

# Relationship of Age and Gender with Total Serum Immunoglobulin E Levels in Adults- A Cross-sectional Study

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## ABSTRACT

**Introduction:** Immunoglobulin E (IgE) plays a crucial role in various allergic diseases. These antibodies are produced in response to allergenic environmental stimuli, and their blood levels strongly correlate with allergy manifestations. Elevated IgE levels have been considered a powerful predictor of future asthma development. While several studies have explored the association between total serum IgE levels and demographic and environmental factors, no such study has been conducted in this region of India.

**Aim:** To estimate total serum IgE levels and examine their association with age and gender in the adult population of Haryana, India.

**Materials and Methods:** A cross-sectional study was conducted in the Department of Respiratory Medicine, Adesh Medical College and Hospital, Shahabad (M), Kurukshetra, Haryana, India. The records of patients, who visited the department between September 2015 and December 2020 were screened. Data on

serum total IgE levels, age, and gender were collected from 360 patients (21-80 years, both sexes) with available information. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 23.0 software.

**Results:** The mean age of the study participants was  $36.80 \pm 18.30$  years. Out of total 360 patients included, 198 (55%) were males and 162 (45%) were females. Male gender (odds ratio=1.68) was a significant ( $p < 0.05$ ) independent risk factor, while age  $\leq 30$  years (odds ratio=1.68) and age 31-50 years (odds ratio=1.15) were insignificant ( $p > 0.05$ ) risk factors for abnormal serum total IgE levels.

**Conclusion:** Significant gender variation was observed in total serum IgE levels, while age showed insignificant variation. Physicians should consider these factors when examining the relationship between serum total IgE levels, allergy markers, and airways disease.

**Keywords:** Antibodies, Asthma, Allergy marker, Inflammatory response

## INTRODUCTION

The IgE serves as a mediator of allergic reactions triggered by exposure to specific allergens [1]. It constitutes approximately 0.05% of total immunoglobulin levels in the body, making it the least abundant isotype [2]. IgE, upon binding to allergens, elicits an inflammatory response, becoming a characteristic feature of various allergic conditions. Previous studies have reported differences in serum total IgE levels based on ethnicity, age, and gender [3,4], although some studies have contradicted these findings and found no significant association between serum IgE and age or gender [5]. Moreover, studies have suggested physiological or environmental disparities in IgE-mediated immune responses between males and females [2,6]. Therefore, demographic and environmental factors may serve as predictors of total IgE levels in adults, which should be considered when examining the relationship between IgE levels, allergy markers, inflammation, and airway disease [6,7].

Due to the global increase in the prevalence of allergic diseases, physicians strive to promptly identify patients with such conditions, and serum total IgE level estimation can aid in achieving this goal. However, it has been observed that interpreting IgE levels should also take into account age and gender differences [1]. Considering these aspects, the present study aimed to assess the relationship between age, gender, and serum total IgE levels among the adult population in a tertiary care health setting in Haryana, as no such study has been conducted in this region of India.

## MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of Respiratory Medicine, Adesh Medical College and

Hospital, Shahabad (M), Kurukshetra. Data were collected from medical records between September 2015 and December 2020 and analysed from February 2021 to July 2021. The study received approval from the Institutional Ethics Committee (vide no. AMCH/IEC/2021/01/03, dated 15.01.2021). As it was a retrospective study utilising patient records, consent from the patients was not required.

**Inclusion criteria:** Patients of either sex, aged between 21-80 years, with available data for the variables of age, gender, and total serum IgE levels, were included in the study.

**Exclusion criteria:** Patients aged  $< 21$  years and those with incomplete data were excluded from the study.

**Sample size calculation:** Assuming that two out of three patients visiting the Department of Respiratory Medicine met the study criteria, with a proportion of 66.7% having abnormal IgE levels, and considering a minimum two-sided 95% confidence interval with a 5% margin of error, the estimated minimum sample size was 342. Therefore, a total of 360 patients were included in the final analysis. The sample size was determined using software (Power analysis and sample size version -16, PASS-16, NCSS, LLC, USA).

