



Letter to the Editor

Prevalence of allergy and asthma in a rural community of children and adults in Bolivian Chaco



Several risk factors are involved in determining the individual susceptibility to asthma and allergy, but the dramatic increase in the prevalence of these conditions in westernized countries in the past thirty years suggests that also the environmental factors play a critical role [1]. Epidemiologic studies conducted in Central Europe showing protection from asthma and allergic disease in children grown up in traditional dairy farms, indicate that children’s contact with farm animals and the associated high microbial exposure are related to the reduced risk [2,3]. It is now widely accepted that reduced early life microbial exposure in the urban environment, particularly in western countries leads to an increased predisposition to chronic allergic conditions, and this theory is known as “Hygiene hypothesis”. According to this hypothesis, allergic disorders, such as rhinitis, asthma, and atopic dermatitis, are the result of a systemic inflammatory reaction triggered by type 2 T helper (Th2) cell-mediated immune responses against ‘innocuous’ antigens, the allergens, due to a reduced microbial burden during childhood, as a consequence of Westernized lifestyle [4]. On the other hand, the type 2 response, beyond the pathogenic role in allergy, plays a crucial role in the protection from helminths infection [5]. The pathogenic or protective role depends mainly on the nature of the targeted antigens and also on the ability to dampen the inflammatory response.

Here we report the results of a study conducted in a rural community of the Chaco region, south-eastern Bolivia, in September 2018, aimed at determining the prevalence of asthma and sensitizations to environmental inhaled allergens in children and adults. The Chaco region is a semi-arid, sparsely populated, homogeneous ecological zone, situated between the latitudes 17°59’–22°21’ South and the longitudes 64°31’–58°51’ West. In this area, a dramatic decrease of soil-transmitted helminthiases (STH), the most prevalent parasitosis worldwide, has been recently reported, from up to 50% in the late 1980’s to less than 1% in 2016 – likely the result of 30 years of preventive chemotherapy (PC) strategy, based on 6-monthly single-dose mebendazole delivery to at-risk groups, such as school-age children and pregnant women [6,7]. Moreover, a significant drop of anti-*S. stercoralis* antibodies seroprevalence was reported from 1987 to 2013, although PC is not effective against this parasite [8]. On the other hand, neither protozoan parasitic infections nor other feco-oral transmitted infection, such as hepatitis A, hepatitis E and *Helicobacter pylori*, showed any substantial decreasing, suggesting that environmental fecal contamination caused by inadequate sanitation, poor hygiene, and unsafe drinking water still persist in this area [7,9].

The surveyed community was Ivamirapinta (municipality of Gutierrez, Cordillera Province, Department of Santa Cruz), a rural village of ≈ 1100 inhabitants, mainly of the Guaraní ethnic group, living in poor dwellings with walls of sticks, straw and clay and thatched roofs. The local economy is based on agriculture and animal farming.

In the community, the study was first explained during a preparatory meeting, involving local health care providers and community

leaders of the Guaraní political organization (Asamblea del Pueblo Guaraní). With their collaboration, the invitation to participate was disseminated to all individuals of the community during public meetings. The study was approved by a local Ethic Committee (Colegio Médico de Santa Cruz, TDEM CITE No. 028/2017) and a written informed consent was obtained by each enrolled participant (or by a parent or a legal guardian, if minor).

A total of 181 subjects have been screened for sensitizations to inhaled allergens, 112 children attending the primary school (60 males, 52 females, mean age 10,03 years) and 69 adults (16 males, 53 females, mean age 40,94 years) among the parents that gave their consent to participate to the study. All the subjects underwent skin prick test for five allergens (dermatophagoides mix, dog dander, cat dander,

