of adverse food reactions remains controversial. This study aimed was to understand the significance of food-specific IgG antibodies among patients who presented with food-dependent gastrointestinal symptoms viz upset stomach, bloating, etc.

Materials and methods: A total of 2,748 cases who underwent testing for specific IgGs for 200+ food items under the 'food intolerance test' over 3 years from Jan 2020 to Dec 2022 across different Indian geographical regions were included in the study. The microarray food IgG assay was used to measure over 215 types of food-specific serum IgG antibodies, with the top 25 most common food IgGs found based on the biological reference interval further analyzed.

Results: Barley (98.70%), pea (96.70%), sheep milk (87.20%), and cow milk (86.40%) were found to be the most prevalent food IgG antibodies. Corn maize, goat milk, cashew nut, pistachio, potato, soya bean, wheat, peanut, and hazelnut were found to be significantly associated with gender. Intolerance to cashew nuts, pistachio, potato, peanut and hazelnut was found to be significantly higher in females than males, whereas only corn maize was found to be significantly higher in males than female. Except for sunflower seed ($p = 0.0551$) all the other 24 food IgG concentrations showed a significant relation with age-group. Intra-group correlation among 25 food items showed a positive correlation between milk (cow) and casein ($r = 0.919$), pea and cola nut ($r = 0.721$), cashew nut, and pistachio ($r = 0.753$). The food intolerance seen in the study was mainly for vegetarian food.

Conclusion: The study emphasizes the role of testing food-specific IgG antibodies in adverse food reactions which may further help in the diagnosis, management, and treatment of patients presenting with food-related gastrointestinal symptoms.

Keywords: Food intolerance, IgG antibody, Microarray.

Indian Journal of Medical Biochemistry (2024): 10.5005/jp-journals-10054-0236

Introduction

Food intolerance, by definition, encompasses a non-immunological response triggered by a food or food component at a dose normally tolerated by the population, and accounts for most adverse food responses.[1] Food intolerance is found to affect up to 20% of the world's population and is more common as compared to food allergy.[2] In 2022, the market for food intolerance products was valued at USD 16.1 billion globally, with gluten-free, lactose-free, and diabetic products leading the list (Food Intolerance Products Market, Food Allergy Market 2022). A food intolerance predominantly involves the digestive system and causes less serious life-threatening symptoms. The double-blind, placebo-controlled food challenge (DBPCFC) is widely regarded as the gold standard for diagnosing adverse food reactions, including food allergies and intolerances. However, due to its inconvenience, expense, and time-consuming nature, it is not always feasible to carry out this type of challenge in large populations, as indicated by the expert panel of the U.S. National Institute of Allergy and Infectious Diseases.[3] Few previous studies suggested the poor response to an IgG-based diet questioning the diagnostic accuracy of food intolerance testing.[4–7] Alpay K et al. reported in their cross-over study on patients with migraines, that there was a reduction in episodes of the migraine attacks in patients when diet restrictions based on IgG antibodies was prescribed.[8] Atkinson W et al. also established that selective food elimination based on IgG has been effective in the treatment of irritable bowel syndrome.[9] There are research studies showing that a low FODMAP diet is useful in the management of functional gastrointestinal symptoms in cases like IBS, where food intolerance is suspected.[10] It is however recommended that exclusion should be followed only for as short time as possible for symptom improvement followed by gradual reintroduction of the individual contents based on the food intolerance results. A recent Indian study suggested that devising elimination diets should be based on individual patients rather than a fixed dietary regimen for all patients as they have been observed to be associated with various demographic factors, regional influence, etc.[11]

[1–5]Department of Clinical Chemistry, Metropolisindia.com, Mumbai, Maharashtra, India

Corresponding Author: Shailesh Desai, Department of Clinical Chemistry, Metropolisindia.com, Mumbai, Maharashtra, India, Phone: +91 7718001683, e-mail: shailesh.desai@metropolisindia.com

How to cite this article: Desai S, Misra M, Jatale R, *et al*. Food-specific IgG Antibody Levels in Indian Subjects: A Retrospective Analytical Study. Indian J Med Biochem 2024;28(3):63–71.

Source of support: Nil

Conflict of interest: None

Objective

The study objective was:

- To study blood IgG profile for food intolerance in the Indian population.
- To determine the relationship between demographic factors, including regional variations with IgG findings.
- To determine Intra-group correlation of food IgG concentrations amongst each other.

Materials and Methods

A retrospective study was conducted on 2,748 cases in Global Reference Lab in Mumbai, India for a period of 3 years from 2020 to 2022. A total of 215 food-specific IgG antibodies were measured using quantitative microarray-based ELISA of which 25 most commonly found food IgG antibodies were included in the study. We have assessed the overall prevalence as well as intra-group association of food-specific IgG antibodies to food items.

Food-specific Serum IgG Assays

The serum/plasma of participants was collected and sent. The concentrations of 215 different food-specific IgGs were measured using Food Print® Microarray 200+ Food IgG 16pt Kit.[12]

Principle of the Test

Around 215 food extracts are applied onto a nitrocellulose pad placed on a glass microscope slide. These food extracts were then incubated with either patient serum or plasma in a sample diluent. Post that, any unbound proteins were washed away, and anti-human IgG conjugated to horseradish peroxidase was added to the pads. This conjugate is bound to food extract-bound IgG antibodies in the primary incubation. The unbound conjugate was removed by washing, and a solution containing 3, 3′5,′5′- tetramethylbenzidine and enzyme substrate was added to detect specific antibody binding. The slides were then washed with distilled water and dried by centrifugation before scanning. The optical densities of the standards, positive and negative controls, and samples were measured using a high-resolution flatbed scanner with associated Genarrayt® reporting software.

