

Relationship between total serum immunoglobulin E level and total eosinophils count with skin reactivity in children with allergic rhinitis and asthma in North Indian population

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Abstract

CONTEXT: Various epidemiological studies have shown association among total serum immunoglobulin E (IgE) levels, blood eosinophilia, skin test reactivity, and allergy prevalence, the details of these associations has still not well determined specially in the Indian population.

AIMS: The aim of this study is to determine the correlation between total serum IgE level, total eosinophils counts (TECs), and skin prick test (SPT) for common aeroallergens in children with allergic rhinitis (AR) and asthma.

SETTINGS AND DESIGN: A prospective, cross sectional, and observational study conducted at Santokba Durlabhji Memorial Hospital, Jaipur, Rajasthan, India, between October 2018 and June 2019.

MATERIALS AND METHODS: A total of 140 children of age 6–18 years diagnosed with AR and Asthma were enrolled. SPT using 18 aeroallergens were performed with the measurement of total serum IgE level and TEC.

RESULTS: Among the total cases, around 77% ($n = 108$) were having positive skin test for one or more allergens, most common allergen was house dust mite. Total serum IgE level was strongly related with skin reactivity in both AR and asthma groups (correlation coefficient = 0.68), and a fair correlation was also observed between TEC and SPT grade in our all study participants ($r = 0.48$).

CONCLUSION: Our study suggested a close relationship between total serum IgE and TEC and skin test reactivity in children with AR and asthma.

Keywords: Aeroallergen, allergic rhinitis, asthma, house dust mite, Rajasthan

Introduction



Allergic diseases affects lives of more than one billion people worldwide;^[1] asthma and allergic rhinitis (AR) are common among them. Fourteen percent children experience asthma symptoms according to global asthma report.^[2] Allergy once considered diseases of rich and of western world, is now increasingly affecting middle income group and poor people in the developing countries. The prevalence of asthma in India estimated to range from 3% to 38%.^{[3],[4]}

AR considered as the most common allergic disease afflicting 10%–30% population globally and more than 50% of atopies in India.^[5]

The response of the immune system of the sensitized person to the allergen as a result of a series of reactions, mediated by many immune mediators, including eosinophils, mast cells, and basophils which can be defined *in vitro* using various parameters such as total immunoglobulin E (IgE), specific IgE, and eosinophil counts.^[6]

It is established that IgE plays a pivotal role in the pathogenesis of allergic diseases. Total serum IgE level and total eosinophil counts (TECs) are widely used as a diagnostic tool for allergic diseases.^[7] In routine clinical practice, a combination of total serum IgE and TEC is used to rule out allergic diseases.

Among various allergens, house dust mite (HDM),^[8] cockroach, mosquito, fungus (*Alternaria*), dog, and cat dander are common indoor allergens implicated in various allergic disorders,^{[9],[10],[11]} while according to aerobiology of North India, *Parthenium*, *Holoptelia*, *Chenopodium* sps., *Cynodon* sps., *Amaranthus* sps., *Ricinus comunis*, *Brassica* sps. and *Zea mays* are some common outdoor allergens.^[12]

Studies have shown strong association among total serum IgE levels, blood eosinophilia, skin test reactivity, and allergy prevalence, the details of these association is still not well determined.^[13]

This study is being conducted in Jaipur, Rajasthan, North India, to compare and correlate total serum IgE levels and TECs to common 18 aeroallergens by skin prick test (SPT), which is considered as gold standard test for the diagnosis of clinical allergy.^[14] We have chosen here 18 most common aeroallergens because of wide prevalence of reactivity to

these allergens in allergic patients which is well established by regional aerobiology and various studies.^{[9],[10],[11],[12]}

Materials and Methods



This was a prospective, observational study conducted at Santokba Durlabhji Memorial Hospital, Jaipur, Rajasthan, India. One hundred and forty children with allergic disease (Asthma and AR) were enrolled between October 2018 and June 2019.

In all cases, sociodemographic data, including age, sex, date of birth, socioeconomic status, etc., and detailed history regarding, presenting symptoms, duration of symptoms, seasonality of symptoms, environmental and precipitating factors history, history of treatment prior to hospitalization, etc., were obtained.

All patients were categorized into urban and rural class according to definition by census of India 2011.

