

Interpretation of food specific immunoglobulin E levels in the context of total IgE

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ABSTRACT

Background: Food specific immunoglobulin E (IgE) (fslgE) cut points are used in the evaluation of food allergies. Concomitant measurement of total IgE (tlgE) is traditionally not obtained. We anecdotally observed elevations in fslgE mirroring tlgE increases, which may confound accurate interpretation.

Objective: To determine whether changes in tlgE were associated with fslgE and whether predictions of fslgE could be formulated based on tlgE.

Methods: We studied children younger than 18 years who had both tlgE and fslgE (egg, n = 136; milk, n = 123; peanut, n = 201; soy, n = 55) obtained simultaneously on 1 or more occasion between January 2008 and February 2011. After institutional review board approval, natural log-transformed (ln) tlgE and fslgE levels were analyzed using univariate and multivariate regression models to assess associations and predict fslgE using tlgE and other covariates.

Results: Soy IgE levels were strongly correlated ($\rho = 0.85$, $P < .001$), whereas egg, milk, and peanut IgE levels were substantially correlated ($\rho = 0.69$, 0.69 , and 0.66 , respectively, $P < .001$) with tlgE. A 1-unit increase in ln(tlgE) was significantly correlated with unit increases in ln(egg IgE) (0.77), ln(milk IgE) (0.84), ln(peanut IgE) (0.87), and ln(soy IgE) (0.89) ($P < .001$). The ln(tlgE)-based univariate models could predict fslgE in the validation data with strong (soy) and substantial (egg, milk, and peanut) predictive ability ($P < .001$).

Conclusion: Our study found significant and parallel relationships between tlgE and fslgE levels to egg, milk, peanut, and soy. It underscores the importance of examining fslgE levels in context of tlgE while making diagnostic and management decisions in children with food allergies.

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Introduction

Food allergies affect approximately 8% of children in the United States, and both the prevalence and disease burden appear to be increasing.^{1,2} Common food allergens in children include egg, milk, peanut, and soy.³ The natural history of each food allergy can be extremely variable. For instance, approximately 80% of egg, milk, and soy allergic children outgrow their allergy by 16 years of age, whereas only 20% of peanut allergic children attain clinical tolerance over a lifetime.^{4–8} Restrictive diets in young children can lead to nutritional deficiencies, including severe malnutrition. Furthermore, food allergies are associated with social, emotional, and psychosocial deficits and an increased risk of repetitive bullying in school.^{9,10} These factors exemplify the importance of expanding our ability to accurately diagnose food allergies and evaluate onset of development of clinical tolerance.

Food specific immunoglobulin E (IgE) (fslgE) tests, in addition to clinical history and skin prick testing, have enhanced our ability to diagnose food allergies. Cut points with validated, decisional, and predictive fslgE levels have further improved our diagnostic accuracy and ability to predict development of clinical tolerance.¹¹

Nevertheless, the utility of fslgE in the management of food allergy has recognized limitations. Variability of results have been observed in relation to multiple factors, such as age and clinical characteristics of the patient population.¹² The quantity of total IgE (tlgE), a nonspecific indicator elevated in patients with allergic conditions, has not hitherto been considered a factor affecting the interpretation of fslgE. Measurement of tlgE is currently not recommended in the evaluation and management of food allergies.¹³

In our clinical practice, we anecdotally observed that fslgE levels often appear to be higher in patients with elevated tlgE levels, causing diagnostic confusion. We therefore postulate the existence of a strong correlation between tlgE and fslgE levels in children with suspected food allergy. Our primary aim was to examine the correlation between tlgE and fslgE (egg, milk, peanut, and soy) levels in children evaluated for food allergy. Our secondary aim was to formulate equations that predict the effect of tlgE on fslgE levels. Understanding the influence of a confounding variable, such as tlgE on fslgE levels, may enable practicing clinicians to better assess children with suspected food allergies.

