

# Total IgE plasma levels vary according to gender and age in Brazilian patients with allergic rhinitis

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**OBJECTIVE:** Allergic rhinitis is a disease that affects the upper airways and causes inflammation of the nasal mucosa and it is mediated by IgE antibodies produced after sensitization to environmental allergens. Previous reports have indicated that this disease affects males more often than females. The objective of this study was to verify whether total IgE plasma levels vary between genders in patients suffering from allergic rhinitis.

**METHODS:** A total of 171 adult patients suffering from allergic rhinitis (55 males and 116 females) were enrolled. Total IgE plasma levels were determined using commercial kits, with 140 IU/mL considered as a reference value. The mean total IgE plasma levels were compared according to gender and age.

**RESULTS:** The mean age of the overall patient group with allergic rhinitis was  $38.4 \pm 19.0$  years and a significant difference in age was observed between genders (males:  $32.2 \pm 17.8$  years; females:  $41.4 \pm 18.9$  years;  $p = 0.0027$ ). Additionally, the mean total IgE plasma levels were higher in males ( $413.0 \pm 143.0$  IU/mL) than in females ( $147.9 \pm 98.0$  IU/mL) ( $p < 0.0001$ ). These differences persisted even when males and females were stratified by age (up to or older than 20 years of age).

**CONCLUSIONS:** In conclusion, total IgE plasma levels are higher in young adult males than in females suffering from allergic rhinitis. Evaluating total IgE plasma levels can be useful to identify patients at risk of allergic rhinitis in areas with low industrial pollution.

**KEYWORDS:** Rhinitis; Allergic; Seasonal; Immunoglobulin E; Respiratory Hypersensitivity; Respiration Disorders.

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## INTRODUCTION

Allergic rhinitis causes inflammation of the nasal mucosa. Its pathogenesis is mediated by IgE antibodies produced after exposure and sensitization to environmental allergens. The most common symptoms are nasal congestion, watery rhinorrhea, sneezing and itching, which revert spontaneously or after treatment. Allergic rhinitis is influenced by environmental and genetic factors (1).

Epidemiological data indicate that the prevalence of allergic rhinitis has increased in developing and developed countries over the last few decades (2-4). Independent studies have demonstrated the differential incidence of this disease between genders. Several studies reported an increased prevalence of allergic rhinitis in young males

than in young females (5-7), although other studies failed to find differences according to gender or age (8,9).

Two studies explored the prevalence of allergic rhinitis in Brazil. One study found that this disease is highly prevalent among children and adolescent males treated at emergency centers (10). Another analysis, a descriptive cross-sectional study on schoolchildren aged 10-14, reported a rate of 33.2% for allergic rhinitis but did not find differences in the frequency between genders (11).

Despite the contradictory data reported in Brazil and elsewhere, surveys accounting for total IgE plasma levels in allergic rhinitis patients are scarce. The aim of the present study was to investigate whether the plasma levels of total IgE differ between genders and according to age among patients suffering from allergic rhinitis.

## PATIENTS AND METHODS

### Ethical considerations

This study was approved by the Research Ethics Faculdade de Medicina de São José do Rio Preto (FAMERP) (Case 085/2008). All patients received broad explanations about the objectives of the study and the procedures that involved the

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collection of biological material. They then signed written consent forms.

### Patient selection

Patients who received medical attention at the Clínica Menino Jesus in São José do Rio Preto, State of São Paulo, Brazil, from March 2009 to December 2011 were eligible for the study. A total of 171 adult patients of both genders (55 males and 116 females) who had regularly visited the clinic for a period of one year and who had been diagnosed with allergic rhinitis were enrolled.

Patients under 18 years old, smokers and those with a history of previous hospitalization due to respiratory diseases were excluded. Patients with a confirmed diagnosis of asthma were also excluded to avoid confounding the results because the immunological mechanisms underlying this disease and allergic rhinitis are similar.

