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A real-world data analysis of distribution and inconsistency between total serum IgE and allergen-specific IgE results in clinical practice

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Abstract

Background: The inconsistency between serum total IgE (tIgE) and allergen-specific IgE (sIgE) results is often encountered in clinical practice, but the distribution and influencing factors of the inconsistent results have not been fully understood.

Objective: The aim of this study was to analyze the distribution and inconsistency between tIgE and sIgE test results.

Methods: A retrospective study, from the electronic medical records of 2139 patients who underwent both tIgE and sIgE tests, from January to December 2023 was reviewed. The tIgE and sIgE results and their distribution, as well as their inconsistency, were analyzed based on sex, age, and disease subgroups.

Results: 36.2% of the patients had a positive sIgE, and 43.7% had an elevated tIgE level. sIgE and tIgE results were discordant in nearly 30% of patients, with no difference between genders, while individuals aged over 60 exhibited a significantly higher inconsistency rate than the other age groups, and the inconsistency rate between tIgE and sIgE results was significantly different among different tIgE levels, sIgE grades, positive allergen count and positive allergen types. In addition, patients with chronic urticaria (CU) had a higher inconsistency rate than those with other allergic diseases, but the difference was not statistically significant.

Conclusions: The overall inconsistency rate between tIgE and sIgE results was about 30%. The elderly group older than 60 years old is more likely to have inconsistent results, and tIgE level, sIgE level, the number and type of positive allergens also affected the consistency of tIgE and sIgE results.

Key words: allergen, specific IgE, total IgE, inconsistency, allergic disease

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Introduction

Immunoglobulin E (IgE), a type of immunoglobulin, is a protein produced by the immune system as part of the immune response to foreign or autologous antigens.[1] It is the least abundant immunoglobulin in the bloodstream but is highly effective in triggering allergic responses. Even exposure to trace allergens can lead to the production of IgE antibodies in atopic individuals.[2]

The concentration of IgE antibodies in the circulation of healthy people is very low (less than 240 ng/mL), However, in allergic people, IgE will be produced in large quantities under the background of allergen exposure and the active of allergic diseases, and the level of circulating IgE antibodies will be significantly increased.[3] Therefore, IgE antibody measurement is an integral part of the diagnostic evaluation of a patient for atopic disease.[4] At present, the most commonly used tests for detecting circulating IgE antibodies are total serum IgE (tIgE) assays and allergen-specific IgE (sIgE) antibody assays.[5]

Since the first solid-phase sandwich immunoassay for the measurement of total was described in 1967, the level of tIgE was considered as the simplest way to identify atopic subjects.[6] tIgE level is commonly tested and found increased in allergic diseases such as allergic rhinitis (AR), asthma (AS), atopic dermatitis (AD) and urticaria,[7,8] and it has also been extensively studied and discussed as a marker which is closely related to the clinical characteristics of these diseases, such as clinical classification, disease activity, severity, treatment response and prognosis. While traditionally tIgE has been employed for the identification of allergic conditions, its elevation is not exclusive to atopy, as it can also be associated with parasitic infections, multiple myeloma, and other non-allergic diseases.[9] This broader association has led to some debate over its specificity as a biomarker. In contrast, although sIgE presents a higher specificity and is considered a more objective diagnostic indicator, its clinical positive rate is not high enough.[5] We believe that a balanced approach, considering both tIgE for screening and sIgE for allergen specificity, can provide a more comprehensive understanding of allergic sensitization.

However, in clinical practice, it is often encountered that the results of tIgE and sIgE are inconsistent, which brings confusion to the clinical interpretation of the results and the determination of their clinical value. At present, reports on the detailed distribution of discordant results between tIgE and sIgE and related influencing factors are extremely limited. This study aims to address this confusion by investigating the distribution and inconsistency of tIgE and sIgE results in clinical practice. These findings would be helpful for clinicians to interpret when tIgE and sIgE results are inconsistent.

Methods

Participants and Data

We included all patients who were tested for both sIgE and serum tIgE at Southwest Hospital during the one-year period from January to December 2023. The diagnoses were established by specialists adhering to established criteria, including the international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for Chronic Urticaria (CU),[10] Chinese Criteria for Atopic Dermatitis (AD),[11] Chinese Society of Allergy Guidelines for the diagnosis of Allergic Rhinitis (AR),[12] and Chinese guidelines for the diagnosis of Asthma (AA).[13] *In our study, we meticulously selected patients based on their principal diagnosis, taking into account the presence of any coexisting allergic conditions in the AD, AR, and AA patient populations. For CU patients, we strictly included only those without other allergic comorbidities*. For those who also underwent sIgE and tIgE testing during this period but did not receive a definitive diagnosis of the aforementioned common allergic diseases after further examination and assessment, they were included as a "negative control (NC)" group in our study. The demographic information of patients, including age and gender, was collected. The patient population was stratified into four age subgroups to account for the varying immunological and clinical aspects of allergic diseases across the lifespan: 0-11 years for the pediatric group, 12-17 years for adolescents, 18-59 years for adults, and 60 and above for the elderly population. The detection of tIgE and sIgE was performed by the laboratory department of Southwest Hospital and the detail tIgE and sIgE test results of the patients were collected. This study was approved by the Ethics Committee of Southwest Hospital of Army Military Medical University (*KY2020152*).

