

## Comment on IgE responses to *Ascaris* and mite tropomyosins are risk factors for asthma

H. Takeuchi<sup>1,2</sup>, A. F. Khan<sup>3</sup>, M. I. Hasan<sup>4</sup>, M. D. H. Hawlader<sup>5</sup>, M. Yunus<sup>4</sup>, K. Zaman<sup>4</sup>, H. R. Chowdhury<sup>6</sup>, S. Takanashi<sup>7</sup>, Y. Wagatsuma<sup>8</sup> and T. Iwata<sup>9</sup>

<sup>1</sup>Department of Community and Global Health, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan, <sup>2</sup>Department of Pediatrics, Funabashi General Hospital, Funabashi, Chiba, Japan, <sup>3</sup>Centre for Nutrition and Food Security, International Centre for Diarrhoeal Disease Research, Bangladesh, Mohakhali, Dhaka, Bangladesh, <sup>4</sup>Centre for Child and Adolescent Health, International Centre for Diarrhoeal Disease Research, Bangladesh, Mohakhali, Dhaka, Bangladesh, <sup>5</sup>Department of Epidemiology, Bangladesh University of Health Sciences, Mirpur, Dhaka, Bangladesh, <sup>6</sup>Global Burden of Disease Group, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Vic, Australia, <sup>7</sup>Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan, <sup>8</sup>Department of Clinical Trial and Clinical Epidemiology, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan and <sup>9</sup>Department of Education for Childcare, Faculty of Child Studies, Tokyo Kasei University, Sayama, Saitama, Japan

We read with great interest the paper by Ahumada *et al.* [1] on the association between asthma symptoms and IgE responses to *Ascaris* and mites in a population living in the tropics. They report for the first time in a nationwide case–control study performed in Columbia that IgE sensitization to house dust mite or *Ascaris* tropomyosin has clinical relevance. They also report that specific IgE to tropomyosins from *Ascaris* and mites strongly correlate and speculate that co-exposure to both mite and *Ascaris* generates conditions to increase the allergic symptoms.

Anti-*Ascaris* IgE has been reported to increase the risk of wheezing in low endemic areas, and we demonstrated previously that elevated anti-*Ascaris* IgE was associated with wheezing in children in rural Bangladesh, where as many as 75% of children were infected with *Ascaris* [2]. A study performed later in the same area of Bangladesh in 2008, when the infection prevalence was 17.4%, reported that anti-*Ascaris* IgE was associated with increased risk of ever asthma in 5-year-old children as well [3]. These findings suggest that anti-*Ascaris* IgE is associated with increased risk of wheezing regardless of exposure levels to *Ascaris*.

The prevalence of asthma in Bangladesh has been increasing over the years. A nationwide cross-sectional survey in 1999 reported 7.3% of asthma prevalence in the children aged 5–14 years [4]. A subsequent study conducted in 2000 among the schoolchildren aged 6–7 years documented 9.1% of current wheezing [5]. Our later

research reported a further increase to a 16% prevalence of current wheezing in 2001 among children aged 5–6 years in a rural area [2], while a 2008 study described a 19.7% prevalence of current wheezing in the same area among 5-year-old children [3]. This sudden increase of the prevalence from 2000 to 2001 and the subsequent slow increase between 2001 and 2008 also attracts our attention. The annual increase in the prevalence of asthma was reported 0.02% for the Indian subcontinent, which includes Bangladesh [6].

On the other hand, the percentage change of *Ascaris* infection in age-standardized prevalence from 1999 to 2013 was -44.8%, and the percentage change in age-standardized years lived with disability (YDLs) from 1999 to 2013 was -80.1%. This percentage decrease in age-standardized YDLs was the highest among all the listed 301 acute and chronic diseases and injuries in 188 countries between 1990 and 2013 [7]. The infection prevalence in Bangladesh also declined drastically after introduction of the national programme of anti-helminthic drug administration for children 24–59 months, initiated in 2004, and an additional programme for primary school-aged children [2,3]. The high prevalence of the infection in 2001 and the subsequent sharp decline until 2008 arrests our attention.

WHO has been implementing a programme since 2001 for people at risk in endemic areas in order to eliminate soil-transmitted helminthic infections to reduce intensity of infection and to protect infected individuals from morbidity related to the worms harboured [8]. Major soil-transmitted helminths are *Ascaris lumbricoides*, *Trichuris trichiura* and *Ancylostoma duodenale*. The morbidity related to the worms harboured listed includes abdominal pain, general malaise and weakness, impaired cognitive and physical development [8]. The people at risk are preschool children and school-age children, women of child bearing age and

### Correspondence:

Haruko Takeuchi, Department of Community and Global Health, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan. E-mail: htakeuchi-tky@umin.net

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

adults in certain occupations such as tea-pickers or miners [8]. WHO targets to eliminate the morbidity due to soil-transmitted helminthiasis in children by treating regularly 75% of the children in endemic areas by 2020 [8]. It is anticipated that helminthic infection will be eradicated in the near future. Despite this advance, an unacceptably large number of people suffering from the infection still remain [8].