Methods

Study Population

We analyzed retrospective data compiled by the Medical Research Department at our tertiary pediatric hospital from January

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2008 to February 2011 after institutional review board exemption of the study protocol based on the use of deidentified data. Our study criteria included children younger than 18 years seen at our tertiary pediatric hospital and affiliated outpatient clinics who had tIgE levels and fslgE levels (egg, milk, peanut, or soy) measured simultaneously on at least 2 occasions. Our data included levels of tIgE and fslgE, patient diagnoses, age at the time of the visit, sex, and ethnicity. Comorbid allergic diseases were defined based on *International Classification of Diseases, Ninth Revision (ICD-9)* codes: asthma (code 493), atopic dermatitis (code 691), and allergic rhinitis (code 477). Our only exclusion criterion was a documented diagnosis of hyperimmunoglobulin E syndrome. Diagnostic cut points, based on well-known, published data, were used as follows: egg, 7 kU/L if older than 2 years and 2 kU/L if 2 years or younger; milk, 15 kU/L if older than 2 years and 5 kU/L if 2 years or younger; peanut, 14 kU/L; and soy, 30 kU/L.^{11,14,15}

IgE Assays

Levels of tIgE were measured using ImmunoCAP with a lower detection limit of less than 2 kU/L. Levels of tIgE with a concentration below the detection limit were assigned a value of 1 kU/L. Levels of fslgE were measured using ImmunoCAP with a current detection range of 0.1 to 100 kU/L. Levels of fslgE with a concentration below the detection limit were assigned a value of 0.1 kU/L, and levels with a concentration above the detection limit were assigned a value of 100 kU/L.

Statistical Analysis

Pearson correlation, univariate, and multivariate regression models were applied to assess the association between tIgE and fslgE levels, taking covariates (age, sex, ethnicity, asthma, atopic dermatitis, and allergic rhinitis) into account. Because of skewed distributions, tIgE and fslgE levels were natural logarithmically transformed, denoted as $\ln(\text{tIgE})$ and $\ln(\text{fslgE})$, for statistical analysis. Regression models were constructed to predict $\ln(\text{fslgE})$ using $\ln(\text{tIgE})$ alone or $\ln(\text{tIgE})$ along with the other covariates. Levels of tIgE from the first clinical visit were used as training data to develop the predictive models for fslgE levels. The predictive ability of the regression models was further assessed using the second clinical visit tIgE and fslgE levels, which served as validation data. To further confirm our finding, we also performed linear regression analysis using $\ln(\text{fslgE})$ as the outcome variable and $\ln(\text{tIgE})$ – $\ln(\text{fslgE})$ as the risk factor. This analysis was performed after data with immeasurably high values of fslgE (exceeding the detection limit of 100) were excluded. We then analyzed the associations between the incremental changes in tIgE levels and fslgE levels between 2 visits. Two-tailed comparisons were made with statistical significance established at $P < .05$. All analyses were conducted using SPSS statistical software, version 18 (SPSS Inc, Chicago, Illinois), and SAS statistical software, version 9.2 (SAS Institute Inc, Cary, North Carolina).

Results

Study criteria was met by 136 patients with fslgE levels to egg, 123 patients with fslgE levels to milk, 201 patients with fslgE levels to peanut, and 55 patients with fslgE levels to soy. Demographic characteristics are summarized in Table 1. The mean age of the children at the initial testing was approximately 2 years. Most children were male, were white, and had commercial insurance. The characteristics of tIgE and fslgE are summarized in Table 2. In the first clinical visit 11 patients with egg IgE levels, 13 patients with milk IgE levels, 16 patients with peanut IgE levels, and 1 patient with soy IgE levels were above the detection limit of the ImmunoCAP assay. In the same data set 57% of egg IgE levels, 41% of milk IgE levels, 38% of peanut IgE levels, and 11% of soy IgE levels