All participants were divided into two disease groups: Predominant Asthma and predominant AR, after detailed medical history and physical examination.

Diagnosis of Asthma was established by Global Initiative for Asthma (GINA) guideline 2018.^[15] Characteristics symptoms pattern on history and evidence of variable airflow limitations (spirometry/reversibility test).

Diagnosis of AR by Allergic Rhinitis and its Impact on Asthma (ARIA) guideline 2007:^[16] Based on symptomatology-rhinorrhea, nasal blockage, nasal itching and sneezing, which are reversible spontaneously or with treatment.

Skin prick test

After detailed history and examination clinical diagnosis of AR and asthma being made (ARIA and GINA guidelines). SPT has been performed for 18 aeroallergen: *Holoptelia*, *Amaranthus spinosus*, *Argemone maxicana*, *Brassica* sps., *Chenopodium* album, *Ricinus communis*, Male and female cockroach, Mosquito, HDMs (D. Farinae, D. Pteronyssinus), *Parthenium* sps., *Zea mays*, *Alternaria*, Cat dander, Dog dander, *Cynodon dactylon* and Grain dust, using standard allergen extracts prepared by Alcure pharma, Delhi. Skin pricks were done using standard protocol with a sterile lancet under all aseptic precautions. Histamine is used as positive control and Normal saline as negative control. Test results were read after 15–20 min. An emergency kit (containing inj. Adrenaline, Hydrocortisone, Chlorpheniramine) was always there at testing site for management of any adverse reaction. Test was considered positive if wheal in any of the allergens was 3 mm or more than the positive control.

Total serum immunoglobulin E and total eosinophils count analysis

Venous blood sample has been taken from each patient and total serum IgE level and TEC was measured.

Statistical analysis

Categorical data has been presented as numbers (percent) and were analyzed using Chi-square test/Fischer exact test as applicable.

Correlation between quantitative variables has been assessed by using Pearson's/spearman correlation coefficient as applicable. For inference of correlation coefficient:

- $r \geq 0.8$ = Very strong correlation
- $0.6-0.8$ = Moderately strong correlation
- $0.3-0.5$ = Good correlation
- <0.3 = Poor/weak correlation.

A Probability $P = 0.05$ was considered as statistically significant.

All statistical analyses were done using Medcalc 16.4 statistical software (Medcalc Software, Ostend, Belgium).

Results



This study was done in Pediatric outpatient department (OPD), at SDM Hospital, Jaipur. Total 140 children (70 Asthma and 70 AR) were enrolled for the study. The following observations were made:

[Table 1] shows basic demographic and geographic data of study subjects. Children enrolled were mostly of age group 6–15 years (93.6%, $n = 131$). There is statistically significant difference ($P = 0.008$) seen in the prevalence of asthma and AR i.e., the asthma is more prevalent in younger children (80%, $n = 56$) as compared to AR (58.6%, $n = 41$). 78.6% ($n = 110$) were male and 21.4% ($n = 30$) female participated in the study. 55.7% ($n = 78$) cases were from rural background and 44.3% ($n = 62$) from urban.

	Allergic rhinitis, n (%)	Asthma, n (%)	Total (n)
Age (years)			
6-10	41 (58.6)	56 (80)	97 (69.3)
11-18	29 (41.4)	14 (20)	43 (30.7)
Gender			
Female	20 (28.6)	10 (14.3)	30 (21.4)
Male	50 (71.4)	60 (85.7)	110 (78.6)
Residence			
Rural	40 (57.1)	38 (54.3)	78 (55.7)
Urban	30 (42.9)	32 (45.7)	62 (44.3)

Table 1: Demographic data of study subjects

[Table 2] depicts the skin test reactivity in AR and asthma groups. 77.1% (108) cases of both AR and asthma showed positive skin test to at least 1 aeroallergen or more. Both groups showed equal skin reactivity in our study, no significant difference seen in both study group.