Performance	*Outcome*
Relative sensitivity	96.6%
Relative specificity	98.8%

Biological reference interval for serum IgG Assay is <24 negative, 24–30 borderline, and >30 positive. Internal IgG standards included in the array are used for deriving the results.

Statistical Analysis

All data recording was done in MS Excel. Continuous variables are written as median values interquartile range (IQR) and range. Discrete variables are summarized in terms of frequencies and percentages. Shapiro–Wilk test determined whether data sets differed from a normal distribution. For comparison of continuous variables (food concentration) between three or more groups (age-group) Kruskal–Wallis test was used and the Mann–Whitney *U* test for two groups (gender). Pearson's correlation coefficient was used to analyze relation between food concentrations among the 25 food items. Regression coefficients and *p*-values were derived from multivariate linear regression models that set gender (male, 0; female, 1) and age as independent variables and the Box Cox transformation food concentrations for 25 foods as dependent variables. Two-sided *p*-value of less than 0.05 was considered to be statistically significant. All statistical test was done using R Studio 2022.07.2 + 576 "Spotted Wakerobin".

Table 1: Baseline characteristics of the study population

Demographic details	*Frequency*	*Percentage (%)*
Age-group (years)		
<18	318	11.57%
18–40	1,222	44.47%
41–60	931	33.88%
>60	277	10.08%
Gender		
Female	1,448	52.69%
Male	1,300	47.31%

Results

The median age of the patients included in the study was 39.6 years. The majority of the cases fall in the younger age-group, i.e., 18–40 years (44.47%) followed by 41–60 years (33.88%). A slightly higher percentage of female cases was observed (52.69% female vs 47.31% male) (Table 1).

Among the top 25 food IgG antibodies, barley showed the highest positivity (98.70%), followed by pea (96.70%), sheep milk (87.20%), cow milk (86.40%) and yeast brewer's (82.30%) (Table 2, Fig. 1).

From the 25 food items, corn (Maize) ($p = 0.002519$), cashew nut ($p = 0.030737$), pistachio ($p = 0.009874$), potato ($p = 0.017957$), peanut ($p = 0.001060$) and hazelnut ($p = 0.000338$) were found to be statistically significant between female and male. Only corn maize concentration was found to be higher in females compared to males with median value 48 vs 44. All the other food items had higher concentrations in males (Table 3).

Except sunflower seed ($p = 0.0551$) all the other 24 food IgG concentrations showed a significant relation with age-group.

Food IgG concentration of milk (sheep), milk (cow), egg white, casein, milk (goat), cashew nut, pistachio, bean (White haricot), almond, potato, soya bean, wheat, bean (red kidney), peanut and gliadin showed a decreasing trend with age-group. While food IgG concentration of barley, pea, yeast (Brewer's), cola nut, corn (maize), agar, and plum showed an increasing trend with age (Table 4).

Overall distribution showed that maximum patients showed intolerance towards gluten-containing grains followed by intolerance for vegetables and dairy/egg. Non-vegetarian food such as meat (4.04%), and fish/seafood (62.26%) showed lower positivity accounting for lesser chances of food intolerance (Table 5).

The majority of the population showed higher intolerance towards vegetarian food items compared to non-vegetarian food.

Regional comparison across India showed that the majority of patients 75.95% ($N = 2,087$) were from the West with lesser contributions from other regions (Table 6).

Table 2: Distribution of food-specific IgG concentrations

			IgG positive (>30 U/mL)	
Sr. No	*Food*	*Type*	*Frequency*	*Percentage*
1	Barley	Grains (gluten-containing)	2,713	98.70%
2	Pea	Vegetables	2,657	96.70%
3	Milk (Sheep)	Dairy/Eggs	2,395	87.20%
4	Milk (Cow)	Dairy/Eggs	2,375	86.40%
5	Yeast (Brewer's)	Miscellaneous	2,261	82.30%
6	Egg white	Dairy/Eggs	2,168	78.90%
7	Cola nut	Miscellaneous	2,163	78.70%
8	Corn (Maize)	Grains (gluten-free)	2,045	74.40%
9	Casein	Dairy/Eggs	2,021	73.50%
10	Milk (Goat)	Dairy/Eggs	1,854	67.50%
11	Cashew nut	Nuts/Seeds	1,820	66.20%
12	Pistachio	Nuts/Seeds	1,762	64.10%
13	Bean (White haricot)	Vegetables	1,684	61.30%
14	Agar	Miscellaneous	1,667	60.70%
15	Almond	Nuts/Seeds	1,626	59.20%
16	Plum	Fruit	1,600	58.20%
17	Potato	Vegetables	1,491	54.30%
18	Soya bean	Vegetables	1,412	51.40%
19	Wheat	Grains (gluten-containing)	1,364	49.60%
20	Bean (Red kidney)	Vegetables	1,296	47.20%
21	Peanut	Nuts/Seeds	1,272	46.30%
22	Gliadin	Grains (gluten-containing)	1,207	43.90%
23	Sunflower seed	Nuts/Seeds	1,203	43.80%
24	Hazelnut	Nuts/Seeds	1,175	42.80%
25	Yeast (Baker's)	Miscellaneous	1,145	41.70%

Figure 1 shows intra-group correlation of 25 food-specific IgG antibodies amongst themselves cell in red determine a high correlation whereas cells in dark green determine no correlation. It was observed that sheep milk, goat milk, and cow milk show a very strong positive correlation among themselves. Similarly, casein was observed to have a strong positive correlation with sheep milk and cow milk. Also, cashew nut with pistachio, corn (maize) with plum, cola nut with plum, and wheat with gliadin were found to have a strong positive correlation (Table 7).

