

Study of Serum IgE levels in Recurrent Respiratory illness in children 6 months to 5 years of age

Vishwakarma R.¹, Sharan A.^{2*}, Reddy P.³, Satyanarayana K.⁴

DOI: <https://doi.org/10.17511/ijpr.2020.i07.05>

¹ Rashmi Vishwakarma, Resident, Department of Pediatrics, Kamineni Hospital, Hyderabad, Telangana, India.


^{2*} Anita Sharan, Associate Professor, Department of Pathology, Dr. DY Patil Medical and College, Mumbai, Maharashtra, India.

³ Priti Reddy, Resident, Department of Pediatrics, Kamineni Hospital, Hyderabad, Telangana, India.

⁴ Satyanarayana K., Professor and Head, Department of Pediatrics, Kamineni Hospital, Hyderabad, Telangana, India.

Objective: The present study was undertaken to study the serum IgE levels in recurrent respiratory tract illnesses in children greater than 6 months to less than 5 years of age and to find the correlation between them. **Methods:** This was a prospective observational cross-sectional study. The study was undertaken to determine the correlation of serum IgE levels with recurrent respiratory tract illness. A total of 99 children were included in this study. 2ml of blood was drawn by peripheral venous phlebotomy in airtight screw-capped plastic vials for measuring serum IgE levels. The Serum IgE level is assessed by chemiluminescence. **Results:** Out of 99 children, 48 children had elevated serum IgE levels and 51 had normal serum IgE levels. Serum IgE levels were significantly higher (66.07%) in males as compared to females (25.58%) with a p-value of 0.0003 (<0.05). The elevation of serum IgE levels was 48.48% in all children (48 out of 99 children). It's noticed that the number of children suffering from RRTI and the number of children with elevated serum IgE levels increased with increasing age. There is a significant increase in serum IgE levels from 10.00% in infancy to 64.10% in the 49-60th month. **Conclusion:** This study showed an increasing number of children with recurrent respiratory tract illness and serum IgE levels with increasing age. Males, preterm and bottle-fed babies are more prone. There was a significant role in a family history of recurrent respiratory tract illness in children with elevated serum IgE levels.

Keywords: Recurrent Respiratory Tract Illness, RTI, Children, Serum IgE, Chemiluminescence

Corresponding Author	How to Cite this Article	To Browse
Anita Sharan, Associate Professor, Department of Pathology, Dr. DY Patil Medical and College, Mumbai, Maharashtra, India. Email: anitsharan@gmail.com	Vishwakarma R, Sharan A, Reddy P, Satyanarayana K. Study of Serum IgE levels in Recurrent Respiratory illness in children 6 months to 5 years of age. <i>Pediatric Rev Int J Pediatr Res.</i> 2020;7(7):344-350. Available From https://pediatrics.medresearch.in/index.php/ijpr/article/view/623	

Manuscript Received
2020-08-30

Review Round 1
2020-09-10

Review Round 2
2020-09-18

Review Round 3

Accepted
2020-09-29

Conflict of Interest
No

Funding
Nil

Ethical Approval
Yes

Plagiarism X-checker
8%

Note



© 2020 by Rashmi Vishwakarma, Anita Sharan, Priti Reddy, Satyanarayana K. and Published by Siddharth Health Research and Social Welfare Society. This is an Open Access article licensed under a Creative Commons Attribution 4.0 International License <https://creativecommons.org/licenses/by/4.0/> unported [CC BY 4.0].



Introduction

Pediatric respiratory tract illness is one of the most common reasons for physician visits and hospitalization and is associated with significant morbidity and mortality. Respiratory illness (RI), mainly involving the upper airways, is common in children and their recurrence constitutes a demanding challenge for the pediatricians.

A child with recurrent respiratory infections presents a difficult diagnostic challenge. It is necessary to discriminate between those with simply-managed causes for their symptoms such as recurrent viral infections or asthma, from the children with more serious underlying pathology such as bronchiectasis or immune dysfunction.