Measurement of serum total IgE (tIgE)

Serum total IgE was measured by immunoturbidimetry, using the Immunoglobulin E (IgE) Immunoassay Reagent (Beckman Coulter, Inc., America) and the IMMAGE 800 System (Beckman Coulter, Inc.). A tIgE test result < 100 IU/mL was defined as negative or normal tIgE, and a tIgE test result ≥ 100 IU/mL was defined as positive or elevated tIgE.

Measurement of allergen-specific IgE (sIgE)

The AllergyScreen System (Mediwiss Analytic, Germany) was used to detect allergen-specific IgE through immunoblotting semi-quantitatively. We tested 29 mixed items, including 18 aeroallergens (*D. pteronyssinus*, *D. farinae*, *Blomia tropicalis*, Cat dander, Dog dander, Cockroach, silk, Dwarf ragweed, Artemisia, Humulus, Quinoa/amaranthus, Juniper/birch, Platanus/ash, alder/poplar /willow/beech/oak/walnut, June grass/ryegrass/timothy, Maple/mulberry/acacia/elm/cypress/paper mulberry, Aspergillus fumigatus, Candida/Penicillium/Mycosporium/Alternaria /Aspergillus niger) and 11 food allergens (Egg yolk, Egg white, Milk, Peanut/soybean, Sesame, Wheat/buckwheat, Cashew/pistachio/hazelnut/almond/walnut, Beef/lamb, Fish, shrimp/crab, Peach/apple/mango/lychee/strawberry). Concentrations of sIgE less than 0.35 IU/mL were considered negative, while concentrations ≥ 0.35 IU/mL were considered positive. Positive results were divided into six levels based on sIgE concentration, with higher levels indicating greater concentration. Level 1 was 0.35-0.69 IU/mL, Level 2 was 0.70-3.49 IU/mL, Level 3 was 3.5-17.49 IU/mL, Level 4 was 17.5-49.9 IU/mL, Level 5 was 50-100 IU/mL, and Level 6 was greater than 100 IU/mL.

Definition of inconsistency

Referring to Yamana's study,[14] we divided the aeroallergens into five subgroups and the food allergens into two subgroups, as shown in **Table S1**. Positive sIgE (sIgE+) was defined as being sensitized to at least one allergen, and the overall sIgE level of the patient was defined as the highest sIgE level of the tested allergens. Positive tIgE was defined as ≥ 100 IU/mL. Consistent results were defined when sIgE and tIgE were both positive or both negative, while inconsistent results were defined when only one of the two was positive and the other was negative.

Statistical analyses

The statistical analyses were conducted by the SPSS (Version 26, SPSS Inc.) software. Categorical measurements were expressed as numbers and percentages, and non-normally distributed numerical measurements were presented as median (percentiles 25th–75th). The Chi-square test and Fisher's exact test were used to analyze categorical variables. We used the Bonferroni method to correct the significance levels for multiple comparisons. The Mann-Whitney U test and the non-parametric Kruskal-Wallis test were utilized to compare non-normally distributed numerical data. A p-value of < 0.05 was considered statistically significant. All the figures were generated by GraphPad (Version 6.0, GraphPad Software Inc.) or Excel.

Results

General information of the patients

A total of 2,139 patients who underwent both tIgE and sIgE tests were enrolled, including 101 with AR, 411 with AD, 139 with AS, and 396 with chronic urticaria (CU), and a negative control group with 1092 patients who did not receive a definitive diagnosis of AR, AD, Asthma, CU, or any other allergic diseases after an exhaustive evaluation by our specialists. Of these patients, 923 (43.2%) were male and 1216 (56.8%) were female, with a median (Interquartile range, IQR) age of 34 (17, 51) years old.

sIgE results in the patients

36.2% of the whole patients were positive for sIgE. Among them, 705 (33.0%) were positive for aeroallergens, and 184 (8.6%) were positive for food allergens. The detailed positive rates for 29 allergens classified as aeroallergens and food are presented in **Figure S1**. The most prevalent allergens subgroup was dust mites, with a positivity rate of 25.6%, followed by pollens (6.9%) and animal-derived food allergens (6.6%) (**Figure 1A**). 53.8% of the dust mite-sIgE positive patients were distributed in level 3 or above, which is the highest proportion among all allergens subgroups, followed by pollen at 39.5% and pets at 33.9% (**Figure 1B**).

