



## Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica,  
Alergología y Asma Pediátrica

[www.elsevier.es/ai](http://www.elsevier.es/ai)



### ORIGINAL ARTICLE

# Changes over time in the prevalence of asthma, rhinitis and atopic eczema in adolescents from Taubaté, São Paulo, Brazil (2005–2012): Relationship with living near a heavily travelled highway



M.F. Toledo<sup>a,\*</sup>, B.M. Saraiva-Romanholo<sup>b,c</sup>, R.C. Oliveira<sup>d</sup>, P.H.N. Saldiva<sup>e</sup>,  
L.F.F. Silva<sup>e</sup>, L.F.C. Nascimento<sup>a</sup>, D. Solé<sup>f</sup>

<sup>a</sup> Department of Medicine, University of Taubaté (UNITAU), Taubaté, São Paulo, Brazil

<sup>b</sup> Experimental Therapeutic Laboratory I (LIM 20), Department of Medicine, University of São Paulo, São Paulo, Brazil

<sup>c</sup> University City of Sao Paulo (UNICID), São Paulo, Brazil

<sup>d</sup> Experimental Air Pollution Laboratory, Department of Pathology, Medical School, University of São Paulo, Sao Paulo, Brazil

<sup>e</sup> Department of Pathology, Faculty of Medicine, University of Sao Paulo, Sao Paulo, Brazil

<sup>f</sup> Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Escola Paulista de Medicina – Federal University of São Paulo, São Paulo, Brazil

Received 13 October 2015; accepted 20 February 2016

Available online 7 July 2016

#### KEYWORDS

Air pollution;  
Allergy;  
Asthma;  
Heavy traffic;  
Highway;  
Residence

#### Abstract

**Background:** The prevalence of allergic diseases is increasing. We evaluated temporal trends in the prevalence of asthma, rhinitis and eczema in adolescents (13–14 years) living in Taubaté, SP, Brazil (2005–2012) and assessed the relationship between these prevalences and the residential proximity to Presidente Dutra Highway (PDH, a heavily travelled highway).

**Methods:** This cross-sectional study of adolescents ( $N=1039$ ) from public and private schools was evaluated using the standard questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC) plus a question about their place of residence in relation to PDH. The data obtained were compared to the 2005 data using a chi-square test or Fisher's exact test. An analysis by groups consisting of two phases (two-step cluster) was used to evaluate the effect of living near PDH.

**Results:** There was a lifetime increase in the prevalence of active asthma (15.3% vs. 20.4%,  $p=0.005$ ) and physician-diagnosed asthma (6.8% vs. 9.2%,  $p=0.06$ ) and a decrease in the symptoms of active rhinitis (36.6% vs. 18.5%) between 2005 and 2012. A high frequency of asthma and rhinitis (18.1% vs. 23.2%, respectively) was observed among adolescents living close or very close to PDH; furthermore, 85.6% of the adolescents without symptoms of asthma or rhinitis lived far from PDH.

\* Corresponding author.

E-mail address: [maristellatol@ig.com.br](mailto:maristellatol@ig.com.br) (M.F. Toledo).

**Conclusion:** An increase in the prevalence of asthma and a decrease in the prevalence of rhinitis were observed during the studied period. Living near PDH was associated with higher rates of asthma, rhinitis, and eczema.

© 2016 Published by Elsevier España, S.L.U. on behalf of SEICAP.