## Study Procedure

Aseptically, 5 mL of venous blood samples were collected from the ante-cubital vein of the subjects after an overnight fasting of 10-12 hours using a dry disposable syringe. The blood was transferred to a sterile, dry, acid-washed vial, allowed to stand for half an hour, and after clot formation, the supernatant was

centrifuged. Total IgE levels were estimated in serum using a two-site immunoenzymometric assay on the TOSOH AIA-360 immunoanalyser. The detectable range of total serum IgE was 3-4000 IU/mL. Measurements below 3 IU/mL or above 4000 IU/mL were expressed as 3 IU/mL or 4000 IU/mL, respectively. A reference value of 214 IU/mL was considered based on the age of the analysed patients [8]. Serum total IgE levels (IU/mL) were further categorised as abnormal (>214) or normal ( $\leq$ 214).

## STATISTICAL ANALYSIS

Continuous variables were presented as mean $\pm$ standard deviation or median (interquartile range), while categorical variables were expressed as frequencies (%). The independent samples t-test was used to compare age between genders, while the Mann-Whitney U test and Kruskal-Wallis H test were used to compare serum total IgE values between genders and age groups, respectively. Spearman's rank correlation coefficient was employed to determine the correlation between age and serum total IgE levels. Classification and Regression Trees (CART) analysis was utilised to visually present homogeneous subgroups for predicting abnormal total IgE levels. Binary logistic regression analysis was used to assess independent predictors of IgE based on age groups and gender. Mean and 95% confidence intervals were represented using error bars. The correlation coefficient between age and IgE levels of the study participants was displayed using a scatter plot. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 23.0 software.

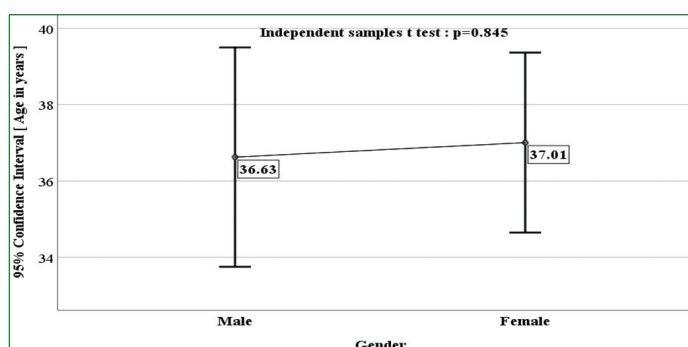
## RESULTS

The present study included a total of 360 outpatients of either sex who visited the Department of Respiratory Medicine for treatment. Among these patients, 198 (55%) were males and 162 (45%) were females. The mean age of the patients was 36.80 $\pm$ 18.30 years. When examining the mean total IgE levels among patients in different age groups, it was found that patients aged  $\leq$ 30 years and those aged >50 years had higher total IgE levels compared to patients in the 31-50 years age group ( $p=0.117$ ) [Table/Fig-1]. The mean age of the study patients was similar between males and females (36.63 years in males vs. 37.01 years in females,  $p=0.845$ ) [Table/Fig-2]. Serum total IgE levels were significantly higher in males (1241.44 $\pm$ 2682.99 IU/mL) compared to females (999.91 $\pm$ 2667.54 IU/mL) ( $p=0.004$ ) [Table/Fig-3].