Skin prick test	Allergic rhinitis, n (%)	Asthma, n (%)	Total, n (%)
Negative	16 (22.9)	16 (22.9)	32 (22.9)
Positive	54 (77.1)	54 (77.1)	108 (77.1)
Total	70 (100)	70 (100)	140 (100)

$\chi^2=0.041$ with 1 degree of freedom; $P=0.840$

Table 2: Skin-prick test positivity among study participants

[Table 3] illustrates the prevalence of different aeroallergens in AR and asthma patients. Common allergens in our study were HDM ($n = 49$, 45.3%), Cockroach ($n = 45$, 41.7%), mosquito ($n = 45$, 41.7%), grain dust ($n = 31$, 28.7%) and haloptelia ($n = 28$, 25.9%). HDM was the commonest offending allergen in Asthma patients (41.4%, $n = 29$) and mosquito (32.9%, $n = 23$) in AR patients.

Allergens	Asthma, n (%)	Total, n (%)
Alternaria	5 (9.2)	5 (4.6)
Argimone	1 (1.8)	3 (2.8)
Brassica	4 (7.4)	10 (9.2)
Chenopodium	7 (12.9)	15 (13.9)
Cockroch (f, m, both)	22 (40.7)	45 (41.7)
Cynadon	7 (12.9)	14 (12.9)
Grain dust	15 (27.8)	31 (28.7)
Haloptelia	13 (24)	28 (25.9)
HDM (Df, Dp, both)	29 (53.7)	49 (45.3)
Mosquito	24 (44.4)	45 (41.7)
Ricinus	6 (11.1)	13 (12)
Zea mays	7 (12.9)	12 (11.1)
Amaranthus	5 (9.2)	8 (7.4)
Dog dander	3 (5.5)	6 (5.5)
Parthenium	6 (11.1)	14 (12.9)

HDM=House dust mite

Table 3: Distribution of study subjects according to prevalence of allergens sensitivity

[Table 4] represents the relation of mean IgE level with SPT positivity. In our study with 140 total subjects, mean IgE level was significantly high (759.5 ± 607.7) in SPT positive cases ($n = 108$) in comparison to SPT negative ($n = 32$) cases (235.4 ± 271.7) ($P < 0.001$).

SPT	n	Mean±SD	Range
SPT positive	108	759.5±607.7	72-2736
SPT negative	32	235.4±271.7	20-1349
t-test=4.731 with 138 degree of freedom; P<0.001 (S). SPT=Skin prick test, SD=Standard deviation, S=Significant			

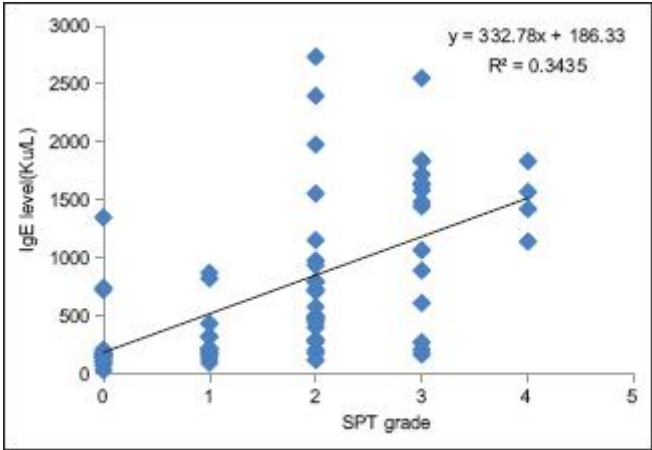
Table 4: Mean immunoglobulin E level of study subjects in relation to skin prick test positivity

[Table 5] shows the relationship of TEC to SPT positivity in study subjects. According to our study analysis, mean of TEC in SPT positive ($n = 108$) was 645.6 ± 487.7 and in SPT negative ($n = 32$) was 370.3 ± 354.5 , which is also significant statistically ($P = 0.004$).

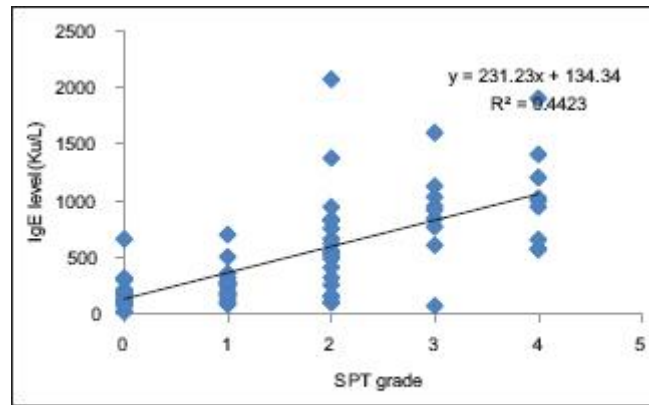
SPT	n	Mean±SD	Range
SPT positive	108	645.6±487.7	0-2810
SPT negative	32	370.3±354.5	0-1720
t-test=2.966 with 138 degree of freedom; P=0.004 (S). SD=Standard deviation, S=Significant, SPT=Skin prick test			