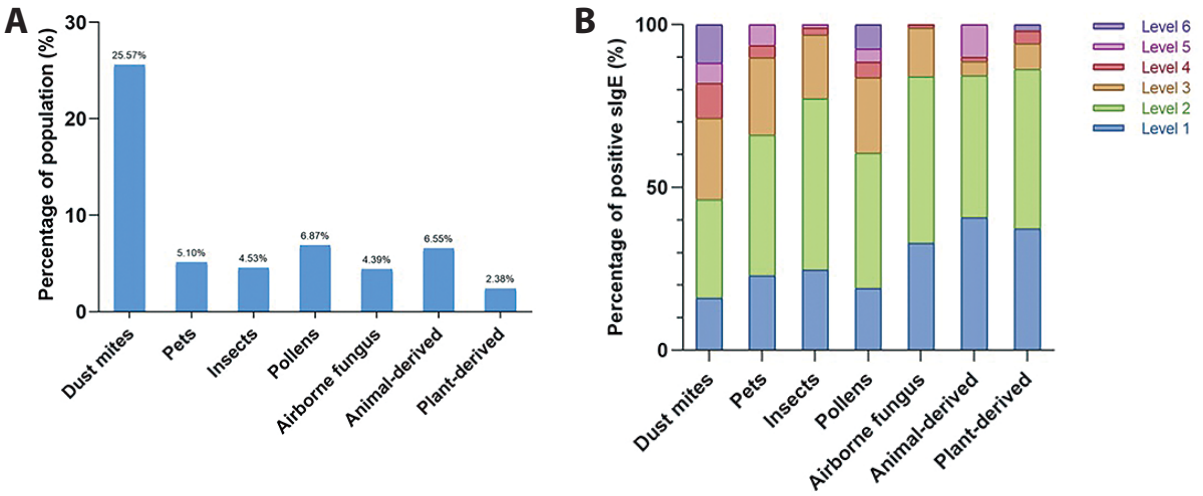

Figure 1. General characteristics of allergen distribution. (A) The positive rates of various allergen subgroups. (B) Comparison of allergen-positive rates in sex. (C) Comparison of allergen-positive rate between age groups. (D) The percentage of sensitization grade (Level 1-6) in the positive sIgE. (E). The positive rate of sIgE in different diseases. CU, chronic urticaria; AD, atopic dermatitis; AS, asthma; AR, allergic rhinoconjunctivitis; NC, negative control. *$p < 0.05$.