Based on a previous report by Sybilski et al. (12), the number of patients enrolled was sufficient to show any differences in total IgE plasma levels between genders with a power exceeding 90%.

### Diagnosis of allergic rhinitis

Allergic rhinitis was diagnosed by an experienced physician (NF) following the criteria of the Second Brazilian Consensus for Rhinitis (1). The clinical history of the patient, any family history of the disease, a physical examination and the patient report (symptoms of rhinitis for more than four days per week for five consecutive weeks) were recorded. The cardinal symptoms considered were nasal congestion; watery rhinorrhea; paroxysmal sneezing and pruritus of the nose, palate and/or eyes.

### Blood sample collection

A 5 mL sample of peripheral blood was drawn from each participant by venous puncture and placed in a vacuum tube without anticoagulant for IgE determination.

### Total IgE plasma level assay

The total IgE plasma levels in the serum samples were measured using commercial ImmunoCAP kits. A reference value of 140 IU/mL was considered, given the ages of the patients analyzed.

### Statistical analysis

The software GraphPad InStat version 3.1 was used to perform calculations. A *t* test was used to compare the mean

values between the two age groups and the mean total IgE plasma levels between genders.

## RESULTS

Data from the 171 patients enrolled in this study are shown in Table 1. The mean age of the overall group of patients with allergic rhinitis, recorded at the time of enrollment, was  $38.4 \pm 19.0$  years old and the mean age varied significantly between genders. The male patients were younger than were the female patients, even when the comparison was restricted within the 25<sup>th</sup> and 75<sup>th</sup> percentiles.

Total IgE plasma levels, measured in IU/mL, were higher in males than in females, even when the comparison was restricted within the 25<sup>th</sup> and 75<sup>th</sup> percentiles. The mean total IgE plasma levels stratified into values up to or above 140 IU/mL showed significant differences between males and females (Figure 1). Table 2 shows the mean total values of IgE levels for males and females when stratified by age (up to or older than 20 years of age). In both of these cases, the mean values were higher in males than in females.

## DISCUSSION

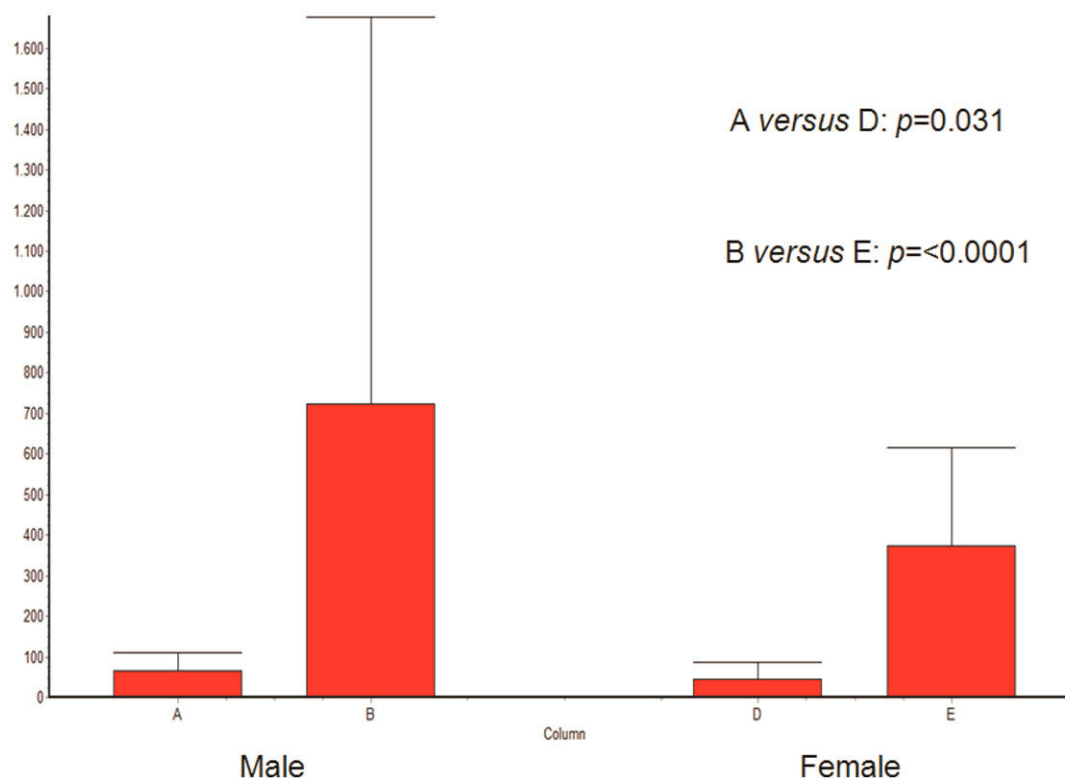
The aim of this study was to determine whether total IgE plasma levels differed between genders and according to age in patients with allergic rhinitis. Antibodies belonging to this class are produced in response to allergenic environmental stimuli and their concentrations and specificities are strongly associated with various manifestations of allergies (13,14).