Table 1

Demographic characteristics of the study participants

Characteristic	Egg (n = 136)	Milk (n = 123)	Peanut (n = 201)	Soy (n = 55)
Initial age, mean (SD), y	2.32 (2.32)	2.08 (2.48)	2.61 (2.27)	1.56 (2.12)
Age at follow-up, mean (SD), y	3.76 (2.56)	3.51 (2.82)	4.08 (2.51)	2.78 (2.33)
Sex, No. (%)				
Female	51 (37.5)	47 (38.2)	78 (38.8)	17 (30.9)
Male	85 (62.5)	76 (61.8)	123 (61.2)	38 (69.1)
Ethnicity, No. (%)				
White	91 (66.9)	80 (65.0)	137 (68.2)	35 (63.6)
African American	17 (12.5)	19 (15.4)	30 (14.9)	7 (12.7)
Hispanic	10 (7.4)	6 (4.9)	6 (3.0)	3 (5.5)
Other	18 (13.2)	18 (14.6)	28 (13.9)	10 (18.2)
Insurance, No. (%)				
Commercial	97 (71.3)	101 (82.1)	168 (83.6)	48 (87.3)
Government	35 (25.7)	20 (16.3)	32 (15.9)	7 (12.7)
Self	4 (2.9)	2 (1.6)	1 (0.5)	0
Diagnoses, No. (%)				
Asthma	65 (47.8)	47 (38.2)	103 (51.2)	15 (27.3)
Atopic dermatitis	86 (63.2)	64 (52.0)	114 (56.7)	26 (47.3)
Allergic rhinitis	77 (56.6)	53 (43.1)	120 (59.7)	23 (41.8)
Noncategorized	23 (16.9)	35 (28.5)	37 (18.4)	19 (34.5)

were above the diagnostic cut points. In all 4 foods analyzed the mean fslgE levels increased from the first to the second clinical visit along with increased tIgE levels.

We observed significant correlation between $\ln(\text{tIgE})$ and $\ln(\text{fslgE})$ for all 4 foods analyzed (Fig 1). There was a substantial correlation between $\ln(\text{tIgE})$ and $\ln(\text{fslgE})$ levels for egg, milk, and peanut ($\rho = 0.69, 0.69$, and 0.66 , respectively, $P < .001$). There was a strong correlation between $\ln(\text{tIgE})$ and $\ln(\text{fslgE})$ levels for soy ($\rho = 0.85$, $P < .001$). In light of substantial and strong correlations between $\ln(\text{tIgE})$ and $\ln(\text{fslgE})$, we performed univariate linear regression to predict $\ln(\text{fslgE})$ using $\ln(\text{tIgE})$. The first clinical visit data were analyzed using the formula $\ln(\text{fslgE}) = a + b \times \ln(\text{tIgE})$ where a is an intercept measuring the baseline $\ln(\text{fslgE})$ value and b is a slope measuring the rate of change in $\ln(\text{fslgE})$ in response to a 1-unit change of $\ln(\text{tIgE})$. The fitted predictive models are as follows:

$$\begin{cases} \ln(\text{egg IgE}) = -2.60 + 0.77 \times \ln(\text{tIgE}) \\ \ln(\text{milk IgE}) = -2.93 + 0.84 \times \ln(\text{tIgE}) \\ \ln(\text{peanut IgE}) = -3.06 + 0.87 \times \ln(\text{tIgE}) \\ \ln(\text{soy IgE}) = -4.62 + 0.89 \times \ln(\text{tIgE}) \end{cases} \quad (1)$$

The univariate linear regression models (1) indicated that a 1-unit increase in $\ln(\text{tIgE})$ was associated with mean (SD) unit

Table 2

IgE characteristics

Characteristic	Initial		Follow-up	
	fslgE	tIgE	fslgE	tIgE
Milk IgE				
Mean (SD)	21.8 (33)	1,130 (3,388)	27.0 (37)	1,281 (3,345)
Median	4.52	134	5.84	269
Maximum	100	23810	100	26090
Egg IgE				
Mean (SD)	21.2 (31)	1,243 (3,478)	21.6 (31)	1,349 (2,632)
Median	5.59	250	5.11	534
Maximum	100	26,090	100	16,990
Peanut IgE				
Mean (SD)	22.5 (31)	834 (2,310)	31.2 (38)	1,036 (2,122)
Median	7.00	214	9.49	349
Maximum	100	23,810	100	16,990
Soy IgE				
Mean (SD)	9.4 (19)	1,873 (4,860)	11.0 (21)	1,982 (4,726)
Median	0.50	128	1.34	269
Maximum	100	23,810	100	26,090

Abbreviations: fslgE, food specific IgE; tIgE, total IgE.