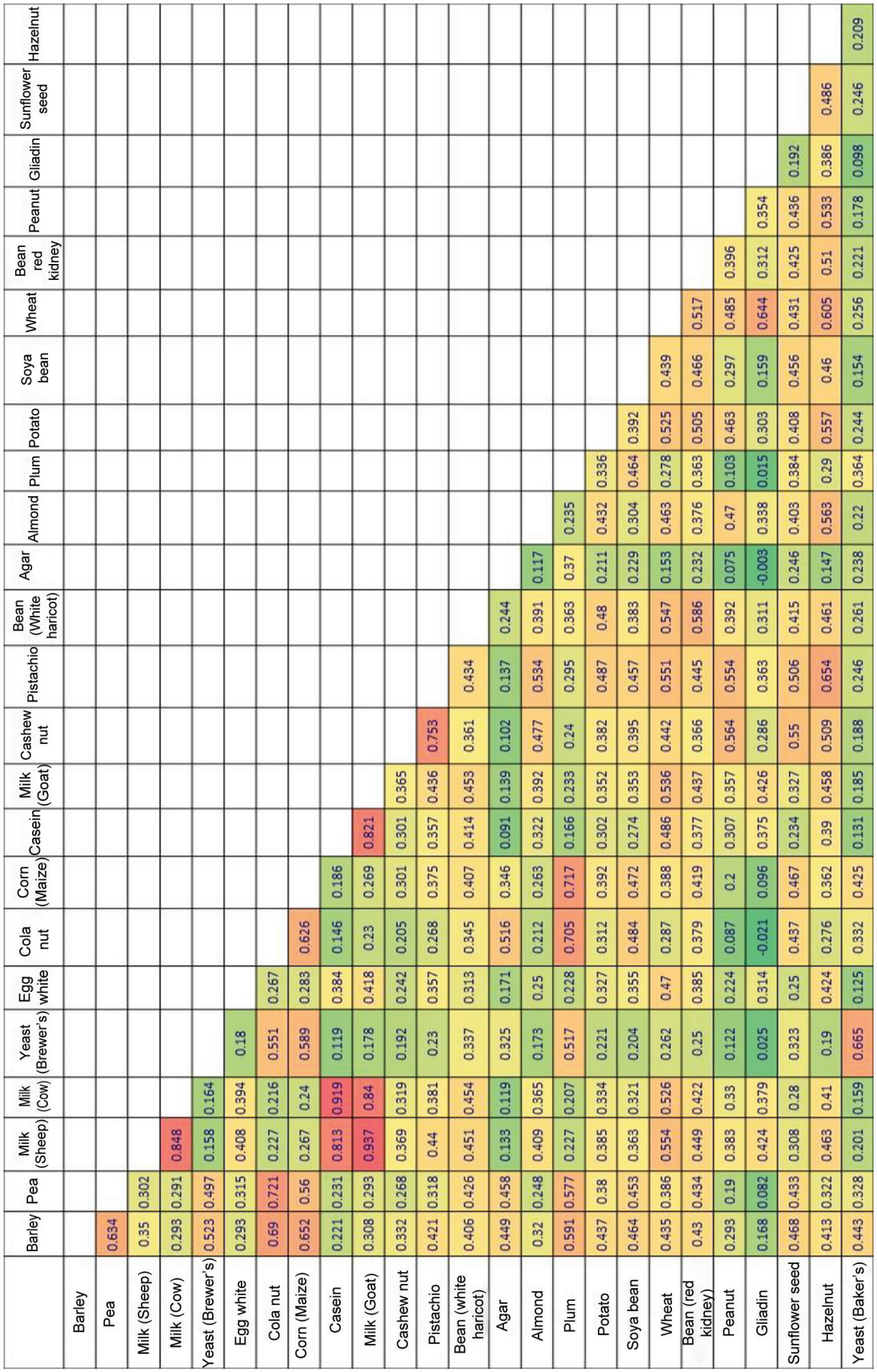
Discussion

This study highlights the serum IgG profile in Indian subjects with self-reported food intolerance in the current study, out of 25 food items tested for IgG antibody positivity, most patients showed intolerance for barley (98.70%), followed by pea (96.70%), sheep milk (87.20%), cow milk (86.40%) and yeast brewer's (82.30%) (Table 2). Shakoor Z et al. reported that, among the 223 food items tested, food-specific IgG against cola nut (80.3%), brewer's yeast (78.9%), and wheat (77.5%) were most common among the patients clinically presenting with symptoms.[13] Another study by Antico A et al., have reported a higher prevalence of specific IgGs against egg (77.8%), milk (62%), and casein (57.8%) among patients suffering from urticarial, asthma, rhinitis, and atopic eczema.[14] In an Indian study by Kumar R et al. conducted among patients suffering from asthma, specific IgG antibodies against cow's milk (56%), tiger nut (48%), and casein (48%) were found to be the most frequently occurring antibodies.[15]

Our study suggested that food intolerance is significantly more common in males than in females, which was in contrast with the observations of a study from China by Zeng Q et al., which had a higher concentration of food-specific IgG in females compared to males for 12 out of 14 food items.[16] Similarly, a study by Pizza V et al. documented higher levels of food-specific IgG levels among females compared to males for 10 out of 11 food items.[17] However, the study conducted by Poulos LM et al. reported that the prevalence of food intolerance is higher among boys than girls.[18] L Chang et al. suggested that despite numerous studies supporting female predisposition for developing food intolerance, some supportive research suggests that there are no gender differences in development of IgG-mediated food intolerance.[19]