The enrolled patient group with allergic rhinitis comprised nonsmokers living in the northwest region of São Paulo State (20° 49' 53" S; 49° 22' 55" W). This region is predominantly used for agriculture and keeping livestock and does not contain major industrial centers (11,15). Smoke and industrial pollution are known risk factors that increase the prevalence of respiratory diseases (16).

Fewer male patients were enrolled in the study compared with the number of females enrolled. The reasons why men seek medical attention less often relative to women are not completely understood. There is evidence in certain countries that the local health systems are not tailored to meet the health needs of men (17). Additionally, in the current study, this difference probably reflects the cultural attitudes of Brazilian males, which are characterized (at

**Table 1 - Mean age and mean values of total IgE plasma levels between male and female patients with allergic rhinitis.**

Characteristics	Males		Females		p
	N	%	N	%	
Total (n = 171)	55	32.2	116	67.8	
Mean age $\pm$ SD	32.2 $\pm$ 17.8		41.4 $\pm$ 18.9		0.0027
Median (range)	29 (18-78)		41.5 (18-85)		
25 <sup>th</sup> percentile (range)	17.2 (18-28)		25.9 (18-41)		
75 <sup>th</sup> percentile (range)	47.9 (32-78)		57.0 (42-85)		
Normal distribution	Yes		No		
Total IgE in plasma					
Mean $\pm$ SD (IU/mL)	413.0 $\pm$ 143.0		147.9 $\pm$ 98.0		<0.0001
Median (range)	144.0 (0.5-4,210)		62.3 (1.5-1,009)		
25 <sup>th</sup> percentile (range)	68.9 (0.5-142.0)		23.4 (1.5-60.6)		
75 <sup>th</sup> percentile (range)	767.1 (150.0-4,210)		272.3 (64.0-1,009)		



**Figure 1** - Mean values of total IgE plasma stratified up to and above 140 IU/mL according to genders.

least in certain regions) by invulnerability, strength and virility, leading them to avoid seeking medical care (18).

In this study, we verified that the mean age of males was lower than that of females, even when the comparison was restricted within the 25<sup>th</sup> and 75<sup>th</sup> percentiles. This observation agrees with the data of Boulet et al. (5) and of Huurre et al. (6), who reported that allergic rhinitis is more common in young men than in women. Additionally, Huurre et al. (6) highlighted that the incidence of allergic rhinitis is even higher in men between the ages of 17 and 22 years. In addition, our data are aligned with those of Lasmar et al. (10), who reported a high prevalence of allergic rhinitis among Brazilian adolescent males in comparison with females.

It has been observed that the first symptoms of allergic rhinitis appear around preschool age, affect males more often than females and can persist through adolescence and adulthood (6,19). This tendency seems to be multifactorial and it has been advocated that the timing regarding the introduction of solid foods and exposure to potential allergens during early life influence maturation of the immune system and susceptibility to allergic rhinitis (19-21).

