Clinical Study

Predictors of Serum Total IgE in a Random Sample of 7–17 Year Old Children

**Sofie Strømgaard,** 1 **Simon Francis Thomsen,** 2 **Mogens Fenger,** 3 and **Vibeke Backer** 1

1 Department of Respiratory Medicine, Bispebjerg Hospital, 2400 Copenhagen, Denmark
2 Department of Dermatology, Bispebjerg Hospital, 2400 Copenhagen, Denmark
3 Department of Clinical Biochemistry, Hvidovre Hospital, 2650 Hvidovre, Denmark

Correspondence should be addressed to Simon Francis Thomsen, sft@city.dk

Received 7 March 2011; Accepted 11 April 2011

1. Introduction

There is only limited knowledge about factors that cause increased serum total immunoglobulin E (IgE) in children. Generally, IgE has been found to be higher in men than in women [1, 2]. However, some studies found this difference only among smokers [3, 4], whereas others have found that the difference was confined to the age group above 55 years [5, 6]. Serum total IgE has been shown to decrease with age with the highest concentrations found in children and adolescents [2, 5, 7]. Some investigations have found this association only in different subgroups of the study populations but results are contradictory [3, 4, 6, 8]. The association between allergic symptoms and serum total IgE has been found to be dependent on atopic status [4, 9, 10]. Notably, subjects with positive skin prick test have higher IgE levels [4, 7]. Rhinitis, wheeze, and current asthma are closely associated with IgE [10]. Furthermore, subjects with occupational exposure to dust or gas have been shown to have higher IgE levels than those not exposed [6]. Most of these studies were on adult populations, whereas some also included children above the age of 15. One study included children older than 11 years and three included children older than 6 years. In one-year olds, IgE has been found to be associated with parental IgE levels [11], whereas some studies have found an effect of alcohol intake on serum total IgE in adults [12]. Smoking has been shown to increase IgE in both men and women [1, 2, 6, 9] but especially in men [3, 8]. Warren et al. found that smoking was associated with increased IgE only in men [8], whereas another study found that the association between smoking and increased IgE was present only in subjects older than 20 years of age [4]. Due to the relatively sparse knowledge of predictors of serum total IgE in children we studied the association between perinatal, demographic, socioeconomic, clinical, paraclinical and early life factors, and serum total IgE in a population sample of children aged 7–17 years.

2. Methods

2.1. Subjects. A random sample of children and adolescents living in Copenhagen, Denmark was invited to take part in a clinical examination [13]. All subjects were drawn at
The participants were told to stop using medications that were not contained antihistamine at least three days before skin testing.

2.4. Bronchial Responsiveness Test. The method of Yan et al. was used for measuring airway responsiveness to inhaled histamine [15]. Each aerosol was inhaled starting with saline and followed by increasing doses of histamine until a cumulative dose of 7.8 μmol had been reached. The test was terminated when the maximum concentration had been reached or when a 20% decline in FEV1 had occurred before the end of the dosing regimen. For all subjects experiencing at least a 20% decline in FEV1 the concentration causing a 20% fall in FEV1 (PD20) was calculated. A positive test result (AHR) was defined as a PD20 below 3.9 μmol.

2.5. Statistical Analysis. Data were analysed with the statistical package SPSS 16.0 (SPSS, Inc., Chicago, IL, USA). Population characteristics were compared using the unpaired t-test for numerical data and the chi-square test for categorical data. To determine the impact of different factors on serum total IgE, we first used univariate linear regression analysis and then multivariate linear regression analysis. The response variable was serum total IgE and the explanatory variables were different perinatal factors, early life factors, socioeconomic factors, demographic factors, clinical, and paraclinical factors. A stipulation of the linear regression analysis is that for each value of the explanatory variable, the values of the response variable should approximately follow the normal distribution. The IgE values in our population did not follow the normal distribution, so we used log (IgE) as the response variable as these data were approximately following the normal distribution. Under the assumption of constant variance, all factors examined were analysed by univariate regression. Based on the univariate analysis, factors that had a relation to serum total IgE that was statistically significant or approaching significance were included in the multivariate analysis. Factors of which we lacked knowledge in a great number of the participating subjects were excluded from the multivariate regression analysis. As a consequence, the multivariate analysis included the factors: birth weight, birth length, smoking in pregnancy, parental disposition to allergy, sex, age, smoking, FEV/FVC, airway hyperresponsiveness, asthma, hay fever, positive skin prick test, and atopic dermatitis. Subjects, on which we did not have information about all of these factors, were excluded from the multivariate analysis. A total of 378 subjects were included in the final model.