We observed that the majority of the cases of high IgG food concentration fell in the young age-group, i.e., 18–40 years (44.47%) followed by 41–60 years (33.88%) which was significant for all the food items tested in the present study (Table 4). In the study conducted by Shakoor Z et al., patients aged between 20 and 39 were compared with 40–60 years of age, and revealed that the younger age-group had higher levels of egg white and gliadin-specific IgG for the 11 most commonly occurring food-specific IgG in their study.[13] A study by Zeng Q et al. found a similar comparison between younger and older age-groups wherein the younger age-group was found to have higher levels of egg-specific IgG antibodies compared with the older age-group.[16] Intestinal mucosa seems to mature with increasing age which may influence food intolerance resulting in differential immune responses to food-specific IgG antibodies. Harduar-Morano et al. reported that elderly people are more prone to experience allergic reactions to foods than the younger populations.[20]

The Indian population has multiple religions, ethnicities, across India and they differ in their food habits remarkably. North Indian population consumed wheat as it is predominantly grown cereal there while rice forms the main part of the diet in Southern and Eastern India. Western and Eastern Coastal lines predominantly consume fish and fish products while milk and dairy products are mainly consumed in states such as the Punjab. Meat is also consumed more or less equally across the Indian population. The majority of the study population was from the Western region of India accounting for 75.95%, which could possibly indicate food intolerance common among this population with self-reported cases (Table 6). While other regions of India accounted for 24.05% of the study population with either fewer self-reported cases of food intolerance or this population did not undergo testing for food intolerance. A study by Lee HJ et al. has highlighted the need to identify region-specific food intolerances



	Barley	Pea	Milk (Sheep)	Milk (Cow)	Yeast (Brewer's)	Egg white	Cola nut	Corn (Maize)	Casein	Milk (Goat)	Cashew nut	Pistachio	Bean (White haricot)	Agar	Almond	Plum	Potato	Soya bean	Wheat	Bean red kidney	Peanut	Gliadin	Sunflower seed	Hazelnut
Barley																								
Pea	0.634																							
Milk (Sheep)	0.35	0.302																						
Milk (Cow)	0.293	0.291	0.848																					
Yeast (Brewer's)	0.523	0.497	0.158	0.164																				
Egg white	0.293	0.315	0.408	0.394	0.18																			
Cola nut	0.69	0.721	0.227	0.216	0.551	0.267																		
Corn (Maize)	0.652	0.56	0.267	0.24	0.589	0.283	0.626																	
Casein	0.221	0.231	0.813	0.919	0.119	0.384	0.146	0.186																
Milk (Goat)	0.308	0.293	0.937	0.84	0.178	0.418	0.23	0.269	0.821															
Cashew nut	0.332	0.268	0.369	0.319	0.192	0.242	0.205	0.301	0.301	0.365														
Pistachio	0.421	0.318	0.44	0.381	0.23	0.357	0.268	0.375	0.357	0.436	0.753													
Bean (white haricot)	0.406	0.426	0.451	0.454	0.337	0.313	0.345	0.407	0.414	0.453	0.361	0.434												
Agar	0.449	0.458	0.133	0.119	0.325	0.171	0.516	0.346	0.091	0.139	0.102	0.137	0.244											
Almond	0.32	0.248	0.409	0.365	0.173	0.25	0.212	0.263	0.322	0.392	0.477	0.534	0.391	0.117										
Plum	0.591	0.577	0.227	0.207	0.517	0.228	0.705	0.717	0.166	0.233	0.24	0.295	0.363	0.37	0.235									
Potato	0.437	0.38	0.385	0.334	0.221	0.327	0.312	0.392	0.302	0.352	0.382	0.487	0.48	0.211	0.432	0.336								
Soya bean	0.464	0.453	0.363	0.321	0.204	0.355	0.484	0.472	0.274	0.353	0.395	0.457	0.383	0.229	0.304	0.464	0.392							
Wheat	0.435	0.386	0.554	0.526	0.262	0.47	0.287	0.388	0.486	0.536	0.442	0.551	0.547	0.153	0.463	0.278	0.525	0.439						
Bean (red kidney)	0.43	0.434	0.449	0.422	0.25	0.385	0.379	0.419	0.377	0.437	0.366	0.445	0.586	0.232	0.376	0.363	0.505	0.466	0.517					
Peanut	0.293	0.19	0.383	0.33	0.122	0.224	0.087	0.2	0.307	0.357	0.564	0.554	0.392	0.075	0.47	0.103	0.463	0.297	0.485	0.396				
Gliadin	0.168	0.082	0.424	0.379	0.025	0.314	-0.021	0.096	0.375	0.426	0.286	0.363	0.311	-0.003	0.338	0.015	0.303	0.159	0.644	0.312	0.354			
Sunflower seed	0.468	0.433	0.308	0.28	0.323	0.25	0.437	0.467	0.234	0.327	0.55	0.506	0.415	0.246	0.403	0.384	0.408	0.456	0.431	0.425	0.436	0.192		
Hazelnut	0.413	0.322	0.463	0.41	0.19	0.424	0.276	0.362	0.39	0.458	0.509	0.654	0.461	0.147	0.563	0.29	0.557	0.46	0.605	0.51	0.533	0.386	0.486	
Yeast (Baker's)	0.443	0.328	0.201	0.159	0.665	0.125	0.332	0.425	0.131	0.185	0.188	0.246	0.261	0.238	0.22	0.364	0.244	0.154	0.256	0.221	0.178	0.098	0.246	0.209

Fig. 1: Intragroup correlation of 25 food-specific IgG antibodies (Dark red determine high correlation while dark green highlights no correlation)