In our study, we did not enroll patients younger than 18 years of age and we did not collect information on the alimentary habits of the enrolled patients. However, it is possible that male patients with allergic rhinitis were exposed to specific environmental stimuli at an early age that made them more prone to developing allergic rhinitis. A recent survey performed in a small area in the north-eastern part of São Paulo State reported allergic rhinitis in more than 30% of schoolchildren aged 10-14 years (11). The authors concluded that although it was within acceptable levels, the pollution caused by the cane trash burning season may have contributed to the rhinitis episodes observed. It is reasonable to suppose that patients sensitized by solid foods and/or by other potential allergens at early age remain symptomatic if they are continuously exposed to environmental pollutants during adulthood.

The mean total IgE plasma levels in the combined enrolled group exceeded the reference value of 140 IU/mL. High levels of total IgE in the plasma reflect, at a least in part, involvement of this class of antibodies in the immunological mechanism underlying certain respiratory

**Table 2** - Mean values for total IgE plasma levels (IU/mL) of males and females aged up to or older than 20 years old.

Age stratification	Male		Female		p
	N	%	N	%	
Up to 20 years of age (n=32)	16	48.5	16	51.5	
Mean IgE $\pm$ SD (IU/mL)		609.7 $\pm$ 385.0		162.3 $\pm$ 92.0	<0.0001
Median (range)		173.0 (0.5-3,186)		91.0 (5.7-594.0)	
Older than 20 years of age (n=139)	39	27.5	100	72.5	
Mean IgE $\pm$ SD (IU/mL)		325.0 $\pm$ 195.0		145.5 $\pm$ 97.0	<0.0001
Median (range)		128.0 (3.4-4,210)		56.0 (1.5-1,009)	



diseases, such as allergic rhinitis (22) and are frequently reported in studies comparing subjects with and without allergic diseases (23,24).

We found significant differences in the mean total IgE plasma levels between male and female patients, even when the comparison was restricted within the 25<sup>th</sup> and 75<sup>th</sup> percentiles. These differences persisted even when both genders were stratified according to the reference value (up to or above 140 IU/mL) and according to age (up to or older than 20 years of age). Our data are consistent with many reports in the literature. It has been observed that males with asthma present higher total IgE plasma levels compared with female patients (25). In addition, adolescents and adult males with bronchial asthma exhibit higher plasma levels of total IgE in response to environmental allergens (26).

The reasons underlying these differences are not completely understood. Allergic rhinitis and asthma have similar immunological mechanisms and it is possible that the factors contributing to the increase in total IgE plasma levels in asthma are involved in the same process in allergic rhinitis (13,14). Barrenas et al. (27) demonstrated that the production of specific inflammatory proteins, although influenced by seasonality, is higher in male patients than in female patients suffering from allergic rhinitis, even after treatment with anti-inflammatory drugs. Yamamoto et al. (28) reported that differences associated with sex are important during the initiation of allergic rhinitis in mice. It is possible that the involvement of IL-4 in the immunological mechanisms regulating the production of IgE antibodies influences the high rates of IgE expression in males compared with females (29).

Boulet et al. (5) demonstrated that the degree of sensitization according to the skin prick test reaches its peak in young adults, regardless of the allergen, then tends to diminish with age. In fact, in the current study, we observed that the mean total IgE plasma levels were higher in males up to 20 years of age but decreased among those older than 20 years of age. Taken together, the findings of this study and those of other reports support the view that male patients with allergic rhinitis have elevated total IgE plasma levels and that this class of antibodies plays an important role in the pathophysiology of this respiratory disease.

This study presents certain limitations and the results must be considered preliminary, as the diagnosis of allergic rhinitis was essentially clinical and no measurements of specific IgE or a skin prick test was performed. However, the study sheds light on the importance of gender and age in the production of total IgE in the plasma of patients suffering from allergic rhinitis, especially in regions where pollution from sugar cane burning has been increasing over the last few decades (11).