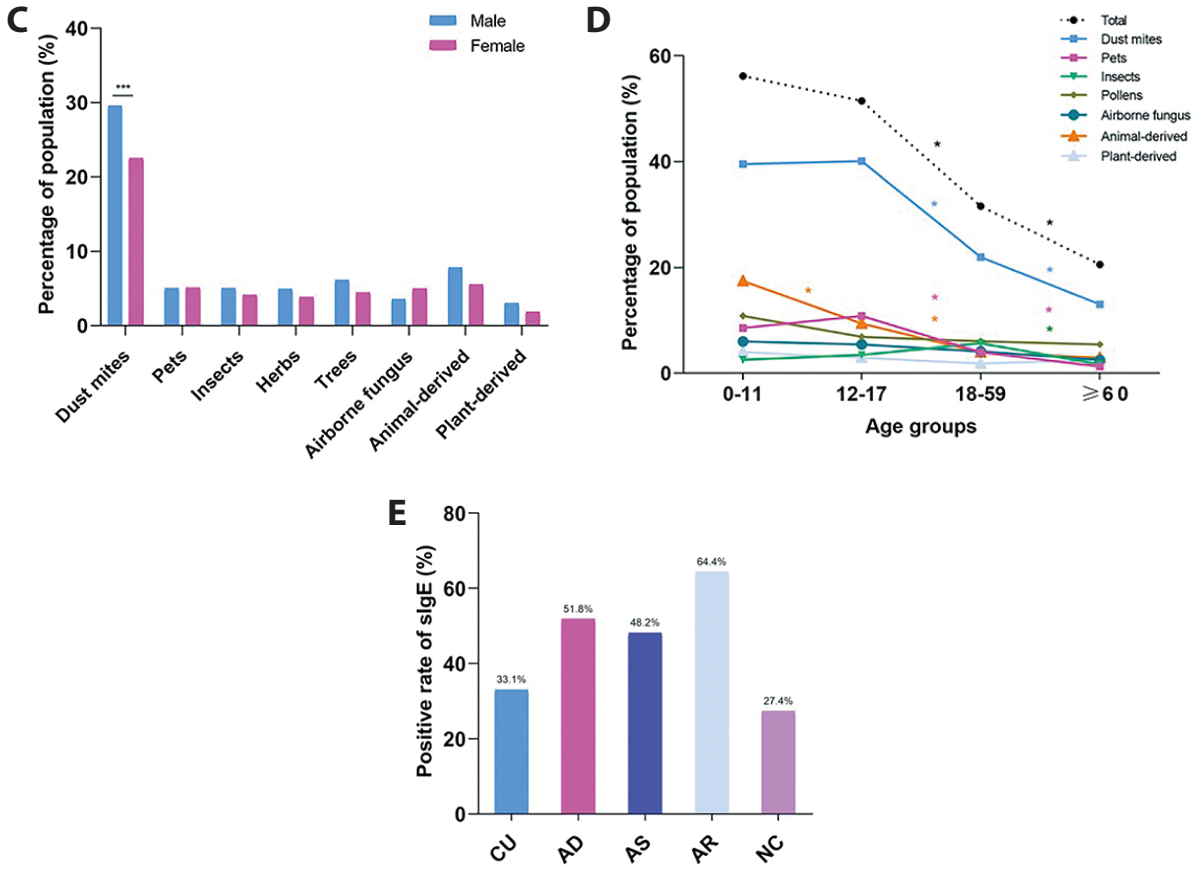

Figure 1. (Continued)

The overall positive rate of sIgE in males was significantly higher than that in females (40.8% vs 32.7%, $p < 0.001$). In different allergen subgroups, dust mites had the highest positive rate both in male and female groups, and its positive rate in males was significantly higher than that in females (29.6% vs. 22.5%, $p < 0.001$). No gender differences were observed in the other allergen subgroups (**Figure 1C**). The overall positive rate of sIgE decreased with age. The positive rate of sIgE was the highest in the 0-11 age group (56.2%), and the lowest in the ≥ 60 age group. In all allergen subgroups, dust mite was the most common allergen in all age groups, and its positive rate also decreased with age (**Figure 1D**). Among different diseases, the positive rate of sIgE in CU patients (33.1%) and other diseases (27.4%) were lower than that in AD, AS and AR (51.8%, 48.2%, 64.4%, respectively) (**Figure 1E**).

tIgE results in the patients

A total of 43.7% of all enrolled participants had elevated tIgE levels, with a median (IQR) tIgE level of 80.0 (29.0, 211.0) IU/mL. Both the tIgE levels and the proportion of elevated tIgE were significantly higher in males than in females ($p < 0.001$). The 18-59 age group had the lowest median (IQR) tIgE levels of 63.2 (24.6, 160.0) IU/mL and the lowest proportion (38.1%) of elevated tIgE compared to the other three age groups ($p < 0.001$) (**Table 1**). There was no significant difference in the level of tIgE and the positive rate of tIgE elevation between CU, AD, AS and AR, but they were all significantly higher than those of other diseases (all $p < 0.05$).

Table 1. tIgE results in different subgroups of patients.

	tIgE (IU/mL), median (IQR)	Elevated tIgE, n (%)
Total (n = 2139)	80.0 (29.0, 211.0)	935 (43.7)
Sex		
Male (n = 923)	106.0 (36.2, 316.0)	478 (51.8)
Female (n = 1216)	64.2 (24.5, 158.0)	457 (37.6)
P	< 0.001	< 0.001
Age (years)		
0-11 (n = 349)	113.0 (36.6, 374.0)[a]	187 (53.6)[a]
12-17 (n = 202)	113.5 (44.9, 382.8)[a]	109 (54.0)[a]
18-59 (n = 1350)	63.2 (24.6, 160.0)[b]	515 (38.1)[b]
≥ 60 (n = 238)	107.0 (43.1, 334.0)[a]	124 (52.1)[a]
P	< 0.001	< 0.001
Diseases		
CU (n = 396)	96.7 (42.8, 193.5)[a]	194 (49.0)[a]
AD (n = 411)	114.0 (38.4, 525.0)[a]	220 (53.5)[a]
AS (n = 139)	83.6 (37.9, 221.0)[a]	64 (46.0)[a,b]
AR (n = 101)	109.0 (34.7, 245.0)[a]	55 (54.5)[a]
NC (n = 1092)	57.7 (21.9, 169.0)[b]	402 (36.8)[b]
P	< 0.001	< 0.001

IQR, Interquartile range; CU, chronic urticaria; AD, atopic dermatitis; AS, asthma; AR, allergic rhinoconjunctivitis; NC, negative control. [ab]Statistical results between pairs are indicated by letters, with the same letters indicating no statistical difference between the two groups and different letters indicating a statistical difference between the two groups. Comparisons among multiple groups were corrected for significance by Bonferroni method.