3. Results

Serum total IgE measurements were available for 421 children. The median value of serum total IgE in the population was 41.8 (Figure 1). In girls, the median value was 33.8, range (2.3–5440), whereas in the boys the median value was 57.4, range (2.1–2173). The geometric mean serum total IgE in the population was 49.3; 60.4 in boys and 41.0 in girls, \( P < .05 \). The proportion of subjects having elevated serum total IgE, asthma, hay fever, atopic dermatitis, and positive skin prick tests were significantly lower in the group of nonrespondents. The subjects, interviewed by telephone, did not differ significantly from the subjects originally included with respect to sex, age, or prevalence of asthma, but there were significantly fewer children with symptoms of hay fever among the group of nonrespondents.
test was not significantly different between boys and girls (Table 1).

The results of the univariate analyses are shown in Table 2. The following factors were significantly associated with serum total IgE: parental allergic predisposition, early life wheezy bronchitis, male sex, airway hyperresponsiveness, asthma, hay fever, positive skin prick test, and atopic dermatitis. After multivariate adjustment positive skin prick test, airway hyperresponsiveness, atopic dermatitis, and parental predisposition remained significant predictors of serum total IgE (Table 3).

4. Discussion

This study showed that positive skin prick test, airway hyperresponsiveness, atopic dermatitis, and parental predisposition to atopic disease were significant predictors of serum total IgE in children, 7–17 years of age. In contrast to some previous studies [1–3, 6, 9] we did not find any effect of smoking on serum total IgE. However, this is consistent with the findings in a study by Sherril et al. that found an effect of smoking on IgE only among subjects older than 20 years of age [4]. The association between serum total IgE and gender that previous studies have found in adults was not found in this study of children. Also, a decreasing tendency for IgE with age [2, 5, 7] was not significant in this study, but a comparison with earlier studies is difficult as these mostly included older age groups and a broader range of ages. The association of atopic disease and positive skin prick test to serum total IgE level is consistent with the results of earlier studies [4, 7, 9, 10]. On the contrary we did not find a significant association between asthma and serum total IgE but this was probably due to a significant effect of airway

Table 1: Population characteristics.

| Variable              | Boys | Girls | Total | P-value |
|-----------------------|------|-------|-------|---------|
| Age                   | 11.8 | 12.5  | 12.2  | .004    |
| Serum total IgE       | 60.4 | 41.0  | 49.3  | .008    |
| High IgE              | 53 (26.4) | 44 (20.0) | 97 (23.0) | .121    |
| Asthma                | 20 (9.0) | 24 (9.3) | 44 (9.2) | .912    |
| Hay fever             | 54 (24.3) | 58 (22.5) | 112 (23.3) | .634    |
| Atopic dermatitis     | 57 (25.7) | 74 (28.7) | 131 (27.3) | .461    |
| Positive skin prick test | 50 (22.9) | 41 (16.3) | 91 (19.4) | .068    |

Table 2: Univariate relationships between different factors and serum total IgE in a sample of children.