Table 5: Mean total eosinophils count level of study subjects in relation to skin prick test positivity

Regarding correlation between IgE level and skin prick reactivity grading, we observed in this study that total serum IgE level is strongly related with skin reactivity in both AR and asthma groups (correlation coefficient = 0.68) as depicted in [Graph 1] and [Graph 2].

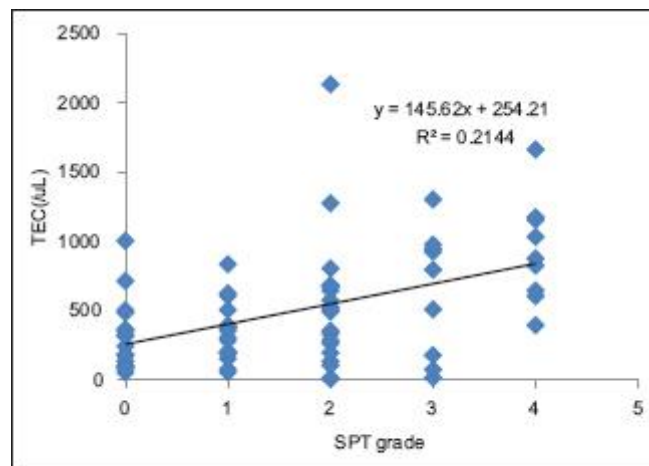


Graph 1: Correlation between immunoglobulin E level (K.u/L) and skin prick test grade in asthma

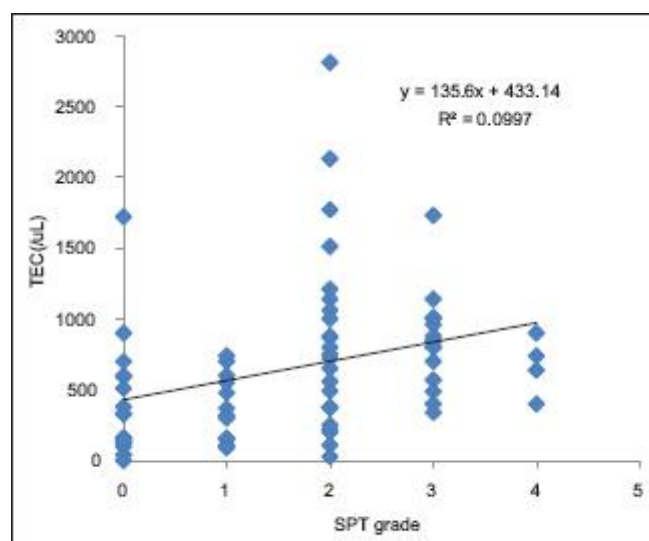


Graph 2: Correlation between immunoglobulin E level (Ku/L) and skin prick test grade in allergic rhinitis

According to pearsons correlation coefficient, not as strong but a good correlation was observed between TEC and SPT grade in our all study subjects ($r = 0.48$) as illustrated by [Graph 3] and [Graph 4].



Graph 3: Correlation between total eosinophils count (/uL) and skin prick test grade in allergic rhinitis



Graph 4: Correlation between total eosinophils count (/uL) and skin prick test grade in asthma

Discussion



This study was carried out to determine correlation between total serum IgE level and TEC with SPT for 18 common aeroallergens in children with AR and asthma. A total 140 pediatric patients (70 AR and 70 asthma), who presented at pediatric OPD at a tertiary care centre in Rajasthan, India, with respiratory allergy were enrolled for the study.

In present study, total 140 patients of aged 6–18 years were enrolled. Most of the cases were below 10 years of age. In this study, there is a significant difference observed between age distribution of AR and asthma groups as the Asthma is more prevalent in younger age group in comparison to AR. Eighty percent of Asthma cases were of age group 6–10 years similar age distribution for asthma was observed in study by Jain *et al.*^[17] and Bayram *et al.*^[18] who found the prevalence of Asthma more in younger age group. Male: female ratio of study subjects was around 4:1 for this study, 78.9% participates were male. 57.1% of cases of AR and 54.3% of cases diagnosed as asthma were from rural background. In a study by Lama *et al.*^[19] their 80% of subjects with asthma were from rural background.