The mutual distribution characteristics of tIgE and sIgE results

We compared the distribution characteristics of the grade of sIgE reaction and the number of positive allergens between the tIgE (+) and tIgE (-) groups. Although the proportion of negative sIgE reactions in the tIgE (-) group (80.6%) was significantly higher than that in the tIgE (+) group (42.1%) ($p < 0.001$), the proportion of positive sIgE reactions of grade 2 or above in the tIgE (-) group was significantly lower than that in the tIgE (+) group (**Figure 2A**). A similar pattern was observed in the number of positive allergen reactions (**Figure 2B**). Approximately 30% of patients with negative sIgE results exhibited positive tIgE results. However, the majority of patients with negative sIgE and positive tIgE results exhibited relatively low tIgE levels (100-499 IU/ml). The proportion of the patients with tIgE levels higher than 500 IU/ml of tIgE was very low, which was significantly different from that of sIgE (+) and tIgE (+) patients ($p < 0.001$) (**Figure 2C**).

Inconsistency analysis between sIgE and tIgE results

The inconsistency analysis among different patient subgroups is shown in **Table 2**. Of the 2,139 individuals included in the analysis, 628 (29.4%) individuals exhibited discordant sIgE and tIgE results. The rate of inconsistency between sIgE and tIgE results in male patients (31.3%) was slightly higher than that in female patients (27.9%), but the difference was not significant ($p = 0.084$). The rate of inconsistency between sIgE and tIgE results in people over 60 years old (43.3%) was significantly higher than that of other age groups ($p < 0.001$). Among different diseases, CU patients had a higher rate of inconsistency between sIgE and tIgE results (34.6%) than that of AD (28.0%), AR (23.8%), AS (26.6%) and other diseases (28.8%), but the difference was not statistically significant ($p = 0.100$).

Figure 2. The distribution characteristics of sIgE level (A) and positive allergen counts (B) in the tIgE+/tIgE- group. (C) The distribution characteristics of tIgE level in sIgE+/sIgE- group. $^{\#}p < 0.05$, $^{*}p < 0.001$.

Table 2. The inconsistency analysis among different subgroups of the patients.

Sex and inconsistency						
Sex	**Male**		**Female**			***P***
Inconsistency Rate, n (%)	289 (31.3)		339 (27.9)			0.084
Age and inconsistency						
Age (years)	**0-11**	**12-17**	**18-59**	**≥ 60**		***P***
Inconsistency Rate, n (%)	101 (28.9)[a]	45 (22.3)[a]	379 (28.1)[a]	103 (43.3)[b]		< 0.001
Diseases and inconsistency						
Diseases	**CU**	**AD**	**AS**	**AR**	**Other**	***P***
Inconsistency Rate, n (%)	137 (34.6)	115 (28.0)	37 (26.6)	24 (23.8)	315 (28.8)	0.100

CU, chronic urticaria; AD, atopic dermatitis; AS, asthma; AR, allergic rhinoconjunctivitis. [ab]Statistical results between pairs are indicated by letters, with the same letters indicating no statistical difference between the two groups and different letters indicating a statistical difference between the two groups. Comparisons among multiple groups were corrected for significance by Bonferroni method.

Table 3 shows the further analysis of the rate of inconsistency between sIgE and tIgE results among different tIgE levels. This analysis revealed that those with tIgE levels in the range of 100-499 IU/mL had the highest inconsistency rate (47.8%), while those with normal tIgE had the lowest inconsistency rate (19.4%). Whereas in the sIgE reaction level, sIgE level 1 exhibited the highest rate of inconsistency between sIgE and tIgE results (58.2%). A negative correlation between allergen sensitization level and inconsistency rate was observed. The characteristics of the inconsistency in positive allergen count were very similar to sIgE level. Patients with only one positive allergen were most likely to have inconsistent results between sIgE and tIgE (49.8%), but the inconsistency rate decreased with the increase of the number of positive allergens. The type of allergen also affected the consistency of sIgE and tIgE results. Patients with positive airborne fungus and food allergens were more likely to have inconsistent sIgE and tIgE results.