## Introduction

The lack of specific diagnostic tests for asthma, rhinitis, and eczema and the use of different assessment methods have prevented the gathering of information about the prevalence of these diseases in epidemiological studies. The *International Study of Asthma and Allergies (ISAAC)* was a turning point in the epidemiological study of asthma, rhinitis and eczema in the paediatric population.<sup>1,2</sup>

The ISAAC enabled temporal comparisons of the prevalence of asthma and allergic diseases in different regions and among regions within a country.<sup>2,3</sup> It allowed the identification of annual increases in the prevalence of asthma among adolescents in several parts of the world, including Africa (+0.16%), Latin America (+0.32%), Northern Europe (+0.26%), Eastern Europe (+0.26%) and India (+0.02%). In contrast, in other regions, such as Oceania (−0.76%), the disease prevalence remained stable or even decreased.<sup>3</sup> ISAAC also reported an increase in the prevalence of rhinitis and eczema, especially in Asia-Pacific countries and in India.<sup>3</sup>

Solé et al.<sup>4</sup> assessed seven Brazilian cities over a 9-year period and found that in 2012, the prevalence of active asthma (wheezing in the last 12 months) among adolescents was highest in São Paulo, in the state of São Paulo (SP) (21.3%), and lowest in Aracaju, in the state of Sergipe (SE) (12.8%). The prevalence of rhinitis was also highest in São Paulo (SP) (47.4%) and lowest in Recife, in the state of Pernambuco (PE) (26.3%), while the prevalence of eczema was highest in Belém, in the state of Pará (PA) (7.9%) and lowest in Aracaju (SE) (3.4%).

Although genetic factors are involved in the occurrence of asthma, their interaction with environmental factors may explain the international variation in the prevalence of this disease.<sup>5</sup>

Several studies identified air pollution as one of the key risk factors for developing or triggering asthma.<sup>6,7,8,9,10</sup> The exposure of asthmatic patients to air pollutants causes oxidative stress over time, which results in damage to the bronchial epithelium, increased airway inflammation, increased bronchial responsiveness and allergic sensitisation.<sup>11,12</sup>

A study conducted in the city of São José dos Campos, Paraíba Valley (SP) demonstrated a significant relationship between air pollutants and an increased number of asthma-related hospitalisations among children up to 10 years of age.<sup>13</sup>

The city of Taubaté (SP) is crossed by the President Dutra Highway (PDH), which is considered the most important Brazilian highway because it links the two main national metropolises (Rio de Janeiro and São Paulo) and passes through one of the richest areas in the country, the Paraíba Valley. The cities located at the margins of the PDH have

undergone rapid expansion, conurbation, and industrialisation in recent years.<sup>14</sup>

The lack of studies investigating the effects of pollutants on the respiratory health of adolescents with asthma and other allergic diseases in Taubaté (SP) prompted our interest in studying these effects and assessing temporal trends in the prevalence of asthma, rhinitis, and eczema in this municipality.

## Materials and methods

This epidemiological cross-sectional study was conducted in the city of Taubaté (SP), which is located 142 km from São Paulo, the state capital. The study included adolescents aged from 13 to 14 years old attending randomly selected public and private schools. The students were asked to answer the ISAAC written questionnaire (ISAAC-WQ) plus one question about the location of their residences in relation to PDH. The participants and their parents/guardians signed informed assent and consent forms, respectively, before their inclusion in the study. The sample size was calculated based on a prevalence of active asthma of 15.3%,<sup>15</sup> 80% power, 5% alpha error and a 4% confidence interval, which resulted in an initial sample size of 500 adolescents. However, considering possible losses of 25% and the stratification of the study population into groups and subgroups, *N* was increased to a minimum of 1000 participants. This present study included only adolescent population in order to make comparisons easier once we used the same age group in a previous study.<sup>15</sup>

According to the answers to the ISAAC-WQ, adolescents were classified as having: **active asthma** (i.e., those who answered “yes” to the question “*Have you had wheezing or whistling in the chest in the last 12 months?*”), **active rhinitis** (those who answered “yes” to the question “*In the past 12 months, have you had a problem with sneezing or a runny nose or a blocked nose when you did not have a cold or the flu?*”) or **eczema** (those who answered “yes” to the question “*Have you had an itchy rash at any time in your life?*”).<sup>3</sup>

The severity of asthma was assessed based on the frequency and severity of symptoms.<sup>16</sup>