| Variable                             | B coefficient | Standard error | P-value |
|--------------------------------------|---------------|----------------|---------|
| Perinatal factor                     |               |                |         |
| Birth weight (per 100 g)             | 0.103         | .063           |         |
| Birth length (per cm)                | 0.018         | .125           |         |
| Gestation (per week)                 | 0.000         | .967           |         |
| Preterm                              | −0.002        | .989           |         |
| Not breastfed                        | −0.019        | .908           |         |
| Supplementation                      | 0.001         | .991           |         |
| Smoking in pregnancy                 | 0.066         | .184           |         |
| Smoking in home                      | −0.056        | .382           |         |
| Parental predisposition              | 0.133         | .013           |         |
| Season of birth                      |               |                | .926    |
| Early life factors                   |               |                |         |
| Pneumonia                            | 0.128         | .117           |         |
| Antibiotics                          | −0.006        | .923           |         |
| Wheezy bronchitis                    | 0.319         | .00040         |         |
| Socioeconomic factors                |               |                |         |
| Mother age                           | −0.004        | .509           |         |
| Mother education                     | 0.096         | .184           |         |
| Mother alone                         | −0.001        | .984           |         |
| Mother smoke                         | −0.107        | .130           |         |
| Father age                           | −0.010        | .110           |         |
| Father education                     | 0.078         | .361           |         |
| Father smoke                         | 0.006         | .941           |         |
| Household income                     | 0.012         | .539           |         |
| Demographic factors                  |               |                |         |
| Sex                                  | 0.168         | .008           |         |
| Age (per year)                       | −0.018        | .101           |         |
| BMI (per unit)                       | 0.006         | .532           |         |
| Smoking                              | −0.217        | .062           |         |
| Clinical and paraclinical factors    |               |                |         |
| FEV/FVC                              | −0.825        | .130           |         |
| AHR                                  | 0.413         | .000002        |         |
| Asthma                               | 0.279         | .011           |         |
| Hay fever                            | 0.387         | .000000        |         |
| Positive skin prick test             | 0.761         | .000000        |         |
| Atopisk dermatitis                   | 0.264         | .0002          |         |

Table 3: Significant predictors of serum total IgE in a random sample of children, 7–17 years of age.

| Variable                             | B coefficient | Standard error | P-value |
|--------------------------------------|---------------|----------------|---------|
| Positive skin prick test             | 0.663         | 0.078          | <.001   |
| Airway hyperresponsiveness           | 0.248         | 0.084          | .003    |
| Atopic dermatitis                    | 0.133         | 0.066          | .046    |
| Parental predisposition              | 0.100         | 0.050          | .047    |
hyperresponsiveness and a strong correlation between this variable and asthma.

The participation rate in this study was quite low. We tried to address this possible bias by making telephone interviews with a random sample of nonparticipants. This showed a comparable distribution of nonparticipants and participants with respect to sex and age but a slightly lower prevalence of hay fever among nonparticipants. A possible parental recall bias cannot be precluded as parents of atopic children may be more aware of factors that could have influenced the development of the disease [16]. Particularly, parental recall bias in this study was defined as symptoms of asthma and/or hay fever in at least one parent when exposed to allergens. This may not be an entirely genetic predisposition as social and environmental factors causing or contributing to the parents’ disease could be shared with the child.

In conclusion, these results show that serum total IgE in children is significantly associated with positive skin prick test, parental predisposition to atopic disease, airway hyperresponsiveness, and atopic dermatitis.

**Conflicts of interest**

The authors declared that there are no conflicts of interest.

**References**

[1] B. Wüthrich, C. Schindler, T. C. Medici, J. P. Zellweger, and P. Leuenberger, "IgE levels, atopy markers and hay fever in relation to age, sex and smoking status in a normal adult Swiss population," *International Archives of Allergy and Immunology*, vol. 111, no. 4, pp. 396–402, 1996.

[2] C. S. Court, D. G. Cook, and D. P. Strachan, "The descriptive epidemiology of house dust mite-specific and total immunoglobulin E in England using a nationally representative sample," *Clinical and Experimental Allergy*, vol. 32, no. 7, pp. 1033–1041, 2002.

[3] E. J. Jensen, B. Pedersen, E. Schmidt, and R. Dahl, "Serum IgE in nonatopic smokers, nonsmokers, and recent exsmokers: relation to lung function, airway symptoms, and atopic predisposition," *Journal of Allergy and Clinical Immunology*, vol. 90, no. 2, pp. 224–229, 1992.