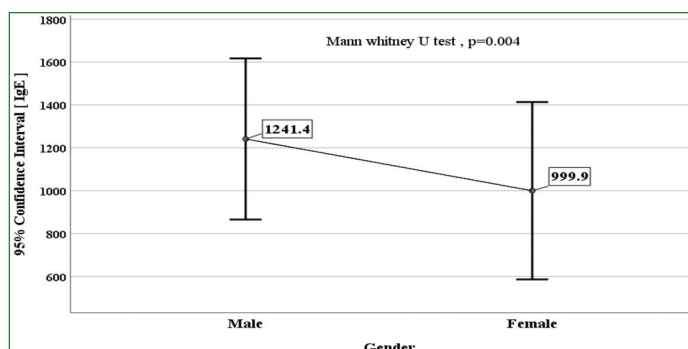
Variables		Mean $\pm$ SD	Median (Q1, Q3)	p-value
Age (in years)		36.80 $\pm$ 18.30	32 (23, 47)	--
IgE (IU/mL)		1132.75 $\pm$ 2675.04	402.30 (122.98, 1162.25)	--
IgE (IU/mL)				
Sex	Male (n=198, 55%)	1241.44 $\pm$ 2682.99	533 (155, 1326)	0.004
	Female (n=162, 45%)	999.91 $\pm$ 2667.54	285 (98.5, 832.7)	
Age groups	$\leq$ 30 years (n=168, 46.7%)	1326.45 $\pm$ 2960.15	510.90 (138.25, 1311.75)	0.117
	31-50 years (n=117, 32.5%)	939.17 $\pm$ 1626.73	384 (120.80, 1013.85)	
	>51 years (n=75, 20.8%)	1000.87 $\pm$ 3260.38	316 (106, 642)	

[Table/Fig-1]: Distribution of IgE and its association with age and gender (N=360). Mann-Whitney U test/Kruskal-Wallis H test was used;  $p<0.05$  significant

Spearman's rank correlation analysis revealed a weak negative correlation between age and serum total IgE levels (correlation coefficient: -0.106,  $p<0.05$ ) [Table/Fig-4]. Univariable binary logistic regression analysis showed that age was not a significant

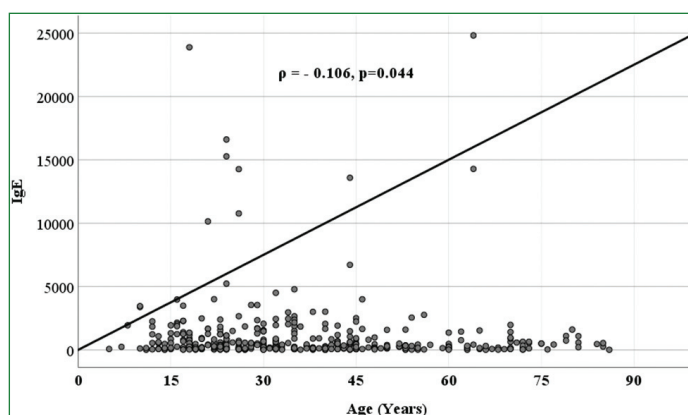


[Table/Fig-2]: Error bar graph showing the almost equal age distribution between male and female study patients.



[Table/Fig-3]: Error bar graph showing the distribution of serum total IgE levels between males and females.

factor, while gender was a significant factor for abnormal total IgE levels. Multivariable binary logistic regression analysis, after adjusting for age, confirmed that male gender was a significant and independent risk factor for abnormal serum total IgE levels [Table/Fig-5].



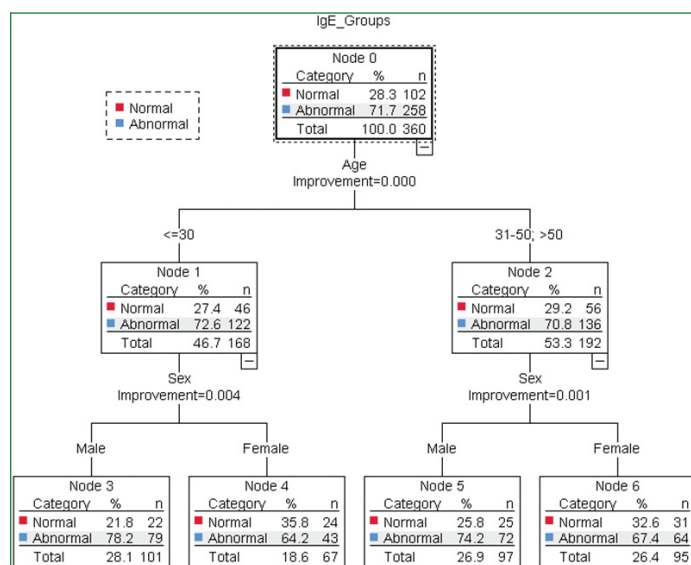
[Table/Fig-4]: Scatter plot showing the weak negative correlation between serum total IgE levels and age of the study participants.