Table 3: Gender and food-specific IgG concentration relationship

	Gender		
	Female	*Male*	
	Median (IQR)	*Median (IQR)*	*p-value*
Barley	75.00 (64–87)	75.50 (63–88)	0.984764
Pea	74 (57–95)	74 (56–94)	0.218380
Milk (Sheep)	64 (42–85)	65 (43.50–88)	0.096567
Milk (Cow)	89 (50–114)	88 (50–116)	0.974682
Yeast (Brewer's)	49 (36–66)	48 (35–61)	0.111655
Egg white	57 (32–90)	58.50 (35–90)	0.234676
Cola nut	59 (35–78)	59 (36–78)	0.717329
Corn (Maize)	48 (31–68)	44 (29–64)	0.002519
Casein	67 (29–99)	66 (28–101)	0.853609
Milk (Goat)	44 (24–66)	45 (25–69)	0.087043
Cashew nut	40 (23–59)	42 (26–62.50)	0.030737
Pistachio	38 (24–59)	42 (25–63)	0.009874
Bean (White haricot)	37 (22.50–55)	37 (23–55)	0.875400
Agar	39 (22–67)	36 (20–64)	0.137401
Almond	35.50 (21–55)	37 (22–57)	0.134994
Plum	37 (18–55)	35 (18–54)	0.479725
Potato	32 (21–46)	34 (23–48)	0.017957
Soya bean	31 (15–48)	32 (15–49)	0.076952
Wheat	30 (21–40)	31 (22–42)	0.075152
Bean (Red kidney)	29 (16–43)	29 (16.50–42)	0.558800
Peanut	28 (18–41)	30 (19–44)	0.001060
Gliadin	26 (15–48)	25 (15–51)	0.419727
Sunflower seed	27 (16–43)	27 (17–44)	0.612115
Hazelnut	26 (15–40)	29 (17–46)	0.000338
Yeast (Baker's)	26 (15–42)	25 (15–42)	0.374623

Table 4: Age and food specific IgG concentration relationship

	Age-group				
	<18	*18–40*	*41–60*	*>60*	
	Median (IQR)	*Median (IQR)*	*Median (IQR)*	*Median (IQR)*	*p-value*
Barley	68 (56–80)	74 (63–85)	79 (67–90)	79 (67.75–91)	<0.0001
Pea	63 (48–81)	76 (59–95)	76 (59–97)	69 (52–91.25)	<0.0001
Milk (Sheep)	83 (63–100)	65 (44–86)	61 (40–83)	53 (33.75–74)	<0.0001
Milk (Cow)	111 (85–127)	90 (53–115)	81 (43–112)	65 (34–100)	<0.0001
Yeast (Brewer's)	34.50 (18–48)	49 (36–62)	50 (38–66.75)	56 (41.75–74)	<0.0001
Egg white	86.50 (51–113)	62 (35–93)	51 (32–79)	43 (27–71.25)	<0.0001
Cola nut	36 (19–52)	60 (38–77)	64 (42.25–83)	62 (33–97)	<0.0001
Corn (Maize)	37 (21–57)	45 (30–63)	49 (33–70)	50 (32–76)	<0.0001
Casein	94.50 (65–116)	68 (32–100)	59 (20–96)	44 (15–80.25)	<0.0001
Milk (Goat)	63 (42–81)	44 (27–66)	42 (21–64)	34 (15–58)	<0.0001
Cashew nut	45 (26–68)	41.50 (24–61)	41 (26–60)	39 (22.75–55)	<0.0001
Pistachio	50 (29–77)	38 (23–59)	40 (24–58)	36 (24–59)	<0.0001

(Contd...)

Table 4: *(Contd...)*

	Age-group				
	<18	*18–40*	*41–60*	*>60*	
	Median (IQR)	*Median (IQR)*	*Median (IQR)*	*Median (IQR)*	*p-value*
Bean (White haricot)	49 (25–66)	36 (23–55)	35 (21–53)	31 (18–50)	<0.0001
Agar	19 (15–34)	38 (22–65)	44 (26–71)	37 (21–64)	<0.0001
Almond	45 (27–63)	33 (21–53)	36 (21–54)	40 (24.75–59)	<0.0001
Plum	23 (15–37)	35 (19–52)	41 (21–58)	46 (17.75–65)	<0.0001
Potato	43 (28–68)	32 (22–44)	31 (21–45)	31 (21–44.25)	<0.0001
Soya bean	37.50 (19–55)	32 (15–49)	30 (15–46)	26 (15–45)	<0.0001
Wheat	44 (35–55)	30 (22–40)	28 (20–37)	26 (19–35)	<0.0001
Bean (Red kidney)	37 (24–54)	29 (17–42)	28 (15–41)	25 (15–39)	<0.0001
Peanut	36 (20–51)	29 (18–42)	28 (18–40)	27 (17.75–40.25)	<0.0001
Gliadin	61 (35–83)	25 (15–47)	21 (15–40)	18 (13–43)	<0.0001
Sunflower seed	26 (15–40)	27 (17–42)	29 (17–45)	27 (15–41)	0.0551
Hazelnut	42 (23–66)	26.50 (16–42)	25 (15–39)	25 (15–39)	<0.0001
Yeast (Baker's)	17 (15–29)	26 (15–41)	27 (15–45)	34 (18.75–52)	<0.0001

