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REVIEW

Recent perspectives on the global epidemiology of childhood eczema

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Abstract The International Study of Asthma and Allergies in Childhood (ISAAC) is the largest epidemiological study ever performed and the only truly global allergy study. This review summarises the childhood eczema-related findings from ISAAC and discusses how these fit into our current understanding of eczema aetiology, with particular emphasis on worldwide time trends in eczema prevalence, climatic and dietary risk factors, breastfeeding, the role of skin barrier impairment and allergic sensitisation.

With close to two million children from 106 countries, ISAAC is the biggest and only allergy study that has taken a truly global approach. ISAAC's strength is the use of uniform validated methods, allowing direct comparison of results between paediatric populations and providing invaluable data on the worldwide burden of allergic disease, time trends in allergy prevalence and severity, as well as major disease risk factors. ISAAC started in 1991 and has so far completed three phases. Phase One measured the symptom prevalence of asthma, rhino-conjunctivitis, and eczema, using a validated questionnaire tool among children aged 6—7 and 13—14 years.[1] This allowed the creation of the first world map of allergic disease prevalence, revealing significant variations in disease burden between countries.[2] Reasons for these variations have been explored first in ecological and then in cross-sectional risk factor analyses as part of Phase Two. Phase Two included around 63,000 children aged 8—12 years from 30 centres in 22 countries. Data was collected through symptom and risk factor questionnaires. Participants were also skin prick tested to environmental allergens and physically examined for flexural eczema. In addition, blood was collected for genetic analyses.[3] Subsequently, Phase Three looked at time trends in disease burden through comparison of prevalence figures with Phase One. As in Phase One, participants were schoolchildren aged 6—7 and 13—14. This review article discusses, in the light of other work, what we have learned from ISAAC about childhood eczema (syn. atopic eczema, atopic dermatitis).[4]

Global prevalence surveys and time trends

Prior to the ISAAC Phase One survey, very little was known about the prevalence of childhood eczema outside of Northern Europe. Phase One collected data from 256,410 children aged 6—7 years in 90 centres and 458,623 participants

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Box 1: Eczema symptoms questionnaire used in ISAAC Phases One to Three (for 6 and 7 year olds the parents answered the questions, whereas older children answered the questions themselves (Phases One and Three). In Phase Two (children aged 8—12) questions were answered by parents):

1. Has your child (have you) ever had an itchy rash which was coming and going for at least six months?
2. Has your child (have you) had this itchy rash at any time in the last 12 months?
3. Has this itchy rash at any time affected any of the following places: folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes? ('flexural eczema in the past 12 months')

If 'yes' to question 3, then additional questions about disease severity were asked:

4. Has this rash cleared completely at any time during the last 12 months?
5. In the past 12 months, how often, on average, has your child (have you) been kept awake at night by this itchy rash? (Never in the last 12 months, less than 1 night per week, 1 or more nights per week)

between 13 and 14 years of age from 153 centres.[5,6] The validated ISAAC eczema questions, which were used in all study centres, are shown in Box 1 . There were significant prevalence differences between paediatric populations for all eczema outcomes in both age groups. For instance, the prevalence of flexural eczema in the past 12 months ranged from less than 2% in Iran to over 16% in Japan and Sweden in the 6—7 years age group and under 1% in Albania to over 15% in a number of Northern European countries among 13 and 14-year-old children. With a few exceptions, prevalences tended to be higher in affluent European and Australasian settings (Japan, Australia, and New Zealand) compared to children in Eastern and Central Europe as well as East Asia.

Phase Three added valuable information on time trends in disease distribution. 302,159 children aged 13—14 years in 105 centers from 55 countries and 187,943 children aged 6—7 years in 64 centres from 35 countries were surveyed from the Phase One study centres, using the same validated questionnaire tool 5—10 years after the initial survey.[7] Overall, in affluent country centres where eczema among 13 and 14 year olds was common, prevalences did not increase further or even decreased, whereas the eczema burden continued to rise in most developing country settings (Figure 1). As for 6—7 year olds, the majority of centres showed an increase in eczema symptoms.

Apart from generating world maps of eczema prevalence, the main outcome of Phases One and Three was that eczema prevalence did not only vary between countries, but there were also differences within populations of the same ethnic background, suggesting that environmental influences play an important role in disease risk. Consequently, a number of ecological and cross-sectional analyses based on the ISAAC data set have examined individual risk factors for eczema.

Climate

One potential explanation for prevalence differences between populations is climate; an area that had previously received little attention with regard to eczema. Based on the Phase One data set, an ecological analysis was conducted using information on long-term climatic conditions in the different study areas from the World Weather Guide.[8] Variables that were examined included latitude, altitude, average outdoor temperature and relative outdoor humidity. The results, which were adjusted for countries' gross national per capita income (GNP), suggest that eczema symptoms correlate positively with latitude and negatively with annual outdoor temperature but none of the other factors. These findings have been supported by cross-sectional studies in Spain and Taiwan[9,10] and could be due to direct climatic influences. Alternatively, behavioural changes triggered by weather are a potential explanation, such as time spent outside in sun, especially as UV light has well-established immuno-suppressive effects and is used as a treatment for eczema.[11] Work that has looked at flare factors in established eczema supports this notion, as lower outdoor temperatures, especially in combination with skin irritants, can contribute to disease worsening, whereas indoor climate seems less important.[12,13] However, the relationship between outdoor climate and disease flares is complex with some children reporting worsening in summer and others in winter, as suggested by a small longitudinal study among German children.[13] Outdoor temperature and humidity as well as seasonal changes in pollen counts are likely to interact,[10,12] and further studies, which also take skin barrier function and hydration status as well as bacterial skin colonisation into account, are required.[14]

Diet

Another potential explanation for prevalence differences between countries are dietary factors. Given how uncommon eczema and other allergies still are in most developing nations, an important question is whether consumption of a 'western' affluent diet (i.e. high intake of refined grains, cured and red meats, as well as saturated and unsaturated fatty acids) is associated with an increase in eczema risk. This was explored in another ecological analysis from ISAAC Phase One, looking at the association between eczema prevalence and per capita consumption of vegetables, olive oil, dietary fibre, fat (total, saturated and unsaturated), protein from various dietary sources, carbohydrates, as well as a number of vitamins. There was a consistent negative association between eczema prevalence and per capita consumption of vegetables, protein from cereal and nuts as well as all fresh and frozen fish, even after adjustment for GNP.[15]

However, such ecological analyses do not allow to directly extrapolate findings from the population to the individual level. A number of longitudinal studies which examined individual dietary components have suggested that a high fish intake during pregnancy has a protective effect on eczema