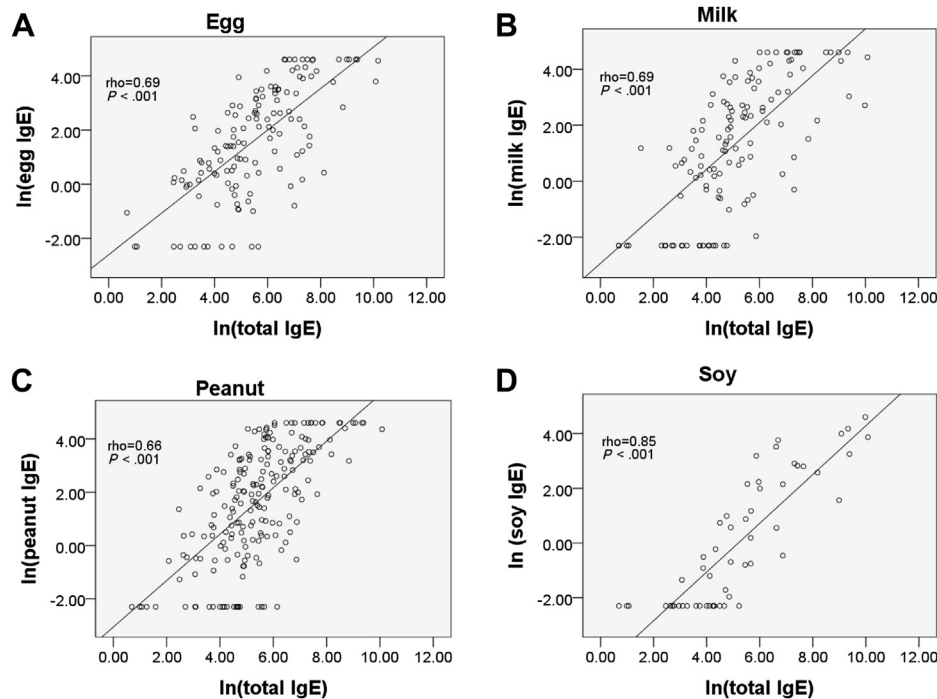


Figure 1. Scatterplots of natural log food specific IgE ($\ln(\text{fsIgE})$) vs natural log total IgE ($\ln(\text{tIgE})$). A, $\ln(\text{egg IgE})$ had a substantial correlation with $\ln(\text{tIgE})$. B, $\ln(\text{milk IgE})$ had a substantial correlation with $\ln(\text{tIgE})$. C, $\ln(\text{peanut IgE})$ had a substantial correlation with $\ln(\text{tIgE})$. D, $\ln(\text{soy IgE})$ had a strong correlation with $\ln(\text{tIgE})$.

increases of 0.77 (0.07) in $\ln(\text{egg IgE})$, 0.84 (0.08) in $\ln(\text{milk IgE})$, 0.87 (0.07) in $\ln(\text{peanut IgE})$, and 0.89 (0.08) in $\ln(\text{soy IgE})$ ($P < .001$). In this model 1 unit was defined as 1 kU/L on IgE testing.

Multivariate analysis was conducted on a general linear model for all 4 foods. Risk factors analyzed included $\ln(\text{tIgE})$, age, sex, ethnicity, and the diagnoses of asthma, atopic dermatitis, and allergic rhinitis (Table 3). Adjusted by these covariates, $\ln(\text{tIgE})$ continued to be significantly associated with $\ln(\text{fsIgE})$ for all 4 foods ($P < .01$). Age was also associated with fsIgE levels to egg. A 1-year increase in age was associated with a 0.27-unit decrease in $\ln(\text{egg IgE})$ ($P < .01$). The fsIgE levels to milk, peanut, and soy were not associated with the covariates based on this analysis. The multivariate analysis using tIgE along with the covariates provided a fair to good explanation for the variation of fsIgE levels ($r^2 = 0.56$ for egg, 0.52 for milk, 0.47 for peanut, and 0.76 for soy).

However, $\ln(\text{tIgE})$ significantly differed by age, ethnicity, atopic dermatitis, and allergic rhinitis (Table 3). A 1-year increase in age was associated with a mean (SD) unit increase of 0.21 (0.03) in

$\ln(\text{tIgE})$ ($P < .01$). African American children had a mean (SD) of 0.51 (0.34) unit higher $\ln(\text{tIgE})$ than white children ($P < .01$). Children with atopic dermatitis had a mean (SD) of 0.66 (0.16) unit higher $\ln(\text{tIgE})$ than those with no atopic dermatitis ($P < .01$). Children with allergic rhinitis had a mean (SD) of 0.33 (0.16) unit higher $\ln(\text{tIgE})$ than children with no allergic rhinitis ($P = .04$). Although these risk factors were significant, they did not provide a good prediction for tIgE ($r^2 = 0.19$) by multivariate analysis.