Table 5: Overall distribution of food intolerance

	Food IgG (N = 2,748)			
	Positive		*Negative*	
	Frequency	*Percentage*	*Frequency*	*Percentage*
Grains (Gluten-containing)	2,724	99.13%	24	0.87%
Vegetables	2,688	97.82%	60	2.18%
Dairy/Egg	2,616	95.20%	132	4.80%
Miscellaneous	2,571	93.56%	177	6.44%
Nuts/Seeds	2,485	90.43%	263	9.57%
Grains (Gluten-free)	2,245	81.70%	503	18.30%
Fruit	2,126	77.37%	622	22.63%
Fish/Sea food	1,711	62.26%	1,037	37.74%
Herbs/Spices	1,335	48.58%	1,413	51.42%
Meat	111	4.04%	2,637	95.96%

Table 6: Region wise distribution of positive food intolerance cases

	Region wise distribution									
	Central (N = 14)		*East (N = 51)*		*North (N = 168)*		*South (N = 428)*		*West (N = 2,087)*	
	N	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*
Dairy/Egg										
Negative	0	0.00%	2	3.92%	10	5.95%	25	5.84%	95	4.55%
Positive	14	100.00%	49	96.08%	158	94.05%	403	94.16%	1992	95.45%
Fish/Seafood										
Negative	4	28.57%	19	37.25%	68	40.48%	146	34.11%	800	38.33%
Positive	10	71.43%	32	62.75%	100	59.52%	282	65.89%	1287	61.67%
Fruits										
Negative	1	7.14%	11	21.57%	47	27.98%	117	27.34%	446	21.37%
Positive	13	92.86%	40	78.43%	121	72.02%	311	72.66%	1641	78.63%

(Contd...)

Table 6: *(Contd...)*

	Region wise distribution									
	Central (N = 14)		*East (N = 51)*		*North (N = 168)*		*South (N = 428)*		*West (N = 2,087)*	
	N	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*
Grains (Gluten-containing)										
Negative	0	0.00%	1	1.96%	1	0.60%	8	1.87%	14	0.67%
Positive	14	100.00%	50	98.04%	167	99.40%	420	98.13%	2073	99.33%
Grains (Gluten-free)										
Negative	2	14.29%	11	21.57%	35	20.83%	95	22.20%	360	17.25%
Positive	12	85.71%	40	78.43%	133	79.17%	333	77.80%	1727	82.75%
Herbs/Spices										
Negative	7	50.00%	25	49.02%	90	53.57%	228	53.27%	1063	50.93%
Positive	7	50.00%	26	50.98%	78	46.43%	200	46.73%	1024	49.07%
Meat										
Negative	13	92.86%	49	96.08%	163	97.02%	411	96.03%	2001	95.88%
Positive	1	7.14%	2	3.92%	5	2.98%	17	3.97%	86	4.12%
Miscellaneous										
Negative	1	7.14%	5	9.80%	11	6.55%	40	9.35%	120	5.75%
Positive	13	92.86%	46	90.20%	157	93.45%	388	90.65%	1967	94.25%
Nuts/Seeds										
Negative	1	7.14%	7	13.73%	14	8.33%	51	11.92%	190	9.10%
Positive	13	92.86%	44	86.27%	154	91.67%	377	88.08%	1897	90.90%
Vegetables										
Negative	0	0.00%	1	1.96%	7	4.17%	13	3.04%	39	1.87%
Positive	14	100.00%	50	98.04%	161	95.83%	415	96.96%	2048	98.13%

with a high prevalence of food items such as whole milk, noodles, pizza, gluten foods, etc., in Korean patients with irritable bowel syndrome. Also, food intolerance due to herbs and spices was found in significant proportion in the Korean population which was least common in our study population.[21]

Vegetarian foods such as gluten-containing grains (99.13%), and vegetables (97.82%) accounted for the most common foodstuffs to be positive for food intolerance while dairy products and eggs contributed to 95.20% for positive food intolerance (Table 5). This was contrary to milk products being the most common cause of food intolerance in a study conducted by Abraham P et al. in patients with Irritable bowel syndrome (IBS).[11] Lactose intolerance is seen in 60% of the Indian population is the most common type of intolerant disease (lactose intolerance; www.medlineplus.gov).[22] As per our study, we found gluten food intolerance due to gluten-rich foods followed by lactose intolerance due to dairy products. Ramakrishna BS reported the prevalence of celiac disease commonly in Northern India especially in state of Ludhiana.[23] Gluten-rich food testing in our study was positive mainly in Northern India accounting for 99.40% and a few central parts of the Indian population. Southern Indian population too has tested positive for gluten-rich foods which is in contrast to various studies mentioning that the prevalence of celiac disease is not significant in the southern population with rice being the major part of the staple diet.[23,24]

Prescribing dietary regimes for patients of IBS gastrointestinal symptoms, states that diets such as FODMAP diets should focus on food intolerance to individual food contents rather than eliminating food groups as a whole. Abraham et al. reported that individuals' intolerance varied widely among a list of high-FODMAP items suggesting that symptomatic individuals should decide on their elimination diets rather than diet just based on the FODMAP content alone among the Indian population.[11] Studies by Hochwallner H et al. and Stapel et al. indicate that food-specific IgGs and IgG subclasses lack diagnostic value for food intolerance as standalone tests that supplement diagnosis along with clinical symptoms as in the case of celiac disease that requires anti-transglutaminase antibody positivity.[7,10,25,26]

Study Limitations

The present study does not include enough data on chronic symptoms for all the patients who participated in this study nor about their symptom exacerbation triggered by food items that they tested positive for. We tested for the presence of serum IgGs against only commonly consumed foods by the Indian population which did not include levels of specific IgG antibodies against pollen and food additives. Also, our study lacks enough data for a definitive diagnosis of the spectrum of conditions associated with food intolerance such as celiac disease, IBS, and lactose intolerance.