Recurrent infectious rhinitis is usually defined as more than five episodes per year and recurrent pharyngitis or tonsillitis more than three episodes within 12 months. It is evident, that only a few appropriate tests are enough helpful to discriminate between a "well-being" child and a patient with immune dysfunction.

Asthma is a chronic inflammatory disorder of the airways involving many cells and cellular elements. The inflammation causes swelling and narrowing of the airway restricting the capability of air to pass through to the lung tissue. The swelling and narrowing of the airways cause recurrent episodes of coughing, wheezing, breathlessness, and chest tightness [1-3].

IgE is the least abundant of the human immunoglobulin classes and was accordingly the last to be discovered in the late 1960s. The concentration of IgE in normal human sera is between 10 and 400 ng/ml⁷. Furthermore, at least in humans, the turnover rate of IgE is much more rapid than that of another immunoglobulin. The half-life of IgE in the circulation is estimated at 2-2.5 days. Sometimes the immune system reacts unnecessarily vigorously against otherwise harmless environmental agents, allergens.

These overreactions are termed hypersensitivity reactions and fall into four subgroups, type's I-IV, depending upon the mechanism behind the action. The type I hypersensitivity reactions are mediated by allergen-specific IgE and are responsible for the clinical manifestation of atopic allergies, such as hay fever, food allergies, eczema, asthma, and anaphylaxis, parasitic infections [4-7].

Materials and methods

Type of study: Prospective observational cross-sectional study.

Sample size: 99 children with inclusion criteria above mentioned.

Inclusion criteria

- Age group > 6 months to < 5 years.
- Children with symptoms of recurrent respiratory tract infections defined as

To diagnose RRTI, at least one of the following criteria needs to be met (Gruppo di Studio di Immunologia della Società Italiana di Pediatria, 1988)

≥ 6 respiratory infections per annum

≥ 1 respiratory infection per month involving the upper airways from September to April

≥ 3 respiratory infections per annum involving the lower airways

Exclusion criteria

- Age less than 6 months
- Congenital heart disease.
- Cerebral palsy.
- Proven Immunodeficiency disorder.

Method of collection of data Approximately 2ml of blood was drawn using aseptic technique by peripheral venous phlebotomy in airtight screw-capped plastic vials for measuring serum IgE levels. The Serum IgE level is assessed by the chemiluminescence method. For accurate comparison to established normal values, a fasting morning serum sample should be obtained. The blood was collected in a plain redtop venipuncture tube without additives or anti-coagulants. The blood was allowed to clot for samples. The specimen is centrifuged to separate the serum from the cells. The usage of contaminated devices was avoided. Repetitive freezing and thawing were avoided. The blood sample collected was transported immediately to the laboratory. Serum IgE levels were measured by the chemiluminescence method.

Normal range: 1-165 IU/ml.

Estimation of serum immunoglobulin: test principle:

Anti-IgE, covalently coupled to Immucap reaction vessel, reacts with the total IgE in the sample. After washing, enzyme-labeled antibodies against IgE are added to form a complex.

After incubation, unbound enzyme anti-IgE is washed away and the bound complex is then incubated with a developing agent. After stopping the reaction, the fluorescence of the eluate is measured. The fluorescence is directly proportional to the concentration of IgE in the sample. To evaluate the test results, the response for the patient samples is compared directly to the response for the calibrators.

Reagents: UniCAP/Pharmacia CAP System™ Washing Solution Product No. 10-9202-01, 2 bottles (400 ml each) of Concentrate, 2 bottles (86 ml each) of additive. The additive contains Surfactant and 5.8 % Kathon CG. The concentrate contains Phosphate buffer and 0.05 % Kathon CG. Store concentrate and additive at 2-8°C until the expiration date. Reconstitute using 5 liters of distilled water, 1 bottle Concentrate, and 1 bottle Additive. Mix thoroughly.

Storage: Allow the samples to thaw in the refrigerator at 2-8° C temperature. Bring the number of samples to be tested to room temperature. Maintain the samples at room temperature during the testing process. Store the sample box back in the refrigerator at 2-8 until the testing is completed on all the samples in the box.

Calculation: The IDM software uses Red bard 5 parameter calculations to graph the calibrator concentrations as a log-log graph. The software then plots the sample response on the calibration curve to calculate the concentration into kU/L, or IU/ml.