We used our patients' second clinical visit data for validation of our analysis and predictive models. The associations among $\ln(\text{tIgE})$, $\ln(\text{fsIgE})$, and risk factors as described above from the second clinical visit were consistent with the findings from the first clinical visit data. Because these risk factors were not significantly associated with $\ln(\text{fsIgE})$ for milk, peanut, and soy, and only age was associated with $\ln(\text{egg IgE})$, incorporating them into our models did not substantially increase the accuracy of predicting $\ln(\text{fsIgE})$. Therefore, predictive models were used for all foods using tIgE levels only as depicted previously. Validation of the equations

Table 3
Multivariate analysis

Variable	$\ln(\text{Soy IgE})$ ($r^2 = 0.56$)		$\ln(\text{Egg IgE})$ ($r^2 = 0.52$)		$\ln(\text{Milk IgE})$ ($r^2 = 0.47$)		$\ln(\text{Peanut IgE})$ ($r^2 = 0.76$)		$\ln(\text{tIgE})$ ($r^2 = 0.19$)	
	Estimate, mean (SD) (β)	P value	Estimate, mean (SD) (β)	P value	Estimate, mean (SD) (β)	P value	Estimate, mean (SD) (β)	P value	Estimate, mean (SD) (β)	P value
Intercept	-2.35 (0.48)	<.01	-2.86 (0.59)	<.01	-2.49 (0.49)	<.01	-4.03 (0.68)	<.01	5.33 (0.17)	<.01
Risk factors										
$\ln(\text{tIgE})$ per 1-unit increase	0.88 (0.08)	<.01	0.92 (0.09)	<.01	0.85 (0.07)	<.01	0.86 (0.09)	<.01		
Age per 1-year increase	-0.27 (0.06)	<.01	-0.08 (0.07)	.26	-0.08 (0.06)	.17	-0.10 (0.09)	.24	0.21 (0.03)	<.01
Sex, female vs male	0.23 (0.26)	.38	-0.54 (0.32)	.09	-0.18 (0.24)	.44	-0.26 (0.38)	.49	-0.20 (0.15)	.18
Ethnicity		.87		.39		.06		.12		<.01
African American vs white	-0.14 (0.37)	.71	-0.65 (0.44)	.14	0.47 (0.33)	.15	1.04 (0.60)	.09	0.62 (0.21)	<.01
Hispanic vs white	-0.01 (0.47)	.98	-0.77 (0.71)	.28	-1.38 (0.68)	.04	-0.70 (0.82)	.40	0.51 (0.34)	.14
Other vs white	-0.29 (0.37)	.43	-0.19 (0.44)	.66	0.35 (0.34)	.30	-0.41 (0.49)	.40	0.56 (0.21)	.01
Asthma vs no asthma	0.11 (0.27)	.68	0.39 (0.36)	.28	0.01 (0.26)	.96	0.13 (0.48)	.79	0.27 (0.17)	.11
AD vs no AD	0.19 (0.27)	.48	0.18 (0.33)	.58	0.30 (0.25)	.22	0.07 (0.40)	.86	0.66 (0.16)	<.01
AR vs no AR	0.32 (0.27)	.23	-0.69 (0.35)	.05	0.35 (0.26)	.18	0.10 (0.41)	.81	0.33 (0.16)	.04

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; $\ln$, natural log transformed; tIgE , total IgE.

revealed a substantial correlation between $\ln(\text{observed fslgE})$ and $\ln(\text{predicted fslgE})$ for egg, milk, and peanut ($\rho = 0.69, 0.67$, and 0.63 , respectively, $P < .001$) and a strong correlation for soy ($\rho = 0.83$, $P < .001$) (Fig 2).

In principle, the correlation between tlgE and fslgE could be spurious if a large fraction of tlgE is in fact composed of fslgE. Our analysis of the association between $\ln(\text{fslgE})$ and $\ln(\text{tlgE}) - \ln(\text{fslgE})$ continued to reveal a significant correlation for each food ($\rho = 0.67$ for egg, 0.66 for milk, 0.62 for peanut, and 0.85 for soy, $P < .001$), further validating our observation.