Based on the symptoms exhibited, adolescents were divided into various subgroups: no allergy symptoms; asthma only; asthma + rhinitis, and other (asthma, rhinitis, and atopic dermatitis). According to their place of residence (proximity to PDH), the participants were divided into the following groups: residing near PDH (N, 200 m to 1 km), very near PDH (VN, less than 200 m) or far from PDH (F, more than 1 km away). These distances were mainly established based on data provided by the “Departamento Nacional de Infraestrutura de Transportes” (DNIT), which recommends a minimum distance of 1 km between residential areas and

two-lane highways<sup>17</sup> and in another study that establishes similar distances from the residences to the highways.<sup>10</sup> Data were collected from January to December 2012. The data were entered in a standard spreadsheet (Excel) and then transferred to SPSS 20.0 software for statistical analysis.

### Statistical analysis

The data were expressed as simple percentages and were compared with the 2005 data<sup>15</sup> using a chi-square test or Fisher's exact test. Cluster analysis was performed to identify homogeneous groups according to the presence of asthma, rhinitis and eczema (based on reported symptoms in the last 12 months) and place of residence. Two-step cluster analysis and the Schwarz–Bayes Information Criterion (SBIC) were used to investigate the similarities and differences among the investigated variables.<sup>18,19</sup> The level of significance was set to 5%. The study was approved by the Ethics and Research Committees of Hospital São Paulo, Escola Paulista de Medicina – Federal University of São Paulo and University of Taubaté (UNITAU).

### Results

A total of 1039 adolescents (51.9% males) participated in the study. Of these, 60.1% were enrolled in public schools, and 39.9% were enrolled in private schools.

Table 1 describes the prevalence of asthma symptoms, rhinitis-related symptoms and the occurrence of eczema among the adolescents for each study year and the comparative analysis. The results showed significant increases in all asthma symptoms except physician-diagnosed asthma, which showed an increasing trend, and dry cough at night over the last 12 months, which exhibited a significant decrease. Regarding rhinitis-related symptoms (Table 1), the comparative analysis showed a significant reduction in "coryza, sneezing or nasal obstruction in the absence of infection", "coryza, sneezing or nasal obstruction in the absence of infection in the last 12 months" and in the occurrence of "rhinitis." However, the prevalence of "nasal problems interfering with daily activities within the past 12 months" showed a significant increase. A significant decrease in the prevalence of atopic eczema from 16.2% to 3.4% was observed (Table 1).

**Table 1** Prevalence of asthma-related symptoms, of rhinitis-related symptoms and of eczema ever among adolescents by study year.

Question	Year				p
	2005 <sup>f</sup>		2012		
	N = 809	95% CI	N = 1039	95% CI	
Wheezing ever	361 (44.6%)	41.2–48.1	578 (55.6%)	52.5–58.7	<0.001
Wheezing in the last 12 months	124 (15.3%)	13.0–18.0	212 (20.4%)	18.0–23.0	0.005
Four or more wheezing attacks in the last 12 months <sup>a</sup>	19 (2.4%)	1.4–3.6	57 (5.5%)	4.2–7.0	0.001
Waking at night <sup>b</sup>	86 (10.7%)	8.6–13.0	194 (18.7%)	16.3–21.2	<0.001
Speech limited by wheezing <sup>b</sup>	14 (1.7%)	1.0–2.9	189 (18.2%)	15.9–20.7	<0.001
Asthma (physician-diagnosed) <sup>c</sup>	55 (6.8%)	5.3–8.7	96 (9.2%)	7.5–11.1	0.060
Wheezing during or after exercise in the last 12 months	109 (13.5%)	11.3–16.0	199 (19.2%)	16.8–21.7	<0.001
Dry cough at night in the last 12 months	268 (33.1%)	30.0–36.4	198 (19.1%)	16.7–21.6	<0.001
Coryza, sneezing, runny nose or nasal blockage without infection	404 (49.9)	46.5–53.4	207 (19.9%)	17.5–22.5	<0.001
Coryza, sneezing, runny nose or nasal blockage without infection in the past 12 months	296 (36.6%)	33.3–40.0	192 (18.5%)	16.1–21.0	<0.001
Nasal problem accompanied by itchy/watery eyes in the past 12 months <sup>d</sup>	143 (17.8%)	15.9–20.5	190 (18.3%)	16.0–20.8	0.784
Nasal problems interfered with daily activities in the past 12 months <sup>e</sup>	156 (39.6%)	34.7–44.6	188 (90.8%)	86.0–94.4	<0.001
Rhinitis ever	304 (37.6%)	34.3–41.0	201 (19.3%)	17.0–21.9	<0.001
Eczema ever	131 (16.2%)	13.7–18.9	35 (3.4%)	2.4–4.7	<0.001