In this study of total 140 subjects, we performed skin prick testing using 18 aeroallergens and was positive of various grades with 1 or more allergens in 77.1% of cases ($n = 108$). Both the study groups, AR and Asthma showed equal incidence of SPT positivity (77.1% each), no significant difference was seen in both groups. Study by Ibekwe and Ibekwe^[14] in 96 allergic patients of Niegeria, showed similar results with SPT i.e., 77% SPT positivity ($n = 74$). Various studies from India and abroad showed high prevalence of SPT positivity. Studies like Siroux *et al.*^[20] found 88.2% ($n = 122$) SPT positivity, Raj *et al.*^[21] 55.6% ($n = 100$), Prasad *et al.*^[22] 89.5% ($n = 43$) and Kumar *et al.*^[23] showed 71.3% ($n = 3040$) SPT positive in their respective studies.

In our study, we found that the commonest offending allergen in asthma patients was HDM (41.4%, $n = 29$) and Cockroach (32.9%, $n = 23$) in AR patients, followed by mosquito (32.1%, $n = 45$), grain dust (22.1%, $n = 31$) and haloptelia (20%, $n = 28$).

Many Indian study showed the similar pattern of allergen sensitization with common allergens. Study by Prasad *et al.*^[22] found the common offending allergens were insects (21.8%, $n = 10$). In Shyna *et al.*^[10] study from South India, HDM was the commonest offending allergen (33%, $n = 20$) similar to our study. Raj *et al.*^[21] found some different pattern of prevalence of sensitization in North India. In their study, Housefly was the commonest allergen, not HDM.

In our study with 140 total subjects, mean IgE level was significantly high (759.5 ku/L) in SPT positive cases in comparison to SPT negative cases (235.4ku/L) ($P < 0.001$), and total IgE level is strongly related to SPT grading in both AR and Asthma patients (correlation coefficient: 0.70 and 0.67 respectively). Kim *et al.*^[24] also found similar relation between SPT positivity and mean IgE in Korean children of 2 age group-6–7 years and 12–13 years. Total IgE levels were higher in children who had a positive SPT response than in those who did not (all $P < 0.001$ at both age groups). Brown *et al.*^[25] found the similar relation between total IgE and SPT. Correlation coefficients between prick responses to individual allergens and total IgE levels were significant from $P < 0.01$ to < 0.001 , Increasing IgE levels are positively correlated with increasing skin reactivity by prick test. But Gharagozlou *et al.*^[26] interestingly found in their study that in the patients with asthma and AR, there was no correlation found between total IgE levels and SPT results ($r = 0.228$, $P = 0.005$ and $r = 0.235$, $P = 0.037$).

TEC were high in SPT positive cases ($n = 108$), in comparison to SPT negative cases ($n = 32$). Mean TEC in SPT positive group was 645.6 ± 487.7 (Standard deviation [SD]) while in SPT negative group it was 370.3 ± 354.5 (SD) which is significant statistically ($P = 0.004$). There is a good correlation between TECs and SPT grade ($r = 0.48$). Similarly Siroux *et al.*^[20] and Deo *et al.*^[27] also found the positive relation between SPT and blood eosinophilia.

Thus, our results seem to confirm the significant relationship between total IgE and TEC with SPT. Regarding the recent studies, SPT itself is one of the most effective measurements of atopy and correlates well with other *in vitro* blood tests like IgE level and eosinophils count (with total IgE level > TEC).

Conclusion



The present study suggests that there is a close relationship between nonspecific allergic markers, namely total serum IgE and TEC and skin test reactivity in children with AR and Asthma. All three parameters can be a predictor of one another in the evaluation of children with allergic conditions. Total serum IgE levels and TECs reflect the severity of the inflammatory processes in allergic disorders, while SPT shows the sensitization of an individual with the specific allergen.

It is recommended that total serum IgE levels and peripheral eosinophil counts should be done in all cases of AR and asthma along with other specific investigations such as skin prick testing, for arriving at a proper diagnosis and management.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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