

Original article

Atopic eczema in children: another harmful sequel of divorce

Background: Different lifestyle factors seem to be associated with the risk for atopic diseases and some studies suggest that stress increases the risk of allergic sensitization, asthma and atopic eczema. Only few studies have investigated the association of early stressful life events and atopic eczema (AE) in children.

Subjects and Methods: Parents of participants of the ongoing LISA birth cohort study were asked to give information on life events, such as severe disease or death of a family member, unemployment, or divorce of the parents. Lifetime prevalence of AE and incidence after the assessment period for life events were compared.

Results: Prevalence of AE until the age of 4 years was 21.4%. Reported life events within the first 2 years were: severe disease (17.5%) or death (8.4%) of a family member, divorce/separation (3.4%), and unemployment (2.7%). Divorce/separation was associated with a significantly [odds ratio (OR) 3.59, 95% confidence interval (CI) 1.69–7.66] increased and disease with a significantly (OR 0.29, 95% CI 0.13–0.68) decreased incidence of AE for the subsequent 2 years of life. No effect was seen for unemployment.

Conclusions: Divorce/separation of the parents and severe disease of a family member influence the risk of developing AE.

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Key words: atopic eczema; children; divorce; life event; psychosomatic.

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Background

Allergies are considered one of the major health concerns of affluent countries. Prevalence of atopy has doubled during the last 20 years. Nowadays, 15–20% of the population in Germany suffer from, at least, one atopic disease and in one-third, allergic sensitization is present (1). Atopic eczema is the most common atopic disease in infants and young children with an average onset at an age of 6–7 months (2). Besides genetic susceptibility, environmental and lifestyle factors are considered to be crucial for the development of atopic diseases. Many

influencing factors have been identified, part of which can be effective as early as in the prenatal period (3–6). Recent studies refer to an even larger influence of lifestyle factors compared with environmental factors (7). Particularly, combinations of different lifestyle factors seem to be associated with the risk for atopic diseases, rather than one factor alone (8, 9). Clinical observations illustrate that psychological factors often precede exacerbations of atopic eczema and skin conditions and it is also assumed that they contribute to their manifestation (10). There is a great body of evidence that stress and other psychological factors are associated with alteration in immune func-

tions, which might subsequently lead to dermatological and other immune-mediated diseases (11, 12). Only few studies have investigated the influence of such psychosocial factors on the development and course of allergies. Some of these studies suggested that stressful life events increase the risk of allergic sensitization, asthma and atopic eczema (13, 14). Very little of this type of research has been performed on younger children and therefore, we investigated this topic in the present study. Stressful life events within the family, such as severe disease or death of a family member, unemployment, or divorce of the parents, which occurred within the first 2 years of life were studied with regard to their association with the later manifestation of atopic eczema.

Subjects and methods

Subjects

Subjects for this study were recruited from the LISA (Einfluss von Lebensbedingungen und Verhaltensweisen auf die Entwicklung von Immunsystem und Allergien im Ost-West-Vergleich) survey, which is an ongoing German birth cohort study on influences of lifestyle factors on the immune system and the development of allergies in childhood. For the LISA study, 3097 healthy mature neonates were enrolled, between November 1997 and January 1999, from obstetrical clinics in the cities of Munich, Leipzig, Wesel and Bad Honnef. Study population and methods of the LISA study have been described in detail earlier (15–17). The aim of the LISA study was to investigate immunoglobulin E (IgE)-dependent allergic diseases in a prospective setting. Data were collected by questionnaires that were sent to the parents shortly after the child's birth, at age 6 months, 1, 1½, 2 and 4 years. For this study, parents of all the 2420 participants, who had stayed in the cohort until the child's fourth birthday and agreed to further participation were contacted. A questionnaire on psychosocial aspects of life and stressful life events was developed and sent to the parents at the beginning of the child's month of birth together with the regular 6-year LISA follow-up documents. The study protocol was approved by the ethics committees of the Bavarian 'Landesärztekammer' and of the University of Leipzig. Written informed consent was obtained from the parents of all participating children prior to the study.