p, chi-square test or Fisher Exact test; 95% CI, 95% confidence interval.

<sup>a</sup> Data missing for two cases from 2005.

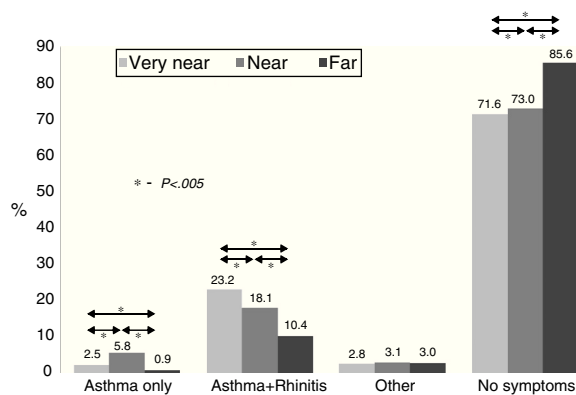
<sup>b</sup> Data missing for two cases from 2005.

<sup>c</sup> Data missing for three cases from 2005.

<sup>d</sup> Data missing for five cases.

<sup>e</sup> Number of respondents: N = 394 (2005) and N = 207 (2012).

<sup>f</sup> Toledo et al.<sup>15</sup>



**Figure 1** Distribution of adolescents by symptom group according to the distance of their home from President Dutra Highway: very near (less than 200 m), near (from 200 m to 1 km) or far (more than 1 km away). Data from 2012.

Fig. 1 shows the distribution of the adolescents according to the symptoms presented and place of residence. Most (85%) who lived far from PDH did not exhibit any disease in the previous 12 months. However, those who lived near or very near PDH exhibited a significantly higher frequency of disease. The combination of asthma and rhinitis was more frequently reported by participants who lived near the highway than by those who lived far from it (23.2% vs. 10.4%); the same pattern was observed for the occurrence of asthma only (5.8% vs. 0.9%).

## Discussion

This cross-sectional study analyses the prevalence of asthma, rhinitis, and eczema and the association between traffic-related air pollution and adverse respiratory and skin health effects in Brazilian adolescents (13–14 years) in 2012. A cross-sectional study with the same methodology was done in 2005 and was used by the authors for comparison of prevalence of asthma and rhinitis symptoms and eczema over time. However, in the 2005 study the effect of air pollution on respiratory and skin health was not evaluated.<sup>15</sup>

This current study has showed an increase on prevalence of asthma and decrease on prevalence of rhinitis and eczema when it was compared in both of our surveys over time.

In the present study, we have found an increase in the prevalence of active asthma and physician-diagnosed asthma compared to the previous study.<sup>15</sup> There was also a possible increase in severity of asthma, particularly asthma symptoms during and after physical exercise (Table 1).