[4] D. L. Sherrill, M. Halonen, and B. Burrows, "Relationships between total serum IgE, atopy, and smoking: a twenty-year follow-up analysis," *Journal of Allergy and Clinical Immunology*, vol. 94, no. 6, pp. 954–962, 1994.

[5] R. A. Barbee, M. Halonen, W. Kaltenborn, M. Lebowitz, and B. Burrows, "A longitudinal study of serum IgE in a community cohort: correlations with age, sex, smoking, and atopic status," *Journal of Allergy and Clinical Immunology*, vol. 79, no. 6, pp. 919–927, 1987.

[6] E. Omenaas, P. Bakke, S. Elsayed, R. Hanoa, and A. Gulsvik, "Total and specific serum IgE levels in adults: relationship to sex, age and environmental factors," *Clinical and Experimental Allergy*, vol. 24, no. 6, pp. 530–539, 1994.

[7] R. A. Barbee, M. Halonen, M. Lebowitz, and B. Burrows, "Distribution of IgE in a community population sample: correlations with age, sex, and allergen skin test reactivity," *Journal of Allergy and Clinical Immunology*, vol. 68, no. 2, pp. 106–111, 1981.

[8] C. P. Warren, V. Holford-Stevens, C. Wong, and J. Manfreda, "The relationship between smoking and total immunoglobulin E levels," *Journal of Allergy and Clinical Immunology*, vol. 69, no. 4, pp. 370–375, 1982.

[9] O. Zetterström, K. Osterman, L. Machado, and S. G. Johansson, "Another smoking hazard: raised serum IgE concentration and increased risk of occupational allergy," *British Medical Journal*, vol. 283, no. 6301, pp. 1215–1217, 1981.

[10] B. Burrows, M. Halonen, M. D. Lebowitz, R. J. Knudson, and R. A. Barbee, "The relationship of serum immunoglobulin E, allergy skin tests, and smoking to respiratory disorders," *Journal of Allergy and Clinical Immunology*, vol. 70, no. 3, pp. 199–204, 1982.

[11] H. A. Orgel, R. N. Hamburger, M. Bazaral et al., "Development of IgE and allergy in infancy," *Journal of Allergy and Clinical Immunology*, vol. 56, no. 4, pp. 296–307, 1975.

[12] A. González-Quintela, C. Vidal, and F. Gude, "Alcohol-induced alterations in serum immunoglobulin e (IgE) levels in human subjects," *Frontiers in Bioscience*, vol. 7, pp. e234–e244, 2002.

[13] S. F. Thomsen, C. S. Ulrik, K. Larsen, and V. Backer, "Change in prevalence of asthma in Danish children and adolescents," *Annals of Allergy, Asthma and Immunology*, vol. 92, no. 5, pp. 506–511, 2004.

[14] R. de Marco, C. Pattaro, F. Locatelli, and C. Svanes, "Influence of early life exposures on incidence and remission of asthma throughout life," *Journal of Allergy and Clinical Immunology*, vol. 113, no. 5, pp. 845–852, 2004.

[15] K. Yan, C. Salome, and A. J. Woolcock, "Rapid method for measurement of bronchial responsiveness," *Thorax*, vol. 38, no. 10, pp. 760–765, 1983.

[16] M. Kulig, R. Bergmann, G. Edenharter, and U. Wahn, "Does allergy in parents depend on allergy in their children? Recall bias in parental questioning of atopic diseases," *Journal of Allergy and Clinical Immunology*, vol. 105, no. 2, part 1, pp. 274–278, 2000.

[17] I. Kummeling, C. Thijs, F. Stelma, M. Huber, P. A. Brandt, and P. C. Dagnelie, "Do parents with an atopic family history adopt a 'prudent' lifestyle for their infant? (KOALA Study)," *Clinical and Experimental Allergy*, vol. 36, no. 4, pp. 489–494, 2006.