Statistical analysis: Continuous data were entered into an excel sheet and analyzed using SPSS (trial version) software. A Chi-square test was used to find an association between elevated serum IgE levels and other variables. The significance level was set at less than 0.05.

Results

The present study was undertaken to determine the correlation of serum IgE levels with recurrent respiratory tract illness. A total of 99 children were included in this study. Elevated serum IgE levels were found in 48.48% of children with recurrent respiratory tract illnesses. Male to Female ratio in recurrent respiratory tract illness with elevated serum IgE levels was 3.4:1 This study showed an increasing number of children with recurrent respiratory tract illness and serum IgE levels with increasing age.

The recurrent respiratory tract illness and elevated serum IgE were less in children who were exclusively breastfed compared to not exclusively breastfed in the initial 6 months of life. Children born at term gestation showed a significant increase in serum IgE levels as compared to those born preterm.

There was a significant role in a family history of recurrent respiratory tract illness in children with elevated serum IgE levels. Serum IgE level was elevated in 50% of children with increased eosinophils, but there was no significant correlation of % of eosinophils and serum IgE levels.

Table-1: Elevated serum IgE levels and gender.

Sex	Elevated serum IgE levels	Normal serum IgE levels
Male (n=56)	37 (66.07%)	19 (33.92%)
Female (n=43)	11 (25.58%)	32 (74.41%)
Total (n=99)	48	51

Table-2: Elevated serum IgE levels-age.

Age group	Number of RRTI children	Number of children with elevated serum IgE levels	%age with elevated IgE levels	P-value
1 - 12 months	10	1	10.0%	0.12
13 -24 months	14	3	21.4%	0.30
25- 36 months	16	9	56.25%	0.07
37 -48 months	20	10	50.00%	0.24
49-60 months	39	25	64.10%	0.001
Total	99	48	48.48%	

Table-3: Elevated serum IgE levels-exclusive breastfeeds.

Breastfeeds	No. Of children with elevated serum IgE levels	No. Of children with normal serum IgE levels
Exclusive breast feeds (n=58)	16 (27.58%)	42 (72.41%)
Not exclusive breast feeds (n=41)	32 (78.04%)	9 (21.95%)
Total (n=99)	48	51

Elevation of serum IgE level was more (78.04%) is not exclusively breastfed as compared to those who were exclusively breastfed (27.58%) with a p-value of 0.0001 (<0.05).

Table-4: Elevated serum IgE levels – gestational age at birth.

Gestational age	Elevated serum IgE levels	Normal serum IgE levels
Term (n=86)	46 (53.48%)	40 (46.51%)
Preterm (n=13)	02 (15.38%)	11 (84.61%)
Total (n=99)	48	51

Out of 48 children with elevated serum IgE levels, 46 (53.48%) were born at term gestation and only 2(15.38%) were born preterm. This is statistically significant with a p-value of 0.01(<0.05).

Table-5: Elevated serum IgE levels –family history of RRTI.

Family history	Number of children with elevated serum IgE levels	Number of children with normal serum IgE levels
Positive (n=20)	17 (85%)	3 (15%)
Negative (n=79)	31 (39.24%)	48 (60.75%)

Serum IgE levels were significantly elevated in 85% of children with a family history of recurrent respiratory tract illnesses with a p-value of 0.001(<0.05).

Table-6: Elevated serum IgE levels-eosinophils.

Eosinophils	Elevated serum IgE levels	Normal serum IgE levels
Elevated (n=8)	4(50.0%)	4(50.0%)
Normal (n=91)	44(48.35%)	47(51.64%)

50% of children with elevated eosinophils had elevated serum IgE levels with p-value 0.93 (>0.05) which is not significant.

Discussion

A child with recurrent respiratory infections presents a difficult diagnostic challenge. It is necessary to discriminate between those with simply-managed causes for their symptoms such as recurrent viral infections or asthma, from the children with more serious underlying pathology such as bronchiectasis or immune dysfunction.