Some studies applying the same methodology have showed similar results. A study assessing temporal trends in the prevalence of asthma among Brazilian adolescents observed a reduction in the average prevalence of active asthma, while the number of cases of severe asthma and physician-diagnosed asthma increased.<sup>20</sup> Another temporal study observed an increase on prevalence of asthma and a reduction in the frequency of physician-diagnosed rhinitis.<sup>21</sup>

The aforementioned increase in the prevalence of active asthma among adolescents from Taubaté from 2005 to 2012 might be related to improvements in asthma diagnoses and

treatment starting in the 2000s. The establishment of the National Plan for the Control of Asthma (Plano Nacional de Controle da Asma – PNCA) and the national pharmaceutical care programme in 2010 were also helpful, as previously observed.<sup>4</sup> The implementation of medical guidelines might have helped to disseminate the term ‘‘asthma’’ among doctors and to more thoroughly standardise the treatment of disease in an empirical manner.<sup>22</sup>

Although living near a highway was not studied in 2005, the present study has showed that the residential proximity of a highway was an important risk factor for asthma and may be associated with the increase in the prevalence of this disease among adolescents from Taubaté and also might be related to the increase in automotive vehicle fleets between 2005 and 2012.<sup>23</sup> This factor is supported by other studies that found a relationship between increased emissions of harmful gases from vehicles and higher asthma prevalences.<sup>24,25</sup>

Although we did not have data on the toxic emissions from the heavy traffic on PDH, we could establish that the prevalence of asthma and other allergic diseases was higher among the participants who lived near or very near the highway, similar to the observations of other studies.<sup>9,10</sup>

Despite the decrease in the rhinitis prevalence among adolescents in Taubaté from 2005 to 2012, there was an increase in the ‘‘nasal problems interference with daily activities in the past 12 months’’. Although rhinitis is considered a trivial and/or transient disease that is less severe than asthma, it can considerably impair the patients’ quality of life, performance, learning at school and productivity at work. The physical, psychological, and social impacts of rhinitis are numerous and affect adults as well as children and adolescents.<sup>26</sup>

The increase in the severity of rhinitis and asthma symptoms observed in the present study might be associated with inadequate treatment or inadequate monitoring of treatments. A lack of adherence to asthma treatment is common among adolescents.<sup>27</sup> Acknowledgement of the central role that patients play in the management of their chronic diseases, including asthma and allergies, patient education makes a major component of the global treatment of such conditions.<sup>28</sup> Certainly, after the epidemiological studies as ISAAC and International treatment guidelines for asthma, there was an improvement in diagnosis, especially for asthma. In our country, a better diagnostic was not followed by better control of this disease, which may partly explain the major severity found.

In this study, the association between asthma and rhinitis symptoms was the most frequent presentation. Those diseases are known to exhibit similar inflammatory mechanisms, and they frequently coexist in the same patient.<sup>29,30</sup> In study conducted in Fortaleza, Ceará<sup>20</sup> the results also showed a significant association between asthma and rhinitis symptoms.

The hypothesis that asthma and rhinitis are different expressions of a single airway disease has consolidated and strengthened the need to develop therapies that target this comorbidity in an integrated manner.<sup>31</sup>

In our study, a comparison of the prevalence rates over a 7-year period demonstrated the increased prevalence of asthma and a decreased prevalence of rhinitis and atopic dermatitis in the same study area and under conditions very

similar to those of the previous study.<sup>15</sup> We believe it likely that by having increased prevalence and severity of asthma symptoms, the symptoms of rhinitis might have been underestimated by adolescents.

The prevalence of asthma and allergy has been widely investigated in the past decades worldwide; however, there is still no consensus on the reasons for the variability in disease prevalence, including the variation in allergic symptoms in different study regions. Genetic, phenotypic and environmental factors might influence those differences,<sup>8,9,32,33,34</sup> which would thus partially explain the differences in the prevalence of the investigated allergic diseases found among the adolescents from Taubaté (SP).

In conclusion, there was an increase in prevalence of active asthma and although physician-diagnosed asthma has also increased, it was not significant. The prevalence of rhinitis and eczema decreased in the city of Taubaté (SP) from 2005 to 2012. The severity of rhinitis increased, and the frequency of asthma and rhinitis symptoms was higher among the adolescents who lived near the PDH than those who lived far from the highway.