Table 7: Association of demographic (age and gender) with serum food-specific IgG concentrations

	Age				*Gender*			
Variable	*Regression coefficient*	*95% CI*	*SE*	*p-value*	*Regression coefficient*	*95% CI*	*SE*	*p-value*
Barley	0.19964	0.1582–0.2411	0.0211	<0.0001	0.01795	(–1.3878)–1.4231	0.7166	0.9800
Pea	0.01015	0.0036–0.0166	0.00332	0.00223	0.146093	(–0.0745)–0.3667	0.1125	0.1942
Milk (Sheep)	–0.070847	(–0.0827)–(–0.0589)	0.0061	<0.0001	–0.394477	(–0.7971–0.00816	0.2053	0.0548
Milk (Cow)	–0.3628	(–0.4215)–(–0.3041)	0.0299	<0.0001	–0.02452	(–2.0173–1.96835	1.0163	0.9810
Yeast (Brewer's)	0.023597	0.02003–0.02715	0.0018	<0.0001	0.095345	(–0.0254–0.2161	0.0616	0.1220
Egg white	–0.008269	(–0.00968)–(–0.006852)	0.0007	<0.0001	–0.03561	(–0.0836–0.0124	0.0245	0.1460
Cola nut	0.023727	0.01941–0.02803	0.0022	<0.0001	–0.039418	(–0.1855)–0.1067	0.0745	0.597
Corn (Maize)	0.015293	0.01134–0.01923	0.0020	<0.0001	0.178215	0.0445–0.3120	0.0682	0.0090
Casein	–0.038908	(–0.0448)–(–0.03293)	0.0030	<0.0001	0.006048	(–0.1967)–0.2088	0.1033	0.953
Milk (Goat)	–0.026699	(–0.03108)–(–0.022308)	0.0022	<0.0001	–0.153642	(–0.3026)–(–0.0047)	0.0759	0.0432
Cashew nut	–0.007117	(–0.011234)–(–0.0029991)	0.0021	0.00071	–0.152208	(–0.2919)–(–0.0126)	0.0712	0.0326
Pistachio	–0.012491	(–0.01678)–(–0.0081948)	0.0022	<0.0001	–0.201299	(–0.3470)–(–0.0556)	0.0743	0.0068
Bean (White haricot)	–0.018228	(–0.022143)–(–0.014312)	0.0019	<0.0001	–0.033732	(–0.1667)–0.0992	0.0677	0.6190
Agar	0.021698	0.016612–0.026784	0.0026	<0.0001	0.143697	(–0.0287)–0.3161	0.0879	0.1020
Almond	–0.002469	(–0.006348)–(0.001410)	0.0019	0.212	–0.098039	(–0.2296)–0.0335	0.0671	0.1440
Plum	0.02383	0.019891–0.027774	0.0020	<0.0001	0.05572	(–0.0779)–0.1894	0.0682	0.414
Potato	–0.01466	(–0.018216)–(–0.011120)	0.0018	<0.0001	–0.13797	(–0.2584)–(–0.0175)	0.0614	0.0247
Soya bean	–0.009348	(–0.013049)–(–0.0056456)	0.0018	<0.0001	–0.129776	(–0.2538)–(–0.0041)	0.0641	0.0429
Wheat	–0.02066	(–0.023193)–(–0.0181440)	0.0013	<0.0001	–0.09921	(–0.1848)–(–0.0135)	0.0436	0.0232
Bean (Red Kidney)	–0.014308	(–0.017655)–(–0.010960)	0.0017	<0.0001	0.038125	(–0.0754)–0.15167	0.0579	0.5100
Peanut	–0.008093	(–0.01142)–(–0.004757)	0.0017	<0.0001	–0.198239	(–0.3114)–(–0.0851)	0.0577	0.0005
Gliadin	–0.010038	(–0.011318)–(–0.008759)	0.00065	<0.0001	–0.02824	(–0.0717)–(0.01521)	0.0221	0.203
Sunflower seed	0.000203	(–0.001128)–(0.0015354)	0.0006	0.765	–0.013135	(–0.0583)–(0.03204)	0.0230	0.569
Hazelnut	–0.00669	(–0.00795)–(–0.00542)	0.0006	<0.0001	–0.08632	(–0.1293)–(–0.0434)	0.0219	<0.001
Yeast (Baker's)	0.006902	0.00546–0.008335	0.0007	<0.0001	0.02465	(–0.02397)–0.073274	0.0248	0.3200

Conclusion

This study provides valuable insights into demographic factors and food-specific IgG concentration. It highlights significant associations between age and food-specific IgG, which may be used in suggesting ag-related changes in subjects of food intolerance. Gender variation in food IgG is also observed, highlighting the importance of considering gender-specific factors in dietary assessments. These finding may help in understanding the spectrum of food intolerance and may be of some help to the treating physician in better management of the patients. Further research in this area can broaden the scope for new strategies, for patient management.