Assessment of exposure and outcome

Questionnaire data were used to assess both atopic eczema as a health outcome and exposure to stressful life events. The primary outcome was defined as physician-diagnosed neurodermatitis, allergic or atopic eczema as reported by the parents in the LISA interviews at age 6 months, 1, 1½, 2 and 4 years. As information on IgE sensitization was not available for all children, we did not follow the revised nomenclature of the Nomenclature Review Committee of the World Allergy Organization (18) and in the following, the term 'atopic eczema' is used to denominate all these types of eczema. As each LISA questionnaire exclusively covered the time period between follow-ups, not only the prevalence but also the incidence of atopic eczema for the first 4 years of life could be obtained. Incidence was computed for three life time intervals: (i) under 1 year (ii) 1 year and (iii) 2 and 3 years old; thus the effect of exposure could be differentiated into concomitant and preceding life events as illustrated in Fig. 1.

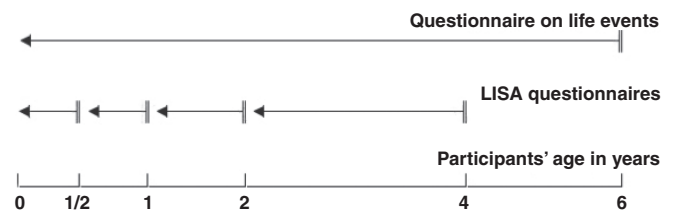


Figure 1. Time of interviews and covered time period.

Data from the LISA questionnaires also comprised information on parental atopy, school education, gender and presence of older siblings, which were considered as potential confounding variables.

The subject of interest was stressful life events within the first 2 years of life of the participating child. The events were based on a commonly used life event scale (19) which enquired about death or severe disease within the family, concerning either the parents themselves, their parents, children, or siblings ('Did you or a member of your family develop a severe physical illness, that lead to hospitalisation or caused this person to be bed-bound for more than ten days?' 'Did a member of your family die?'). Furthermore, it was asked whether one of the parents had been unemployed ('Have you or your spouse been unemployed for more than three months?') and whether a divorce or separation ('Did you experience a separation or divorce from your partner?') had occurred. All life events were obtained retrospectively for the last 6 years, i.e. the lifetime of the participating child, and parents were to state the year of occurrence. For our analysis, life events were dichotomized and considered only if they occurred in 1998, 1999 or 2000, as this was seen as the best approximation of events within the first 2 years of life, which appear to represent the critical period for immune modulation with long-term consequences (20).

Statistical methods

We performed descriptive statistics and tested differences in prevalences and incidences by chi-squared test, in which P -values < 0.05 were considered statistically significant. Crude associations between life events, confounding factors and health outcomes were described using odds ratios (ORs) with 95% confidence intervals (CI) as indicator for stability. Multiple logistic regression analysis was performed to calculate ORs adjusted for potential confounders (aOR). Variable and model selection were performed by backward elimination, using the log-likelihood ratio test, which is a method for testing a simpler model against a more complex model (21). The starting model included incidence and prevalence of atopic eczema as dependent variables, different life events as exposure variables and gender, maternal school education, parental history of atopy and presence of older siblings as potential confounding variables. All calculations were performed by using the statistical software package SPSS 13.0.

Results

Of the 2420 questionnaires on life events that were sent to all remaining participants of the LISA Study, a total of 1930 questionnaires (response rate 79.6%) were returned and could be merged with the corresponding LISA questionnaires. The majority of questionnaires was completed by the mothers (94.5%). Basic characteristics and

Table 1. Basis characteristics of the study population ($N = 1930$)*

Variables	Frequency <i>n/N (%)</i>
Physician diagnosed atopic eczema	
Life time prevalence until fourth birthday	412/1924 (21.4)
Incidence under age 1 year	191/1920 (9.9)
Incidence age 1 year	123/1725 (7.1)
Incidence age 2 and 3 years	98/1525 (6.4)
Life event before 2 years of age	497/1918 (25.9)
Death of a family member	161/1910 (8.4)
Severe disease of a family member	335/1914 (17.5)
Unemployment	52/1912 (2.7)
Divorce/separation	65/1909 (3.4)
Gender	
Male	990/1924 (51.5)
Female	934/1924 (48.5)
Maternal school education†	
High	1069/1910 (55.4)
Intermediate	705/1910 (36.5)
Low	136/1910 (7.0)
Parental history of atopy	1018/1919 (53.0)
Presence of older siblings	906/1924 (47.1)

*Participants of the LISA Study who had stayed in the cohort until the child's fourth birthday and returned the questionnaire on life events.