Because we had data from 2 clinical visits for each study participant, we analyzed the changes in tlgE levels and fslgE levels from one visit to the next. The results revealed significant correlations between tlgE and fslgE for more than one visit ($\rho = 0.55$ for egg, 0.55 for milk, 0.70 for peanut, and 0.75 for soy, $P < .001$); 78% of visits had consistent shifts in IgE levels.

Discussion

Current guidelines do not endorse the utility of total IgE levels in the diagnosis and management of food allergies.¹³ However, we demonstrate significant correlations between tlgE and fslgE levels to egg, milk, peanut, and soy in our study. We additionally present novel and simple predictive equations to predict the role of tlgE levels on fslgE levels. Our results therefore underscore the importance of examining fslgE levels in context of tlgE while making diagnostic and management decisions in children with food allergies.

Our study aimed to provide an evidence base for our preliminary clinical observations of parallel elevations in tlgE and fslgE levels and of changes in the levels of fslgE mirroring changes in tlgE levels. In our clinical practice we have noticed that in some children with positive levels of fslgE and elevated tlgE levels, the fslgE levels went up in subsequent follow-up evaluations concomitantly with increases in tlgE levels. This was particularly seen in children with atopic dermatitis, in whom a total IgE level is a demonstrated marker of disease activity and in whom food allergies are suspect

triggers.^{16–18} This unexpected increase in fslgE levels at the follow-up visit was puzzling and frustrating to families, who were hoping for a downward trend hinting at onset of clinical tolerance. In addition to causing challenges with monitoring the possibility of “outgrowing” the food allergy, the observed association between levels of tlgE and fslgE appeared to cause occasional diagnostic dilemmas. We anecdotally observed that children with elevated tlgE levels had fslgE levels that did not match our clinical suspicion based on history. We suspected that elevations in the tlgE levels might have caused artifactual elevation of fslgE levels above published cut points, generating recommendations of food restrictions and alterations in family lifestyle.

Other researchers have attempted to explore the clinical conundrums caused by the relationship between levels of tlgE and fslgE. Matricardi et al¹⁹ studied the evolution of serum tlgE and select environmental and food allergen specific IgE at various time points from birth up to 13 years of age and their relation to symptomatic respiratory allergies at 13 years of age. They observed that tlgE levels evolved in parallel with the overall food allergen specific IgE levels after the age of 5 years and identified a temporal relationship between increases in tlgE levels and the onset of respiratory allergies and specific sensitization. Sinclair and Peters²⁰ were concerned about the potential link between elevated tlgE and allergen specific IgE causing borderline elevations in specific IgE levels that would be deemed positive but were of uncertain relevance and significant expense. They made the interesting observation that children with very low total IgE levels (<10 kU/L) and nonspecific symptoms rarely had allergen specific IgE present, suggesting that testing in this subset of children was not routinely warranted. Similar to our study, they found an increase in the number of patients with positive and higher levels of allergen specific IgE accompanying elevations in tlgE, although notably they did not use cut points to define a positive test result.

Few studies have attempted to assess the potential value of tlgE levels in accurately predicting the presence of food allergy. Mehl et al²¹ compared the utility of the fslgE/tlgE ratio to fslgE levels