Variables	Univariable analysis			Multivariable analysis		
	Odds ratio	95% CI	p-value	Adjusted odds ratio	95% CI	p-value
Age in years			0.931			0.901
$\leq$ 30	1.10	0.60, 2.01	0.754	1.13	0.62, 2.08	0.686
31-50	1.01	0.54, 1.92	0.968	1.15	0.60, 2.21	0.673
>50	Ref			Ref		
Gender						
Male	1.65	1.04, 2.62	0.033	1.68	1.05, 2.68	0.032
Female	Ref			Ref		

[Table/Fig-5]: Predictors of the IgE from the demographic variables (N=360). Binary logistic regression model used.  $p<0.05$  significant

Furthermore, using the CART method to stratify patients based on abnormal and normal serum total IgE levels, it was found that an age cut-off of  $\leq$ 30 years and >30 years was useful in dividing patients into these groups. Additionally, there was a significantly

higher proportion of male patients with abnormal serum total IgE levels in each age group, suggesting that an age cut-off of  $\leq 30$  years, along with male gender, are risk factors for abnormal serum total IgE levels [Table/Fig-6].



**[Table/Fig-6]:** Classification And Regression Trees (CART) analysis showing the stratification of the study patients into sub-groups with normal and abnormal serum total IgE levels based on age groups and gender.

## DISCUSSION

Allergic disorders are increasing worldwide, and the IgE-mediated inflammatory immune response is a characteristic feature of these diseases. Serum IgE levels can serve as important biomarker and potential target for the treatment of allergic conditions. This study aimed to investigate the relationship between age, gender, and serum total IgE levels in adult patients attending respiratory medicine outpatient departments. The study found significantly higher serum total IgE levels in males compared to females, which is consistent with previous research [6,7,9]. Several studies have reported higher plasma levels of IgE in males, particularly among younger age groups [6,10]. The higher prevalence of smoking in men may contribute to this trend, as suggested by other studies [10,11]. The underlying molecular mechanisms or pathophysiological differences explaining this gender difference remain unclear. However, sex hormones and the involvement of IL-4 in regulating IgE production have been proposed as possible factors [7,12]. It is worth noting that some studies did not find gender differences in serum total IgE levels [13,14]. Although smoking history was not available in the present study, the observed difference in serum IgE levels between males and females was substantial enough to outweigh any potential influence of smoking.

Furthermore, there was a weak negative correlation between total serum IgE levels and patient age. Previous studies in adults have shown mixed results regarding the impact of age on IgE levels [2,15,16]. Some studies reported higher serum IgE levels in certain age groups, while others found no correlation. It is possible that the predominance of patients in a specific age group may contribute to differences in IgE levels [2]. Other studies have suggested that IgE production does not decline with aging due to impaired regulatory function during senescence [15,16]. However, in the present study, after adjusting for age, gender remained a significant risk factor for abnormal IgE levels. Additionally, an age cut-off of  $\leq 30$  years and  $>30$  years was found to be useful in differentiating patients with normal and abnormal IgE levels, with this trend being more evident in males. Therefore, demographic factors were identified as predictors of serum total IgE levels in the adult population. Previous studies have shown that total serum IgE levels can identify patients at risk of allergic diseases such as

asthma [17]. In addition, male gender and age  $\leq 30$  years were identified as independent risk factors for abnormal serum total IgE levels. These findings should be considered by physicians when assessing the relationship between serum IgE levels, allergy markers, and airway diseases.

## Limitation(s)

Limitations of the present study include the lack of information on factors that could potentially influence IgE levels, such as smoking history, disease severity, environmental exposures, and seasonal variations. Additionally, specific IgE measurements or skin prick tests were not performed.