The present study was undertaken to determine the correlation of serum IgE levels with recurrent respiratory tract illness. A total of 99 children were included in this study.

Studies by Satwani et al and Dhar S et al showed that clinical activity of the disease as recorded by the "SCORAD" index can be used as an indicator of the hematological abnormalities as well as to some extent as a prognostic indicator.

A family history of atopy correlates with the hematological abnormalities only if both parents are involved and bronchial asthma is the only associated atopic condition that correlates with the parameters of the disease [8,9].

Stempel DA et al did a prospective longitudinal study and studied the incidence, clinical manifestations, and infectious etiology of respiratory illnesses observed in a were correlated with serum IgE values, which were used as objective markers of atopy. The incidence of upper respiratory illness or middle ear disease showed no correlation with IgE values.

The number and types of viral infections are distributed evenly throughout the population. The results suggest that children with recurrent URI or MED deserve evaluation for allergy only if there are other clinical findings suggestive of atopy. Foucard T et al on the other hand developed allergen-specific IgE and IgG antibodies in pollen-allergic children given immunotherapy.

After treatment, thirteen children tolerated ten to 10,000 times more allergen than before by naso-conjunctival challenge tests. Ten of the children reacted to the same allergen dilution as before and two reacted to a ten times weaker extract. Clinical improvement was accompanied by increased tolerance in most patients.

In the present study, serum IgE levels were elevated in 48.48 % of the children, near comparable to the study done by Satwani et al (64.37%), and very high (85%) in Stempel et al and was noticed very low (32%) in Foucard et al which could be due to the variable number of children in different studies [8-11]. Nagayama Y et al saw total and specific IgE responses in the acute and recovery phases of respiratory infections in children.

The results indicated that these infections might alter the production of total IgE and IgE specific to common allergens unrelated to the infectious agents. Borish L studied total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma. In patients with severe or difficult-to-treat asthma from the TENOR study, higher total IgE levels were observed in males, children, smokers, nonwhite racial/ethnic groups, and adults with the childhood-onset disease.

Also, IgE levels are associated with asthma severity among younger patients.

In the current study number of boys with elevated serum IgE was more than girls, which is statistically significant ($p=0.0003$) Similar results were seen in the studies done by Satwani et al (65%) and Borish L et al (66.5%) The factor responsible for this result could be that, the boys are more exposed to the outdoor activities, hence, increased chances of getting exposed to respiratory infections and allergens [8,12-13].

Petridou ET et al did an investigation that suggests an IgE-mediated allergic response among women with BC in comparison to their controls. The finding needs confirmation by immuno-epidemiological investigation to clarify the directionality of this association and whether laboratory-ascertained atopy can be considered as a risk-marker of susceptibility in the development of BC Johnsson V et al studied that Serum IgE level was determined in 76 monozygous and 81 dizygous like-sexed twin pairs representing adult twins living in the Helsinki area. Monozygous twin pairs were frequently concordant concerning elevated IgE levels, although some pairs were strikingly discordant, indicating that there is a wide range of phenotypic expression for each genotype [14,15]. In the current study, the number of children with elevated serum IgE levels significantly increased with increasing age with a p-value of 0.01. This is by the study conducted on Greek children, by Petridou et al, in children aged 1 month to 14 years, total IgE levels increased by almost 80% per year until 5 years of age. Similarly in a study by Johnsson et al (USA), a 60% increase in IgE levels was observed from birth to 4 years of age. Hamid Habib et al too had significantly increased serum IgE levels with increasing age with p-value 0.001 [14-16].

In the current study, serum IgE levels are significantly elevated (78.04%) in children who were weaned off earlier (before 6 months of age) with a p-value of 0.01 Similar results 60% of elevation of serum IgE levels with early weaning was seen in the study by Satwani H et al with p-value <0.01 and little less, 50% elevation of serum IgE with early weaning were seen in A L Wright et al with p-value <0.005 . In the current study, children born as preterm were less likely to have elevated serum IgE levels as compared to those who were born at term gestation. These values are near the study by Siltanen et al in the study "Preterm birth reduces the atopy in adults" showing 69% elevation of serum IgE levels in children born at term gestation [8,15,16,17].