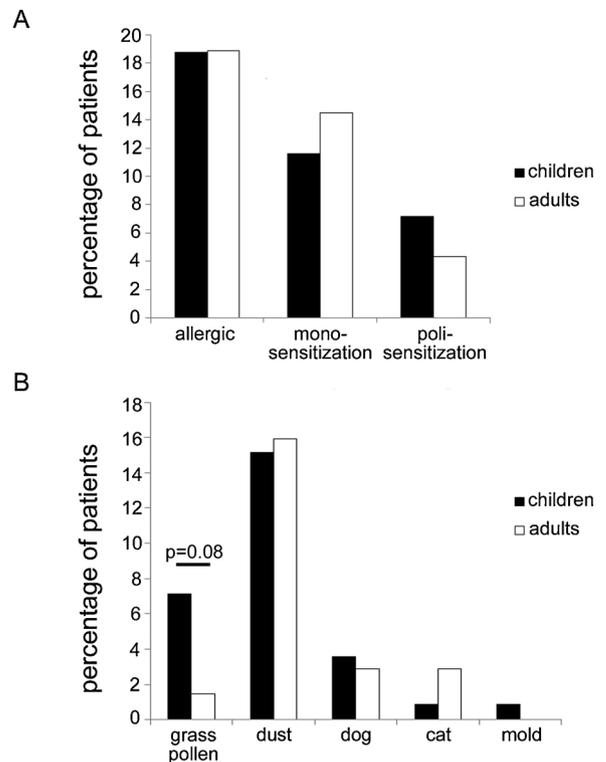


Fig. 1. Prevalence of allergic sensitizations among adults and children. Frequencies of patients with skin prick test positivity, with one sensitization, or with more than one sensitization respect to the whole population (A) Frequencies of skin prick test positivity to the indicated allergen (B). Black columns represent the population of children, the white columns represent the adults). p value was calculated, by using squared Chi test.

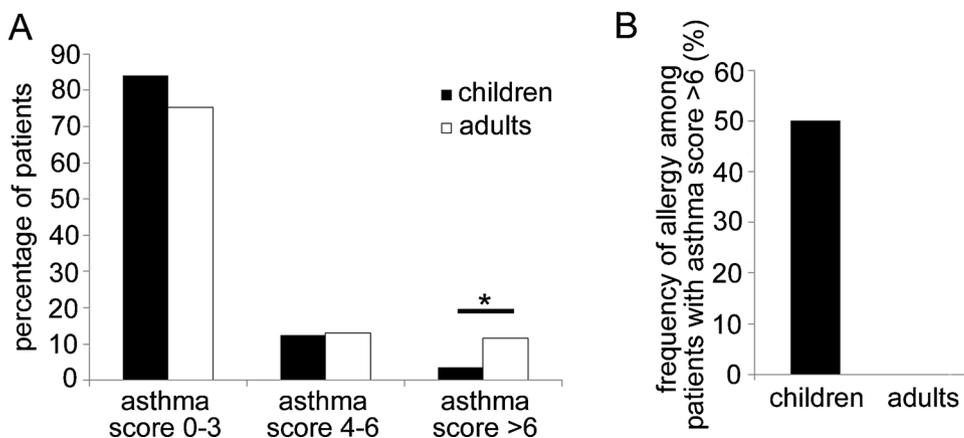


Fig. 2. Prevalence of asthma symptoms in adults and children.

Frequencies of patients belonging to the three different categories according to asthma score (A). Prevalence of allergy among the group with the highest asthma score (B).

Black columns represent the population of children, the white columns represent the adults).

* $p < 0.05$, by using squared Chi test.

Alternaria alternata, and grass pollen mix, all from Lofarma, Milan, Italy). For those participants that had also asthma symptoms, such as wheezing, chest tightness, cough, and so on, also a spirometry test was performed (CareFusion, Hoechberg, Germany). In order to screen the population for asthmatic symptoms, each participant was invited to fill a questionnaire. The score in the questionnaire was directly correlated to the gravity of asthma symptoms. The score represented the sum of the following parameters: numbers of dyspnea events during the last years (from 0 to 3), numbers of episodes of cough without fever during the last year (from 0 to 3), previous diagnosis of asthma (no = 0, yes = 3).

The prevalence of skin prick test positivity in the whole population was similar to the one reported in literature [10], and, more importantly, there were no differences between children and adults (Fig. 1A). Anyway, the sensitization to more than one allergen was more likely in children than in adults (Fig. 1A). Even if this observation was limited to only five allergens and, as consequence, we cannot state that adults are monosensitized at all, this data prompted us to investigate if a difference in the prevalence of single sensitizations existed. As shown in Fig. 1B we found a difference of grass pollen sensitization between children and adults ($p = 0.08$), while no differences emerged for other allergens.

Regarding asthma, we found an higher prevalence in adults, but it was not associated to allergic sensitizations (Fig. 2). Indeed, beyond the adults with the highest score in the questionnaire, no allergic patients were found, suggesting that they have the so-called intrinsic asthma. On the other hand, about a half of asthmatic children were also sensitized to one or more allergens.

The results of the study allow us to make at least two speculations.

The first one is about the relationships between helminths infection and allergic sensitizations. It has been recently reported that infection with *Schistosoma mansoni* may selectively protect from birch tree and grass pollen allergy, thanks to the presence of carbohydrate determinants (CCDs) that cross-react with similar glycans present in helminths and plants [11]. According to this hypothesis *S. mansoni* IgG antibodies, that are cross-reactive with allergens, may behave as blocking antibodies, thereby inhibiting allergic sensitization in susceptible individuals. In our study population, we observed that grass pollen sensitization is virtually absent in adults, highly exposed to intestinal helminthiasis in their childhood, whereas it emerges in younger generations, grown up in different epidemiological conditions.