## Ethical disclosures

**Confidentiality of data.** The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all of the patients included in the study have received sufficient information and have given their informed consent in writing to participate in the study.

**Right to privacy and informed consent.** The authors must have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence must be in possession of this document.

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

## Conflict of interest

The authors have no conflict of interest to declare.

## References

- Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee Report. *Allergy*. 2004;59:469–78.
- Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J*. 1995;8:483–91.
- Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases 1 and 3 repeat multicountry cross-sectional surveys. *Lancet*. 2006;368:733–43.
- Solé D, Rosário-Filho NA, Sarinho ES, Camelo-Nunes IC, Barreto BA, Medeiros ML, et al. Prevalence of asthma and allergic diseases in adolescents: nine-year follow-up study (2003–2012). *J Pediatr (Rio J)*. 2015;91:30–5.
- Subbarao P, Mandhane PJ, Sears MR. Asthma: epidemiology, etiology and risk factors. *CMAJ*. 2009;181:E181–90.
- Newman NC, Ryan PH, Huang B, Beck AF, Sauers HS, Kahn RS. Traffic-related air pollution and asthma hospital readmission in children: a longitudinal cohort study. *J Pediatr*. 2014;164, 1396.e1–1402.e1.
- Gonzalez-Barcala FJ, Pertega S, Garnelo L, Castro TP, Sampedro M, Lastres JS, et al. Truck traffic related air pollution associated with asthma symptoms in young boys: a cross-sectional study. *Public Health*. 2013;127:275–81.
- Kaszniak-Kocot J, Kowalska M, Górny RL, Niesler A, Wypych-Ślusarska A. Environmental risk factors for respiratory symptoms and childhood asthma. *Ann Agric Environ Med*. 2010;17:221–9.
- Ripabelli G, Tamburro M, Sammarco M, de Laurentiis G, Bianco A. Asthma prevalence and risk factors among children and adolescents living around an industrial area: a cross-sectional study. *BMC Public Health*. 2013;13:1038.
- Porebski G, Woźniak M, Czarnobilska E. Residential proximity to major roadways is associated with increased prevalence of allergic respiratory symptoms in children. *Ann Agric Environ Med*. 2014;21:760–6.
- Bernstein JA, Alexis N, Barnes C, Bernstein IL, Nel A, Peden D, et al. Health effects of air pollution. *J Allergy Clin Immunol*. 2004;114:1116–23.
- Gavett SH, Koren HS. The role of particulate matter in exacerbation of atopic asthma. *Int Arch Allergy Immunol*. 2001;124:109–12.
- Amâncio CT, Costa Nascimento LF. Asthma and ambient pollutants: a time series study. *Rev Assoc Med Bras*. 2012;58:302–7.
- Wikipédia. Presidente Dutra Highway in Rodovia Presidente Dutra; 2015. Available at: [http://pt.wikipedia.org/wiki/Rodovia\\_Presidente\\_Dutra](http://pt.wikipedia.org/wiki/Rodovia_Presidente_Dutra) [accessed 18.04.15].
- Toledo MF, Rozov T, Leone C. Prevalence of asthma and allergies in 13- to 14-year-old adolescents and the frequency of risk factors in carriers of current asthma in Taubaté, São Paulo, Brazil. *Allergol Immunopathol (Madr)*. 2011;235:1–7.
- Yarnell JW, Stevenson MR, MacMahon J, Shields M, McCrum EE, Patterson CC, et al. Smoking, atopy and certain furry pets are major determinants of respiratory symptoms in children: the International Study of Asthma and Allergies in Childhood Study (Ireland). *Clin Exp Allergy*. 2003.
- Manual de acesso de propriedades marginais a rodovias federais [Internet], Rio de Janeiro; 2006. Available at: <http://www.dnit.gov.br/download/rodovias/operacoes-rodoviaras/faixa-de-dominio/manual-de-acesso-de-prop-marginais-a-rod.-federais-ipr-728.pdf> [accessed 17.04.15].
- Zhang T, Ramakrishnan R, Livny M. BIRCH: an efficient data clustering method for very large databases. New York: ACM; 1996. Available at: <http://www.cs.sfu.ca/CourseCentral/459/han/papers/zhang96.pdf> [accessed 17.04.15].
- Chiu T, Fang D, Chen J, Wang Y, Jeris C. Robust and scalable clustering algorithm for mixed type attributes in Large Database Environment. In: Proceedings of the Seventh ACM SIGKDD International Conference on Knowledge Discovery and Data Mining. 2001. p. 263.
- Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. *J Allergy Clin Immunol*. 2009;124:1251–8.
- de Luna MFG, Fischer GB, de Luna JRG, da Silva MGC, de Almeida PC, Chiesa D. Prevalences of asthma and rhinitis among adolescents in the city of Fortaleza, Brazil: temporal changes. *J Bras Pneumol*. 2013;39:128–37.