†High: 12 years of schooling or more ('Fach-Hochschulreife'; intermediate: 10 years of schooling 'Mittlere Reife'; low: 9 years of schooling or less 'Hauptschulabschluss'.

potential confounding factors of the study population are given in Table 1. Lifetime prevalence of atopic eczema until the age of 4 years was 21.4% and 53% had a parental history of atopy. Level of maternal education was very high with 55.4% of mothers having had ≥ 12 years of schooling. Any stressful life event within the first 2 years of life of the participating child was reported by 25.9% of the parents. These life events were mostly disease (17.5%) or death (8.4%) of a family member, and fewer cases of divorce or separation of the parents (3.4%) and periods of unemployment (2.7%); 6.1% of all parents reported more than one of these life events. The most common combination was severe disease and death of a family member, which was reported by 4.5% of the parents.

We compared children whose parents had reported a life event within the first 2 years, with all children without such life events (internal control group). Data on development of atopic eczema in children with or without life event within the first 2 years of life are presented in Table 2. Unemployment of at least one of the parents was the only event that did not have any effect on lifetime prevalence at the fourth birthday or incidence of atopic eczema in the participants. Divorce or separation of the parents was associated with a significantly ($P = 0.04$) increased prevalence (32.3%) of atopic eczema in their children compared with 21.2% in the group without divorce or separation. The incidence increased significantly only for the two years after the parents' separation in the group of 2- and 3-year olds (18.8% vs. 6.0%,

Table 2. Development of atopic eczema for children with or without life event within the first 2 years of life

	Life events	
	Death (<i>n</i> = 161)	No death (<i>n</i> = 1749)
Prevalence of atopic eczema	15.6	22.0
Incidence under age 1 year	9.4	10.0
Incidence age 1 year	4.1	7.5
Incidence age 2 and 3 years	3.0	6.7
	Disease (<i>n</i> = 335)	No disease (<i>n</i> = 1579)
	Unemployment (<i>n</i> = 52)	No unemployment (<i>n</i> = 1860)
Prevalence of atopic eczema	16.2*	22.5
Incidence under age 1 year	8.4	10.2
Incidence age 1 year	6.6	7.3
Incidence age 2 and 3 years	2.2**	7.2
	Divorce/separation (<i>n</i> = 65)	No divorce/separation (<i>n</i> = 1844)
Prevalence of atopic eczema	32.3*	21.1
Incidence under age 1 year	10.9	9.9
Incidence age 1 year	8.8	7.2
Incidence age 2 and 3 years	18.8**	6.0

* $P < 0.05$, ** $P < 0.01$ (chi-squared test).

Values are given as percentages.

$P = 0.001$), but not in the younger infants. An opposite effect was seen for severe disease or death of a family member. Both were associated with a decreased prevalence of atopic eczema (16.2% vs. 22.5%; 15.6% vs. 22.0%); for disease this decrease was significant ($P = 0.01$). Again the incidence was decreased in the 2- and 3-year olds (2.2% vs. 7.2%; 3.0% vs. 6.7%) but not in the younger infants. This difference also was significant for severe disease ($P = 0.004$) but not for death. The prevalence of atopic eczema was also associated with parental history of atopy ($P < 0.001$) and maternal education level ($P = 0.02$) in the chi-squared test but not with gender or presence of older siblings.

Logistic regression analysis on the lifetime prevalence at the fourth birthday confirmed that children were at significantly higher risk (OR 1.78; 95% CI 1.05–3.04) for atopic eczema if they had experienced divorce or separation of their parents in the first 2 years of life. Severe disease of a family member significantly decreased the risk (OR 0.67; 95% CI 0.49–0.91) of atopic eczema; for death (OR 0.66; 95% CI 0.42–1.02) this association was not significant. Multiple logistic regression analysis with adjustment for the four potential confounding variables, gender, presence of older siblings, maternal school education and parental history of atopy, led to only marginal changes in the effect estimates, indicating a very

Table 3. Association between life events within the first two years of life and atopic eczema