The second consideration regards the difference in asthma prevalence between children and adults. The higher prevalence of asthma in adults is not associated to allergy. Indeed, none of asthmatic adults showed any allergic sensitization, whereas half of asthmatic children were sensitized to at least one allergen. Asthmatic symptoms in adults are indeed frequently associated to cold season and represent probably the consequence of respiratory infections.

In summary, our study, even if limited to a restricted population,

represents an useful picture to try to understand the intriguing relationships among infections, allergy, and asthma. The reduction of intestinal helminths infections did not affect the overall prevalence of allergy in our population, but may play a role in the emergence of pollen sensitizations in younger generations. On the other hand, asthma symptoms seem to be more related to respiratory infection than to allergy, and, as a consequence, the improvement of living conditions in the last two-three decades probably concurred to a reduction of its prevalence.

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References

- [1] M. Stein, C.L. Hrusch, J. Gozdz, C. Igartua, V. Pivniouk, S.E. Murray, J.G. Ledford, M. Marques Dos Santos, R.L. Anderson, N. Metwali, J.W. Neilson, R.M. Maier, J.A. Gilbert, M. Holbreich, P.S. Thorne, F.D. Martinez, E. von Mutius, D. Vercelli, C. Ober, A.I. Sperling, Innate immunity and asthma risk in amish and hutterite farm children, *N. Engl. J. Med.* 375 (5) (2016) 411–421.
- [2] M.J. Ege, M. Mayer, A.C. Normand, et al., Exposure to environmental microorganisms and childhood asthma, *N. Engl. J. Med.* 364 (2011) 701–709.
- [3] M.J. Ege, D.P. Strachan, W.O. Cookson, et al., Gene-environment interaction for childhood asthma and exposure to farming in Central Europe, *J. Allergy Clin. Immunol.* 127 (2011) 138–144.
- [4] S. Romagnani, The increased prevalence of allergy and the hygiene hypothesis: missing immune deviation, reduced immune suppression, or both? *Immunology* 112 (3) (2004) 352–363.
- [5] L. Cosmi, F. Liotta, L. Maggi, F. Annunziato, Role of type 2 innate lymphoid cells in allergic diseases, *Curr. Allergy Asthma Rep.* 17 (10) (2017) 66.
- [6] WHO, Helminth Control in School-age Children, World Health Organization, Geneva, 2011.
- [7] M. Spinicci, F. Macchioni, D. Rojo, H. Gamboa, A.L. Villagrán, Y. Vallejos, M. Strohmeier, M. Roselli, S. Gabrielli, G. Cancrini, J. Monasterio, P. Castellanos, G.A. Paredes, S. Maury, A. Zárate, R. Rocabado, P. Olliaro, A. Montresor, A. Bartoloni, Scaling down of a deworming programme among school-age children after a thirty-year successful intervention in the Bolivian Chaco, *Trop. Med. Int. Health* 23 (6) (2018) 616–621.
- [8] M. Spinicci, F. Macchioni, A. Mantella, S. Gabrielli, M. Roselli, D. Rojo Mayaregua, et al., Seroepidemiological trend of strongyloidiasis in the Bolivian Chaco (1987–2013) in the absence of disease-specific control measures, *Trop. Med. Int. Health* 22 (2017) 1457–1462.
- [9] I. Campolmi, M. Spinicci, D.R. Mayaregua, H.G. Barahona, A. Mantella, Y. Lara, M. Roselli, M. Strohmeier, G. Corti, F. Tolari, J.M. Pinckert, H.R. Dalton, A. Bartoloni, Seroprevalence of Hepatitis A Virus, Hepatitis E Virus, and *Helicobacter pylori* in Rural Communities of the Bolivian Chaco, 2013, *Am. J. Trop. Med. Hyg.* 98 (5) (2018) 1275–1280.
- [10] A. Fiocchi, R. Pawankar, C. Cuello-García, K. Ahn, S. Al-Hammadi, A. Agarwal, K. Beyer, W. Burks, G.W. Canonica, M. Ebisawa, S. Gandhi, R. Kamenwa, B.W. Lee, H. Li, S. Prescott, J.J. Riva, L. Rosenwasser, H. Sampson, M. Spigler, L. Terracciano, A. Vereda-Ortiz, S. Wasserman, J.J. Yepes-Nuñez, J.L. Brożek, H.J. Schünemann,

World allergy Organization-McMaster university guidelines for allergic disease prevention (GLAD-P): probiotics, *World Allergy Organ. J.* 8 (1) (2015) 4.

- [11] J.E. Igetei, M. El-Faham, S. Liddell, G. Schramm, M.J. Doenhoff, Antigenic cross-reactivity between *Schistosoma mansoni* and pollen allergens from the birch tree (*Betula verrucosa*) and Timothy grass (*Phleum pratense*): involvement of shared glycan epitopes and implications for the hygiene hypothesis, *Int. J. Parasitol.* 48 (5) (2018) 345–357.

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