Table 3. Inconsistency rates among various sIgE and tIgE groups.

tIgE level and inconsistency						
tIgE (IU/mL)	**< 100**	**100-499**	**500-999**	**≥ 1000**		***P***
Inconsistency Rate, n (%)	234 (19.4)[a]	322 (47.8)[b]	40 (33.3)[c]	32 (22.7)[a,c]		< 0.001
sIgE level and inconsistency						
sIgE Level	**Negative**	**Level 1**	**Level 2**	**Level 3**	**Level 4-6**	***P***
Inconsistency Rate, n (%)	394 (28.9)[a]	85 (58.2)[b]	103 (38.7)[c]	36 (20.7)[a]	10 (5.3)[d]	< 0.001
Positive allergen count and inconsistency						
Allergen count	**0**	**1**	**2**	**3**	**≥ 4**	***P***
Inconsistency Rate, n (%)	394 (28.9)[a]	147 (49.8)[b]	61 (30.8)[b]	14 (11.3)[c]	12 (7.6)[c]	< 0.001
Allergen types and inconsistency						
Allergen types	**Dust mites**	**Pets**	**Insects**	**Pollens**	**Airborne fungus**	**Food allergens**	***P***
Inconsistency Rate, n (%)	119 (21.8)[a]	18 (16.5)[a]	12 (12.4)[a]	36 (24.5)[a,b]	34 (36.2)[b]	61 (33.2)[b]	< 0.001

[abcd]Statistical results between pairs are indicated by letters, with the same letters indicating no statistical difference between the two groups and different letters indicating a statistical difference between the two groups. Comparisons among multiple groups were corrected for significance by Bonferroni method.

Discussion

Our research sheds light on the patterns of sIgE and tIgE test results within the authentic clinical landscape of China, emphasizing the variations in IgE sensitization profiles across different allergen types, genders, age groups, and disease classifications. Our investigation found that the positive rate for inhaled allergen-sIgE was substantially higher than that for food allergens in the patient population we examined, with a notable prevalence of sensitization to dust mites. This aligns with similar findings from past studies. Although the positive rate for food allergen sIgE is relatively low and its clinical relevance to the clinical symptoms of traditional allergic diseases such as AR,[15] AS,[16] and AD[17] is less significant, the historical clinical approach has not prioritized the positive outcomes of food allergen testing in diagnosing allergies. Nonetheless, positive results for food allergens, especially at higher levels, are valuable for suggesting an atopic predisposition in patients and can offer support in the diagnosis of atopic diseases. Our study revealed a notably higher rate of positive sIgE and levels of tIgE in male patients compared to females, a pattern echoed in literature,[18,19] which may suggest the influence of hormonal or genetic factors on the allergic sensitization process.[20] The observed decrease in sIgE positivity with advancing age presents an intriguing trend. The 0-11 age group showed the highest positivity rates, likely due to the immature development of the immune system and increased sensitivity of children to environmental allergens.[21] A decline in sIgE positivity in the older age groups could be attributed to the aging immune system, lifelong changes in allergen exposure, or the 'allergic march,' where early sensitivities may wane.[22] The 18-59 age group, characteristic of full immune system maturity, displayed the lowest median tIgE levels, suggesting a potential for developed tolerance and controlled IgE production.[23] Although the difference was not significant, the lower sIgE positivity rates in CU compared to AD, AS, and AR suggest that the pathophysiology of CU may differ from the other allergic diseases. This could be indicative of non-IgE-mediated mechanisms in CU patients.[24]

In clinical practice, it is routine to utilize both sIgE and tIgE results in concert to assess a patient's atopy and to forecast their responses to anti-IgE treatments or allergen-specific immunotherapy. Despite the prevalence of this approach, concrete data regarding the specific distribution of consistency between sIgE and tIgE outcomes have been notably absent from the literature. Through the data presented in this study, we can see that the positive correlation between tIgE and sIgE is clear, which was previously confirmed,[25] but the inconsistency between tIgE and sIgE is also clearly visible in this study. In clinical practice, most doctors recommend that patients with suspected allergic diseases should be tested for tIgE first, and patients with high tIgE levels should be tested for specific IgE.[4,26] However, Al-Mughales et al. reported that the sensitivity of total IgE was 78.6%, while the specificity was only 41.8%.[27] As shown in the results of this study, patients with positive or even high levels of sIgE or multiple allergens positive but tIgE negative are not uncommon. For such patients, if only tIgE test is performed for various reasons, the atopic background will often be overlooked.

What is the distribution of inconsistency between tIgE and sIgE results, and what factors affect the consistency of the results between the two, which is of great concern to physicians in clinical practice.[28] The present study aimed to investigate the inconsistency between tIgE and sIgE results. Our findings revealed that there is a significant inconsistency rate of about 30% between tIgE and sIgE results. To our knowledge, there are no previously reported data addressing this issue. As widely recognized, tIgE reflects the overall IgE levels in serum and can be affected by a range of non-allergic conditions, including parasitic infections, certain autoimmune diseases, and malignancies.[29,30] In clinical practice, once these factors that induce abnormal tIgE levels are excluded, the clinical value of tIgE in allergic diseases is enhanced. Nevertheless, the inconsistency between tIgE and sIgE results can still pose challenges in the diagnosis and assessment of diseases. Therefore, analyzing the influencing factors behind these inconsistencies and examining their specific distribution characteristics can enable us to better interpret these results.