WHO estimated in 2013 that there were over 270 million preschool children and 600 million school-age children in need of treatment of the diseases [8]. The organization recommends the target countries in the tropics to treat the children once a year when the infection prevalence of soil-transmitted helminths in the community is between 20% and 50%, and twice a year when the prevalence is over 50%. According to the Country X indicators of soil-transmitted helminthiasis of WHO in 2013, national coverage of the preventive treatment of soil-transmitted helminthiasis in Bangladesh was 100% among preschool-aged children and 80% among school-age children [9]. The programme coverage is expressed by the fraction using the total number of the annual treatment children receive in the community as the numerator, and the population of the children in the target age group as the denominator. In other words, when 10 children receive treatment twice a year, the number of children treated is counted as '20'. As the treatment of deworming is conducted twice a year per child in Bangladesh, the actual annual number of the children who received treatment should be half of WHO's estimate. Accordingly, the Bangladesh government is going to reduce the number of annual treatment to one because the national coverage of the children treated regularly is approaching 75%.

Ahumada *et al.* [1] hypothesize that co-exposure to both mite and *Ascaris* generates conditions to increase the allergic symptoms. Hawlader *et al.* [3] found that anti-*Ascaris* IgE was significantly associated with anti-DP IgE in rural Bangladesh, in addition to the fact that anti-*Ascaris* IgE is associated with ever asthma. We again focus on the high prevalence of *Ascaris* infection in 2001 and the subsequent sharp decline until 2008. We also focus on the sudden increase in asthma prevalence in 2001 followed by the slow increase during

2001 and 2008. Wheezing illness in this area might be part of the morbidity related to the worms harboured. However, if it is part of the morbidity, there should have been a decline in the prevalence of wheezing after 2001. Similarly, if *Ascaris* infection suppresses asthma, there should have been a continuing increase in the prevalence of asthma. These findings mentioned above, together with the results of the studies including ours, have led us to speculate that the subsequent increase in the asthma prevalence after 2001 had been suppressed by the national deworming programme. Bangladesh might have been in the era of co-exposure to both mite and *Ascaris* in 2001. Although the national coverage of the children treated regularly is approaching 75%, the programme is for severe infection and morbidity. There still remain a large number of lightly infected children without symptoms. It is, therefore, of extreme importance to examine the impact of *Ascaris* infection on the development of asthma, in addition to the described morbidity, among the children at risk, testing the immunological status in Bangladesh in its rapid transition in the prevalence of both asthma and *Ascaris* infection. We would hope to see children cope well with wheezing illnesses in Bangladesh based on the scientific findings, including the findings in the present study.

### Acknowledgements

The authors thank the children who participated in our previous studies and offered us their precious blood and stool, and their guardians who accompanied the children. We thank the field research staffs for vigorous data collection, too. We also thank Dr. Tariq Anwar, Mr. Joytsnamoy Chakraborty, Dr. Mahbubur Rahman, Dr. Shams El Arifeen, Dr. Abdullar Baqui, Professor David Sack, former Executive Director of ICDDR, B, Dr. Hirotsugu Kano, Dr. Shinji Nakahara and Dr Shizue Sunami for overall encouragement.

### Conflict of interest

The authors declare no conflict of interest.

### References

- Ahumada V, García E, Dennis R *et al.* IgE responses to *Ascaris* and mite tropomyosins are risk factors for asthma. *Clin Exp Allergy* 2015; 45:1189–200.
- Takeuchi H, Zaman K, Takahashi J *et al.* High titre of anti-*Ascaris* immunoglobulin E associated with bronchial asthma symptoms in 5-year-old rural Bangladeshi children. *Clin Exp Allergy* 2008; 38:276–82.
- Hawlader MD, Ma E, Noguchi E *et al.* *Ascaris* lumbricoides infection as a risk factor for asthma and atopy in rural Bangladeshi children. *Trop Med Health* 2014; 42:77–85.
- Hassan MR, Kabir AR, Mahmud AM *et al.* Self-reported asthma symptoms in children and adults of Bangladesh: findings of the National Asthma Prevalence Study. *Int J Epidemiol* 2002; 31:483–8.
- Kabir ML, Rahman F, Hassan MQ, Ahamed F, Mridha MA. Asthma, atopic eczema and allergic rhino-conjunctivitis in school children. *Mymensingh Med J* 2005; 14:41–5.
- Pearce N, Ait-Khaled N, Beasley R *et al.* Worldwide trends in the prevalence of asthma symptoms: phase III of the

- International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007; **62**:758–66.
- 7 Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; pii: S0140-6736(15)60692-4.
- 8 Media centre Soil-transmitted helminth infections. Fact sheet N°336 Updated May 2015. <http://www.who.int/media-centre/factsheets/fs336/en/>.
- 9 Soil-transmitted helminthiasis. Country X indicators. [http://www.who.int/neglected\\_diseases/preventive\\_chemotherapy/sth/db/?units=minimal&region=all&country=bgd&countries=bgd&year=2013](http://www.who.int/neglected_diseases/preventive_chemotherapy/sth/db/?units=minimal&region=all&country=bgd&countries=bgd&year=2013) (Last accessed 2 December 2015).