In conclusion, this study demonstrates that total IgE plasma levels are higher in young adult males than in females suffering from allergic rhinitis. Evaluating total IgE plasma levels can be useful to identify patients at risk of allergic rhinitis in areas with low industrial pollution.

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## AUTHOR CONTRIBUTIONS

Couto TA was responsible for organizing the data and generating the plot and tables. Falsarella N was responsible for recruiting patients and performing the clinical diagnoses of allergic rhinitis. Brandão de Mattos CC contributed to the design of the study. Mattos LC conceived and designed the study, analyzed the results and wrote the manuscript.

## REFERENCES

- Segundo Consenso Brasileiro sobre Rinites. Rev Bras Alerg Immunopatol. 2006;29(1):1-30. (Second Brazilian Consensus about Rhinitis 2006) Available from: <http://www.asbai.org.br/revistas/Vol291/consenso.pdf>. Accessed in 2012 (July 30).
- Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. N Engl J Med. 2002;347(12):911-20.
- Halken S. Prevention of allergic disease in childhood: clinical and epidemiological aspects of primary and secondary allergy prevention. Pediatr Allergy Immunol. 2004;15 Suppl 16:4-5,9-32.
- Piau JP, Massot C, Moreau D, Ait-Khaled N, Bouayad Z, Mohammad Y et al. Assessing allergic rhinitis in developing countries. Int J Tuberc Lung Dis. 2010;14(4):506-12.
- Boulet LP, Turcotte H, Laprise C, Lavertu C, Bédard PM, Lavoie A et al. Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma. Clin Exp Allergy. 1997;27(1):52-9, <http://dx.doi.org/10.1111/j.1365-2222.1997.tb00672.x>.
- Huurre TM, Aro HM, Jaakkola JJK. Incidence and Prevalence of Asthma and Allergic Rhinitis: A Cohort Study of Finnish Adolescents. J Asthma. 2004;41(3):311-7, <http://dx.doi.org/10.1081/JAS-120026088>.
- 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, <http://dx.doi.org/10.3132/perj.2007.00006>.
- Nathan RA, Meltzer EO, Selner JC, Storms W. Prevalence of allergic rhinitis in the United States. J Allergy Clin Immunol. 1997;99(6):S808-14, [http://dx.doi.org/10.1016/S0091-6749\(97\)80040-1](http://dx.doi.org/10.1016/S0091-6749(97)80040-1).
- Linneberg A, Nielsen NH, Madsen F, Frølund L, Dirksen A, Jørgensen T. Increasing prevalence of allergic rhinitis symptoms in an adult Danish population. Allergy. 1999;54(11):1194-8, <http://dx.doi.org/10.1034/j.1398-9995.1999.00180.x>.
- Lasmar LM, Camargos PA, Ordonez AB, Gaspar GR, Campos EG, Ribeiro GA. Prevalence of allergic rhinitis and its impact on the use of emergency care services in a group of children and adolescents with moderate to severe persistent asthma. J Pediatr (Rio J). 2007; 83(6):555-61, <http://dx.doi.org/10.2223/JPED.1727>.
- Riguera D, Andre PA, Zaneta DMT. Sugar cane burning pollution and respiratory symptoms in schoolchildren in Monte Aprazível, Southeastern Brazil. Rev Saúde Pública. 2011;45(5):878-86, <http://dx.doi.org/10.1590/S0034-89102011005000052>.
- Sybilski AJ, Doboszynska A, Samolinski B. Total and specific antigen IgE levels in umbilical cord blood. Eur J Med Res. 2009;14 Suppl 4: 233-6.
- Togias A. Rhinitis and asthma: evidence for respiratory system integration. J Allergy Clin Immunol. 2003;111(6):1171-83;quiz 1184, <http://dx.doi.org/10.1067/mai.2003.1592>.
- Baiardini I, Baido F, Brandi S, et al. ARIA-suggested drugs for allergic rhinitis: what impact on quality of life? A GA2LEN review. Allergy. 2008;63(6):660-9, <http://dx.doi.org/10.1111/j.1398-9995.2008.01649.x>.
- SEADE. Fundação Sistema Estadual de Análise de Dados. Secretaria de Planejamento e Desenvolvimento Regional. Perfil Regional. Região Administrativa de São José do Rio Preto. 2009. Available from: [http://www.seade.gov.br/produtos/perfil\\_regional/index.php](http://www.seade.gov.br/produtos/perfil_regional/index.php). Accessed in 2012 (July 30).
- Lee SY, Chang YS, Cho SH. Allergic diseases and air pollution. Asia Pac Allergy. 2013;3(3):145-54, <http://dx.doi.org/10.5415/apallergy.2013.3.3.145>.
- Smith JA, Braunack-Mayer A, Wittert G. What do we know about men's help-seeking and health service use? Med J Aust. 2006;184(2):81-3.
- Gomes R, Nascimento EF, Araújo FC. Why do men use health services less than women? Explanations by men with low versus higher education. Cad Saude Publica. 2007;23(3):565-74, <http://dx.doi.org/10.1590/S0102-311X2007000300015>.
- Alm B, Goksör E, Thengilsdottir H, Pettersson R, Möllborg P, Norvenius G, et al. Early protective and risk factors for allergic rhinitis at age 4½ years. Pediatr Allergy Immunol. 2011;22(4):398-404, <http://dx.doi.org/10.1111/j.1399-3038.2011.01153.x>.
- Bjorksten B. Environmental influences on the development of the immune system: consequences for disease outcome. Nestle Nutr Workshop Ser Pediatr Program. Basel, Karger. 2008;61:243-54.
- Cunningham-Rundles S, Lin H, Ho-Lin D, Dnistrian A, Cassileth BR, Perlman JM. Role of nutrients in the development of neonatal immune