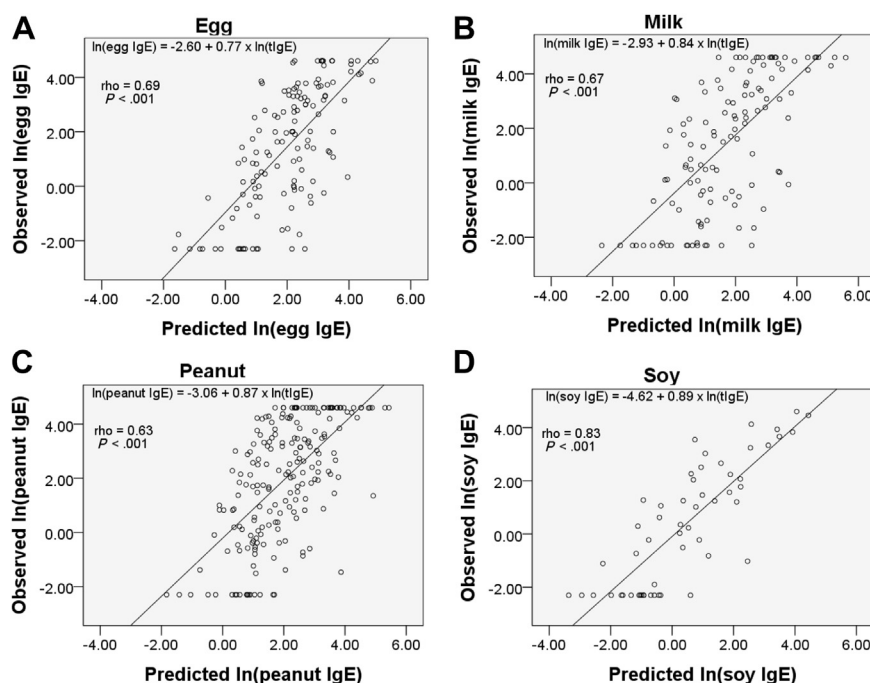


Figure 2. Scatterplots of observed natural log food specific IgE ($\ln[\text{fslgE}]$) vs predicted natural $\ln(\text{fslgE})$. A, Observed $\ln(\text{egg IgE})$ had a substantial correlation with predicted $\ln(\text{egg IgE})$. B, Observed $\ln(\text{milk IgE})$ had a substantial correlation with predicted $\ln(\text{milk IgE})$. C, Observed $\ln(\text{peanut IgE})$ had a substantial correlation with predicted $\ln(\text{peanut IgE})$. D, Observed $\ln(\text{soy IgE})$ had a strong correlation with predicted $\ln(\text{peanut IgE})$.

alone in diagnosing symptomatic food allergy (milk, egg, wheat, and soy) by correlating it with the outcomes of oral food challenges. The sensitivity and specificity of the decision points of the ratio were similar to those of fslgE levels alone; therefore, the researchers concluded that calculations of the fslgE/tIgE ratio for diagnosing symptomatic food allergy offered no clinical benefit compared with obtaining fslgE alone for cow's milk, egg, or wheat. DunnGalvin and colleagues²² formulated a predictive model that successfully predicted the outcome of oral food challenges. However, unlike our study, they used tIgE minus specific IgE as one of the 6 major independent indicators in their model.

Our results indicate substantial to strong correlations between tIgE and fslgE levels and emphasize the importance of interpreting fslgE levels against the backdrop of tIgE in the evaluation of food allergy. We additionally developed simple predictive models to predict fslgE levels based on tIgE levels. Although our predictive equations need to be validated in future prospective, randomized studies, we believe they have the potential to enhance meaningful interpretation of recommended predictive fslgE cut points. Using our models clinicians would be able to calculate a predicted fslgE level for egg, milk, peanut, or soy based on the patient's tIgE level and compare this to the patient's observed fslgE level. An observed fslgE level less than the predicted level may indicate a false-positive result vs sensitization. If the other clinical and laboratory variables are favorable, performance of an oral food challenge may then be considered as an option to confirm the suspicion of absence of clinical food allergy.

Our study has limitations that we would like to acknowledge. Because this is a retrospective analysis, clinical details that may have enhanced interpretation of our laboratory results were not available. The determination of patient diagnoses, which were used in our multivariate analysis, was limited by the accuracy of data entry into the electronic medical record. Our laboratory does not routinely dilute sera to measure levels of fslgE above the detection limit of the ImmunoCAP assay (100 kU/L). Therefore, levels of fslgE above the detection limit were assigned a value of 100 kU/L. Our study was also limited by the relatively homogenous patient population of white males with a mean age of 2 years. Our models require further validation in a more heterogeneous population before results can be extrapolated to all pediatric populations.

In conclusion, our study demonstrates that fslgE should be interpreted in the context of tIgE. We developed novel equations to predict fslgE levels that may enable practitioners to better assess the role of tIgE in influencing the interpretation of diagnostic food allergy tests. Our results suggest there is utility in obtaining tIgE levels in addition to clinical history, skin prick testing, and fslgE measurement in the diagnosis and management of food allergies in children. We hope to conduct future prospective, randomized studies to validate, refine, and determine clinical utility of our predictive models against oral food challenges, the current diagnostic criterion standard.

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