## CONCLUSION(S)

The present study suggests that male patients have a higher risk of elevated total serum IgE levels, even after adjusting for age. Although age or age groups are not independent predictors of elevated IgE levels, individuals below 50 years of age showed a non-significantly higher risk compared to those above 50 years. High serum total IgE levels in individuals below 50 years may indicate underlying inflammatory changes in the lungs, predisposing them to the development of asthma in the future. Therefore, male patients, especially those below 50 years, should be cautious and manage their IgE levels with appropriate medical advice. It is recommended to conduct similar studies in the region, including additional variables that may act as confounding factors, to accurately evaluate the standardised measurement of serum IgE levels and its independent factors. This will contribute to improving clinical practices in the future, particularly in northern India.

## REFERENCES

- Tu YL, Chang SW, Tsai HJ, Chen LC, Lee WI, Hua MC, et al. Total serum IgE in a population-based study of Asian children in Taiwan: Reference value and significance in the diagnosis of allergy. *PLOS One*. 2013;8(11):e80996.
- Choi BG, Lee YW, Choe YB, Ahn KJ. Total serum immunoglobulin E level and specific allergens in adults with skin diseases. *Indian J Dermatol Venerol Leprol*. 2018;84(2):148-52.
- Lama M, Chatterjee M, Chaudhuri TK. Total serum immunoglobulin E in children with asthma. *Ind J Clin Biochem*. 2013;28(2):197-200.
- 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):247-53.
- Criqui MH, Seibles JA, Hamburger RN, Coughlin SS, Gabriel S. Epidemiology of immunoglobulin E levels in a defined population. *Ann Allergy*. 1990;64(3):308-13.
- Couto TA, Falsarella N, Brandao de Mattos CC, Mattos LC. Total IgE plasma levels vary according to gender and age in Brazilian patients with allergic rhinitis. *Clinics (Sao Paulo)*. 2014;69(11):74-44.
- Chen W, Mempel M, Schober W, Behrendt H, Ring J. Gender difference, sex hormones, and immediate type hypersensitivity reactions. *Allergy*. 2008;63(11):1418-27.
- Wittig HJ, Belloit J, De Fillipi I, Royal G. Age-related serum immunoglobulin E levels in healthy subjects and in patients with allergic disease. *J Allergy Clin Immunol*. 1980;66(4):305-13.
- Osman M, Hansell AL, Simpson CR, Hollowell J, Helms PJ. Gender-specific presentations for asthma, allergic rhinitis and eczema in primary care. *Prim Care Respir J*. 2007;16(1):28-35.
- Rajendra C, Zoratti E, Havstad S, Nicholas C, Wegienka G, Cross MT, et al. Relationships between total and allergen-specific serum IgE concentrations and lung function in young adults. *Ann Allergy Asthma Immunol*. 2012;108(6):429-34.
- Tsukioka K, Toyabe SI, Akazawa K. Total and specific IgE levels in adolescents and adults with bronchial asthma. *Nihon Koryoku Gakkai Zasshi*. 2010;48(6):409-18.
- Okano M, Satoskar AR, Abe M, Harn Da Jr, Okano M, Nishizaki K, et al. Interleukin-4-independent production of Th2 cytokines by nasal lymphocytes and nasal eosinophilia in murine allergic rhinitis. *Allergy*. 2000;55(8):723-31.
- Chung HL. Clinical significance of serum IgE. *Korean J Pediatr*. 2007;50(5):416-21.
- Kerkhof M, Droste JH, de Monchy JG, Schouten JP, Rijcken B. Distribution of total serum IgE and specific IgE to common aeroallergens by sex and age, and their relationship to each other in a random sample of Dutch population aged 20-70 years. *Dutch ECRHS Group, European Community Respiratory Health Study. Allergy*. 1996;51(11):770-76.
- Amici MD, Ciprandi G. The age impact on serum total and allergen-specific IgE. *Allergy Asthma Immunol Res*. 2013;5(3):170-74.

- [16] Carosso A, Bugiani M, Migliore E, Anto JM, DeMarco R. Reference values of total serum IgE and their significance in the diagnosis of allergy in young European adults. *Int Arch Allergy Immunol*. 2007;142(3):230-38.
- [17] Razi E, Moosavi. Serum total IgE levels and total eosinophils counts: Relationship with treatment response in patients with acute asthma. *J Bras Pneumol*. 2010;36(1):23-28.

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