Habib H worked on the role of both serum total IgE levels and the absolute eosinophils count, total IgE alone, absolute eosinophils count as a marker of allergy in children. It was concluded that serum total IgE level and absolute eosinophils count, total IgE alone and absolute eosinophils count alone are not a good predictor of allergy in children except that the absolute eosinophils count can be considered as a strong predictor of atopic dermatitis in children. It's found that as the child age increases the positivity of all the tests increases also. A Study of Serum IgE Levels among Children of 6 Months to 5 Years of Age Group Gandhi SS, Rao KR. et al showed that an increasing number of children with recurrent respiratory tract illness and serum IgE levels with increasing age [18-19].

Respiratory morbidity is a major health problem among children. The aim of this study by Siltanen M et al was to compare the background of respiratory problems of children born preterm with that of children born full-term, with special reference to atopy. In conclusion, they demonstrated a significant difference between groups in the association of atopy with respiratory problems.

However, although atopy was not associated with a lifetime prevalence of respiratory symptoms in prematurely born children, an atopic predisposition in them was found to associate with the persistence of wheezing. Croner S et al on other hand did IgE screening in 1701 newborn infants and the development of atopic disease during infancy. There was a significant elevation of serum IgE levels (with a p-value of 0.001) in children with a positive family history of recurrent respiratory tract illness [18-19].

The present results are near to the study by S Croner et al, which had a family history of RRTI in 70% of the children. In this study, 50% of children with increased eosinophils showed elevated serum IgE levels with a p-value of 0.93 (>0.05), which is not significant. Razi E et al studied serum total IgE levels and total eosinophil counts and their relationship with treatment response in patients with acute asthma. On the basis of these findings, they concluded that serum total IgE levels, peripheral white blood cell counts, and eosinophil counts cannot predict the response to the pharmacological treatment of patients with acute asthma. The current study is not following the study by Ebrahim et al, which showed a significant correlation between serum IgE levels and eosinophils with a p-value of 0.001 [18-20].

Conclusion

This study showed an increasing number of children with recurrent respiratory tract illness and serum IgE levels with increasing age. Males, preterm and bottle-fed babies are more prone. There was a significant role in a family history of recurrent respiratory tract illness in children with elevated serum IgE levels. The majority of studies are following the present study, however, some studies results are contrary to what was inferred. Therefore more studies with a large sample size are needed to derive a conclusion.

What does the study add to the existing knowledge

An increasing number of children with recurrent respiratory tract illness and serum IgE levels with increasing age. Males, preterm and bottle-fed babies are more prone. There was a significant role in a family history of recurrent respiratory tract illness in children with elevated serum IgE levels. More studies with a large sample size are needed to derive a conclusion

Author's contribution

Dr. Rashmi Vishwakarma: Concept and data collection, **Dr. Anita Sharan:** Data collection and statistical analysis, **Dr. Priti Reddy:** Data collection and references, **Dr. K. Satyanarayana:** Discussion and guidance