Hence, our analysis has provided an in-depth examination of the distribution of inconsistencies between tIgE and sIgE, with an emphasis on uncovering the possible factors responsible for these inconsistent findings. By comparing data from different disease groups, we found patients with CU had a higher rate of inconsistency than those with classical allergic disease. However, the difference was not statistically significant, indicating that while CU patients may tend to have more inconsistencies but need to be further confirmed. Our findings demonstrate that CU patients do not exhibit significantly different levels of tIgE compared to those with other classical allergic diseases. However, the positivity rate for sIgE is considerably lower in CU, likely due to the focus on exogenous allergens in presently sIgE assays. We speculate that the pathophysiology of CU involves a greater contribution from endogenous allergens, or autoallergens, which may not be adequately captured by presently clinical standard sIgE testing, thus potentially reducing the concordance between tIgE and sIgE results in clinical settings. Furthermore, the complexity of CU's etiology extends beyond the type I allergic reactions induced by both exogenous and endogenous allergens. It also encompasses autoimmune mechanisms, coagulation irregularities, and other non-immune pathways, all of which could influence the alignment of tIgE and sIgE test outcomes in CU patients during clinical assessments.[31] In summary, the inconsistency between sIgE and tIgE results is more pronounced in CU, attributed to its varied pathogenic mechanisms, as opposed to classical allergic diseases. However, validation of this observation necessitates additional research involving larger cohorts.

We further analyzed the impact of other factors on the consistency of tIgE and sIgE results. We found individuals over 60 years old had a significantly higher rate of inconsistency compared to other age groups. This could be due to a variety of factors, including a decline in immune system function with age or other age-related health conditions that could affect tIgE levels.[32] It also suggests that tIgE test results in older adults should be interpreted more cautiously. What's more, we found patients with tIgE levels between 100-499 IU/mL had the highest inconsistency rate (47.8%). This suggests that moderate elevations in tIgE may be particularly incongruent with sIgE levels, possibly indicating a broader sensitization profile or other non-allergic factors influencing IgE levels. In our study, sIgE level 1 had the highest rate of inconsistency (58.2%), and there was a negative correlation between the level of allergen sensitization and the inconsistency rate. This implies that patients with lower levels of sIgE (indicating less sensitization) are more likely to have inconsistent tIgE results. Similarly, patients with only one positive allergen were most likely to have inconsistent results (49.8%), whereas the inconsistency rate decreased with an increasing number of positive allergens. This could suggest that poly-sensitized patients may have more congruent sIgE and tIgE levels, possibly reflecting a more robust allergic response.[33] Overall, the discordance between sIgE and tIgE results is subject to a multitude of influences, such as the patient's age, the quantity and diversity of allergens sensitizing the patient, and the level of sensitization.

This study has some limitations. First, this study was conducted at a single hospital, which limits the generalizability of the findings. Second, while the sample size of 2139 patients is substantial, it may not be fully representative of the broader population, especially considering the diverse range of allergic diseases and their prevalence in different age groups and geographical locations. Third, this study does not provide longitudinal data, which would be useful for understanding the temporal relationship between tIgE and sIgE levels and the progression of allergic diseases. Additionally, this study did not account for the impact of disease severity on the results, which is a significant factor that could influence the outcomes. Further studies are needed to address these limitations.

Conclusion

While this study offers a comprehensive analysis of sIgE and tIgE distribution among various patient subgroups, revealing a notable 30% inconsistency rate between the two, it is clear that our findings require further validation. The identified differences in IgE sensitization based on allergen type, gender, age, and disease category, as well as the higher inconsistency rate in the elderly, provide a foundation for future research. Our study indicates a complex interplay between tIgE and sIgE in allergic diseases, suggesting that clinical interpretation of these measurements should be approached with caution. Further studies, potentially with longitudinal designs and larger, more diverse populations, are essential to confirm our results and explore the implications for allergy diagnostics and patient management.

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Conflict of interest

The authors declare that they have no competing interests.

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Author contributions

- XY and QC designed the study and performed the analysis and manuscript preparation.
- AC, HW, SL and SD collected data.
- ZS and BN designed the study, performed the data analysis and reviewed the manuscript.
- All authors have read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Southwest Hospital of Army Military Medical University. Consent (KY2020152) was waived by the ethics committee. The hospital gave permission to extract information from the database.

Availability of data and materials

The datasets generated during the current study are available from the corresponding author upon reasonable request.