Orcid

Alap Christy https://orcid.org/0000-0002-1411-2279

References

1. Tuck CJ, Biesiekierski JR, Schmid-Grendelmeier P, et al. Food intolerances. Nutrients 2019;11(7):1684. DOI: 10.3390/nu11071684.
2. Chafen JJ, Newberry SJ, Riedl MA, et al. Diagnosing and managing common food allergies: A systematic review. JAMA 2010;303(18): 1848–1856. DOI: 10.1001/jama.2010.582.
3. Scott-Taylor TH, J OBH, Strobel S. Correlation of allergen-specific IgG subclass antibodies and T lymphocyte cytokine responses in children with multiple food allergies. Pediatr Allergy Immunol 2010;21(6):935–944. DOI: 10.1111/j.1399-3038.2010.01025.x.
4. Barnes RM. IgG and IgA antibodies to dietary antigens in food allergy and intolerance. Clin Exp Allergy 1995;25(suppl 1):7–9. DOI: 10.1111/j.1365-2222.1995.tb01124.x.
5. Zar S, Benson MJ, Kumar D. Food-specific serum IgG4 and IgE titers to common food antigens in irritable bowel syndrome. Am J Gastroenterol 2005;100(7):1550–1557. DOI: 10.1111/j.1572-0241.2005.41348.x.
6. Teuber SS, Porch-Curren C. Unproved diagnostic and therapeutic approaches to food allergy and intolerance. Curr Opin Allergy Clin Imunol 2003;3(3):217–221. DOI: 10.1097/00130832-200306000-00011.
7. Hochwallner H, Schulmeister U, Swoboda I, et al. Patients suffering from non-IgE-mediated cow's milk protein intolerance cannot be diagnosed based on IgG subclass or IgA responses to milk allergens. Allergy 2011;66(9):1201–1207. DOI: 10.1111/j.1398-9995.2011.02635.x.
8. Alpay K, Ertas M, Orhan EK, et al. Diet restriction in migraine, based on IgG against foods: A clinical double-blind, randomised, cross-over trial. Cephalalgia 2010;30(7):829–837. DOI: 10.1177/0333102410361404.
9. Atkinson W, Sheldon TA, Shaath N, et al. Food elimination based on IgG antibodies in irritable bowel syndrome: A randomised controlled trial. Gut 2004;53(10):1459–1464. DOI: 10.1136/gut.2003.037697.
10. Lomer MCE. Review article: The aetiology, diagnosis, mechanisms and clinical evidence for food intolerance. Aliment Pharmacol Ther 2015;41(3):262–275. DOI: 10.1111/apt.13041.
11. Abraham P, Dhoble P, Desai D, et al. Self-reported food intolerances in an Indian population: Need for individualization rather than a universal low-FODMAP diet. JGH Open 2023;7(11):772–776. DOI: 10.1002/jgh3.12981.
12. Shreffler WG, Lencer DA, Bardina L, et al. IgE and IgG4 epitope mapping by microarray immunoassay reveals the diversity of immune response to the peanut allergburten, Ara h 2. J Allergy Clin Immunol 2005;116(4):893–899. DOI: 10.1016/j.jaci.2005.06.033.
13. Shakoor Z, Alfaif A, Walamro B, et al. Prevalence of IgG-mediated food intolerance among patients with allergic symptoms. Annals of Saudi Medicine 2016;36(6):386–390. DOI: https://doi.org/10.5144/0256-4947.2016.386.
14. Antico A, Pagani M, Vescovi PP, et al. Food-specific IgG4 lack diagnostic value in adult patients with chronic urticaria and other suspected allergy skin symptoms. Int Arch Allergy Immunol 2011;155(1):52–56. DOI: 10.1159/000318736.
15. Kumar R, Kumar M, Singh M, et al. Prevalence of food intolerance in bronchial asthma in India. Indian J Allergy Asthma Immunol 2013;27(2):121–128. DOI: 10.4103/0972-6691.124394.
16. Zeng Q, Dong S-Y, Wu L-X, et al. Variable food-specific IgG antibody levels in healthy and symptomatic Chinese adults. PloS One 2013;8(1):e53612. DOI: 10.1371/journal.pone.0053612.
17. Pizza V, Mainenti M, Iannuzzi S, et al. Food intolerance in migraine. Pharmacologyonline 2013;1:18–24. Available from: https://pharmacologyonline.silae.it/files/archives/2013/vol1/PhOL_2013_1_A004_024_Pizza.pdf.
18. Poulos LM, Waters AM, Correll PK, et al. Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993–1994 to 2004–2005. J Allergy Clin Immunol 2007;120(4):878–884. DOI: 10.1016/j.jaci.2007.07.040.
19. Liu XJ, Zhu TT, Zeng R, et al. [An epidemiological study of food intolerance in 2434 children]. Zhongguo Dang Dai Er Ke Za Zhi 2013;15(7):550–554. Chinese. PMID: 23866277.
20. Harduar-Morano L, Simon MR, Watkins S, et al. A population based epidemiologic study of emergency department visits for anaphylaxis in Florida. J Allergy Clin Immunol 2011;128(3):594–600.e591. DOI: 10.1016/j.jaci.2011.04.049.
21. Lee HJ, Kim HJ, Kang EH, et al. Self-reported food intolerance in Korean patients with irritable bowel syndrome. J Neurogastroenterol Motil 2019;25(2):222–232. DOI: 10.5056/jnm18125.
22. Bhatnagar S, Aggarwal R. Lactose intolerance. BMJ 2007;334:1331. DOI: 10.1136/bmj.39252.524375.80.
23. Ramakrishna BS. Celiac disease: Can we avert the impending epidemic in India? Indian J Med Res 2011;133(1):5–8. PMID: 21321413.
24. Gupta R, Reddy DN, Makharia GK, et al. Indian task force for celiac disease: Current status. World J Gastroenterol 2009;15(48):6028–6033. DOI: 10.3748/wjg.15.6028.
25. Stapel SO, Asero R, Ballmer-Weber BK, et al. Testing for IgG4 against foods is not recommended as a diagnostic tool: EAACI task force report. Allergy 2008;63(7):793–796. DOI: 10.1111/j.1398-9995.2008.01705.x.
26. Gargano D, Appanna R, Santonicola A, et al. Food allergy and intolerance: A narrative review on nutritional concerns. Nutrients 2021;13(5):1638. DOI: 10.3390/nu13051638.