Reference

- Bellanti JA, Olivieri D, Serrano E. Ribosomal immunostimulation. *Bio Drugs*. 2003;17(5)355-67. doi: 10.2165/00063030-200317050-00005 [Crossref]
- Graham NM. The epidemiology of acute respiratory infections in children and adults- a global perspective. *Epidemiol Rev*. 1990;12;149-178. doi: 10.1093/oxfordjournals.epirev.a036050 [Crossref]
- Teele DW, Klein JO, Rosner B. Greater Boston Otitis Media Study Group, Epidemiology of otitis media during the first seven years of life in children in greater Boston- a prospective, cohort study. *J Infect Dis*. 1989;160(1)83-94. doi: 10.1093/infdis/160.1.83 [Crossref]
- Ishizaka K, Ishizaka T. Identification of γ E-antibodies as a carrier of reaginic activity. *J Immunol*. 1967;99(6)1187-1198. [Crossref]
- Kleine-Tebbe J, Poulsen LK, Hamilton RG. Quality management in IgE-based allergy diagnostics. *J Lab Med*. 2016;40(2)81-96. doi: 10.1515/labmed-2016-0013 [Crossref]
- Bennich HH, Ishizaka K, Johansson SG, Rowe DS, Stanworth DR, Terry WD. Immunoglobulin E- a new class of human immunoglobulin. *Immunol*. 1968;15(3)323. [Crossref]
- Kochwa S, Terry WD, Capra JD, Yang NL. Structural studies of immunoglobulin EI Physicochemical studies of the IgE molecule. *Ann New York Acad Sci*. 1971;190;49-70. doi: 10.1111/j.1749-6632.1971.tb13523.x [Crossref]
- Satwani H, Rehman A, Ashraf S, Hassan A. Is serum total IgE levels a good predictor of allergies in children. *J Pak Med Assoc*. 2009;59(10)698-702. [Crossref]
- Dhar S, Malakar R, Chattopadhyay S, Dhar S, Banerjee R, Ghosh A. Correlation of the severity of atopic dermatitis with absolute eosinophil counts in peripheral blood and serum IgE levels. *Indian J Dermatol Venereol Leprol*. 2005;71(4)246. doi: 10.4103/0378-6323.16615 [Crossref]
- Stempel DA, Clyde Jr WA, Henderson FW, Collier AM. Serum IgE levels and the clinical expression of respiratory illnesses. *J Pediatr*. 1980;97(2)185-190. doi: 10.1016/s0022-3476(80)80471-9 [Crossref]
- Foucard T, Johansson SG. Allergen-specific IgE and IgG antibodies in pollen-allergic children given immunotherapy for 2-6 years. *Clin Experiment Allerg*. 1978;8(3)249-257. doi: 10.1111/j.1365-2222.1978.tb03221.x [Crossref]
- Nagayama Y, Sakurai N, Kojima S, Funabashi S. Total and specific IgE responses in the acute and recovery phases of respiratory infections in children. *J Asthma*. 1987;24(3)159-166. doi: 10.3109/02770908709070932 [Crossref]

13. Borish L, Chipps B, Deniz Y, Gujrathi S, Zheng B, Dolan CM. TENOR Study Group, Total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma. *Ann Allergy, Asthma Immunol.* 2005;95(3)247-253.
doi: 10.1016/S1081-1206(10)61221-5 [Crossref]
14. Petridou ET, Chavelas C, Dikaloti SK, Dessypris N, Terzidis A, Nikoulis DI, et al. Breast cancer risk in relation to most prevalent IgE specific antibodies- a case control study in Greece. *Anticancer Res.* 2007;27(3B)1709-1713.
[Crossref]
15. Sistonen P, Johnsson V, Koskenvuo M, Aho K. Serum IgE levels in twins. *Human heredity.* 1980;30(3)155-158.
doi: 10.1159/000153120 [Crossref]
16. Habib H, Tayeb M, Qutub M, Samkari J. Total IgE and Absolute Eosinophils Count as a Predictor of Allergic Diseases in Children. *Egyptian J Hospital Med.* 2010;40(1)365-374.
doi: 10.12816/ejhm.2010.17385 [Crossref]
17. Gandhi SS, Rao KR, Kokiwar P. Clinical study of recurrent respiratory tract illness among pediatric patients. *International Journal of Contemporary Pediatrics.* 2016;3(1)210-213.
[Crossref]
18. Siltanen M, Savilahti E, Pohjavuori M, Kajosaari M. Respiratory symptoms and lung function in relation to atopy in children born preterm. *Pediatr pulmonol.* 2004;37(1)43-49.
doi: 10.1002/ppul.10402 [Crossref]
19. Croner S, Kjellman NI, Eriksson B, Roth A. IgE screening in 1701 newborn infants and the development of atopic disease during infancy. *Arch Dis Childhood.* 1982;57(5)364-368.
doi: 10.1136/adc.57.5.364 [Crossref]
20. Razi E, Moosavi GA. Serum total IgE levels and total eosinophil counts relationship with treatment response in patients with acute asthma. *Jornal Brasileiro De Pneumologia.* 2010;36(1)23-28.
doi: 10.1590/S1806-37132010000100006 [Crossref]