22. Sociedade Brasileira de Pneumologia. Diretrizes da Sociedade Brasileira de Pneumologia e Tisiologia para o Manejo da Asma. *J Bras Pneumol*. 2012;38:S1–46.
23. IBGE. Instituto Brasileiro de Geografia e Estatística; 2014. Available at: <http://cidades.ibge.gov.br/xtras/perfil.php?codmun=355410> [accessed 18.04.15].
24. Lee YL, Lin YC, Hsiue TR, Hwang BF, Guo YL. Indoor and outdoor environmental exposures, parental atopy, and physician-diagnosed asthma in Taiwanese schoolchildren. *Pediatrics*. 2003;112:e389.
25. Nicolussi FH, Santos APM, André SCS, Veiga TB, Takayanagi AMM. Air pollution and respiratory allergic diseases in schoolchildren. *Rev Saude Pub*. 2014;48:327–30.
26. Camelo-Nunes IC, Solé D. Allergic rhinitis: indicators of quality of life. *J Bras Pneumol*. 2010;36:124–33.
27. Buston KM, Wood SF. Non-compliance amongst adolescents with asthma: listening to what they tell us about self-management. *Fam Pract*. 2000;17:134–8.
28. Grover C, Goel N, Armour C, Van Asperen PP, Gaur SN, Moles RJ, et al. Medication education program for Indian children with asthma: a feasibility study. *Niger J Clin Pract*. 2016;19:76–84.
29. Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop Group, World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001;108 5 Suppl.:S147–334.
30. Cagnani CE, Solé D, Díaz SN, Zernotti ME, Sisul JC, Borges MS, et al. Actualización de rinitis alérgica y su impacto en el asma (ARIA 2008). La perspectiva latinoamericana. *Rev Alerg Mex*. 2009;56:56–63.
31. Andrade CR, Camargos PAM, Ibiapina CC, Alvim CG, Drummond A, Vilaça D, et al. Comorbidade asma e rinite alérgica: inter-relações entre as vias aéreas superiores e inferiores. *Rev Med Minas Gerais*. 2009;19 4 Suppl. 5:S19–24.
32. Vercelli D. Discovering susceptibility genes for asthma and allergy. *Nat Rev Immunol*. 2008;8:169–82.
33. Farrokhi S, Gheybi MK, Movahhed A, Dehdari R, Gooya M, Keshvari S, et al. Prevalence and risk factors of asthma and allergic diseases in primary schoolchildren living in Bushehr, Iran: phase I, III ISAAC protocol. *Iran J Allergy Asthma Immunol*. 2014;13:348–55.
34. Shirinde J, Wichmann J, Vayi K. Association between wheeze and selected air pollution sources in an air pollution priority area in South Africa: a cross-sectional study. *Environ Health*. 2014;13:32.