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Supplementary Material

Table S1. Subgroups of allergens.

Subgroups	Allergens
Dust mites	*Dermatophagoides pteronyssinus* (*D. pteronyssinus*), *D. farinae*, *Blomia tropicalis*
Pets	Cat dander, Dog dander
Insects	Cockroach, Silk
Pollens	Dwarf ragweed, Artemisia, Humulus, Quinoa/amaranthus, Juniper/birch, Platanus/ash, Alder/poplar /willow/beech/oak/walnut, June grass/ryegrass/timothy, Maple/mulberry/acacia/elm/cypress/paper mulberry
Airborne fungus	Aspergillus fumigatus, Candida/Penicillium/Mycosporium/Alternaria /Aspergillus niger
Animal-derived food allergens	Egg yolk, Egg white, Milk, Beef/lamb, Fish, Shrimp/crab
Plant-derived food allergens	Peanut/soybean, Sesame, Wheat/buckwheat, Cashew/pistachio/hazelnut/almond/walnut, Peach/apple/mango/lychee/strawberry

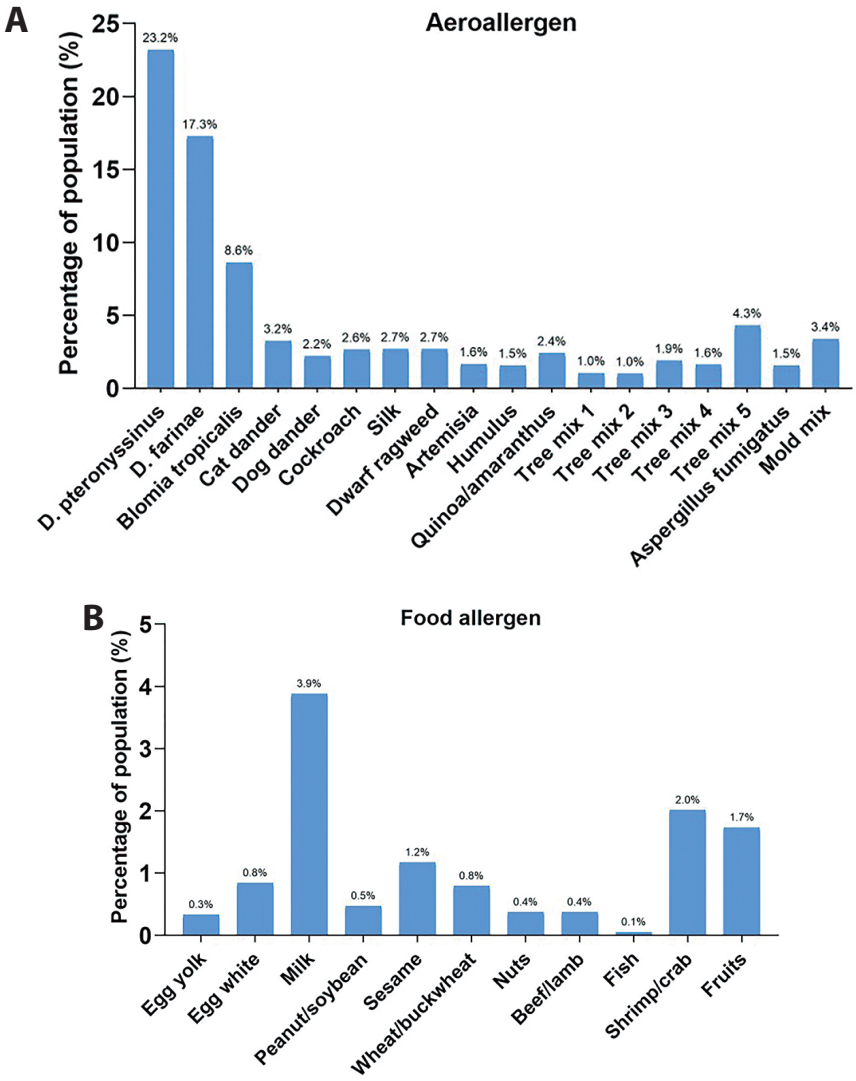

Figure S1. Positive rate of all tested allergens. (A) Positive rate of aeroallergens. (B) Positive rate of food allergens. Tree mix 1: juniper/birch; Tree mix 2: platanus/ash; Tree mix 3: alder/poplar /willow/beech/oak/walnut, Tree mix 4: june grass/ryegrass/timothy; Tree mix 5: maple/mulberry/acacia/elm/cypress/paper mulberry; Mold mix: Candida/Penicillium/Mycosporium/Alternaria /Aspergillus niger; Nuts: cashew/pistachio/hazelnut/almond/walnut; Fruits: peach/apple/mango/lychee/strawberry.