- response. *Nutr Rev.* 2009;67(Suppl 2):S152-63, <http://dx.doi.org/10.1111/j.1753-4887.2009.00236.x>.
22. Razi E, Moosavi GA. Serum total IgE levels and total eosinophil counts: relationship with treatment response in patients with acute asthma. *J Bras Pneumol.* 2010;36(1):23-8.
23. Hamilton RG, Adkinson NF. Clinical laboratory assessment of IgE-dependent hypersensitivity. *J Allergy Clin Immunol.* 2003;111(2 Suppl):S687-701, <http://dx.doi.org/10.1067/mai.2003.123>.
24. Kim JS, O'Gorman MRG. Common In Vitro Tests for Allergy and Immunology. *Allergy Asthma Proc.* 2004;25(4 Suppl 1):S57-8.
25. 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, <http://dx.doi.org/10.1016/j.anai.2012.04.008>.
26. Tsukioka K, Toyabe S, Akazawa K. Total and specific IgE levels in adolescents and adults with bronchial asthma. *Nihon Kokyuki Gakkai Zasshi.* 2010;48(6):409-18.
27. Barrenäs F, Andersson B, Cardell LO, Langston M, Mobini R, Perkins A, et al. Gender differences in inflammatory proteins and pathways in seasonal allergic rhinitis. *Cytokine.* 2008;42(3):325-9, <http://dx.doi.org/10.1016/j.cyto.2008.03.004>.
28. Yamamoto T, Okano M, Ono T, Nakayama E, Yoshino T, Satoskar AR, et al. Sex-related differences in the initiation of allergic rhinitis in mice. *Allergy.* 2001;56(6):525-31, <http://dx.doi.org/10.1034/j.1398-9995.2001.056006525.x>.
29. Okano M, Satoskar AR, Abe M, Harn DA Jr, Okano M, Nishizaki K, et al. Interleukin-4-independent production of T<sub>H</sub>2 cytokines by nasal lymphocytes and nasal eosinophilia in murine allergic rhinitis. *Allergy.* 2000;55(8):723-31, <http://dx.doi.org/10.1034/j.1398-9995.2000.00429.x>.