Variables	Prevalence of atopic eczema	
	OR (95% CI)	aOR (95% CI)
Life event		
Death of a family member	0.66 (0.42–1.02)	0.67 (0.43–1.04)
Severe disease of a family member	0.67 (0.49–0.91)	0.64 (0.47–0.89)
Divorce/separation	1.78 (1.05–3.04)	1.86 (1.09–3.19)
Unemployment	0.96 (0.50–1.92)	1.03 (0.52–2.03)
	Incidence age 2 and 3 years	
	OR (95% CI)	aOR (95% CI)
Life event		
Death of a family member	0.44 (0.16–1.22)	0.44 (0.16–1.21)
Severe disease of a family member	0.29 (0.13–0.65)	0.30 (0.13–0.70)
Divorce/separation	3.59 (1.69–7.66)	3.78 (1.76–8.10)
Unemployment	0.71 (0.17–2.99)	0.76 (0.18–3.19)

aOR adjusted for gender, maternal school education, parental history of atopy, older siblings.

minor confounding effect. Details on crude and adjusted ORs are presented in Table 3.

If the incidence of atopic eczema at age 2 and 3 years instead of prevalence was employed as the outcome variable, effect estimates were enlarged. Divorce/separation of the parents was now associated with a threefold risk (OR 3.59; 95% CI 1.69–7.66) and severe disease of a family member with a reduced risk by two-thirds (OR 0.29; 95% CI 0.13–0.65). Still, no significant association of death (OR 0.44; 95% CI 0.16–1.22) with incidence of atopic eczema could be seen. Adjustment for potential confounding variables led to only marginal changes in the effect estimates (Table 3). No association was seen when incidences in the first and second year of life, i.e. the life time period concomitant to the reported life events, were employed as outcome variables (data not shown).

Discussion

The aim of this study was to examine the development of atopic eczema in children who had experienced life events with a great psychosocial impact in their first 2 years of life.

There is substantiated knowledge that stress can lead to aggravation of symptoms of asthma (22–24) as well as atopic eczema (25), even after effects were controlled for demographic and medical factors. Information on the impact of stress on the onset of atopic diseases is sparse. One retrospective study of Finnish students suggested that preceding or concomitant stressful life events may promote the manifestation of asthma and allergic rhinoconjunctivitis. No association was found for atopic eczema. The authors proposed that this was due to the

common onset of atopic eczema at an very early age (13). In a prospective Swedish study, among children who had been internationally relocated for at least 1 year, development of sensitization was more common than in control children who had stayed at home. The stress related to moving abroad was suggested as a possible factor associated with the increased risk of atopy (14).

In the present study, children whose parents had divorced or separated were at a higher risk for atopic eczema, whereas children whose parents had reported a severe disease of a family member were at a lower risk. The change of prevalence of atopic eczema for each of these events, could be put down to the change of incidence at age 2 and 3 years, i.e. the time period subsequent to the corresponding life event. The incidence of atopic eczema for the first 2 years of life was not significantly different between the groups, indicating that concomitant life events did not show any effect on the manifestation of atopic eczema. Our results regarding the increased risk for atopic eczema after parental separation are in accordance with some studies in asthmatics. In a retrospective psychological study, early onset of asthma was associated with more separation experiences from a close friend or relative (26). One American study in children at genetic risk for asthma found an association of early problems in coping and parenting with the later onset of asthma. Parenting difficulties included problems with infant caregiving as well as components of maternal functioning, such as postpartum depression and inadequate marital support (27). Results of the Norwegian Psychosocial Risk for Allergic Development (PRAD) study also show that parental interaction and difficulties influence the risk of developing symptoms of asthma (28) and a Swedish study identified functional family interaction and a supportive social network as significant aspects in the course of atopic illness in early childhood (29). A study from the Mayo Clinic investigated separation anxiety disorders in children and found a significant association with increased risk for atopic disorders in these children (30). In our study, we did not assess subjectively perceived stress, which would have been possible for the parents only, but it is assumable that divorce or separation causes stress for the affected parents and probably involves inadequate family interactions, problems in parenting and separation experiences for their children, factors that can again lead to stress.

The negative association of reported severe disease of a family member and the subsequent decreased risk for atopic eczema in children is reasonably surprising. As life events were assessed retrospectively and as we had to rely on parents' recall of the events, one needs to discuss a potential reporting bias in this context. It is conceivable that a supportive family network and closer family interaction are associated with a lower eczema risk on the one hand and a higher reporting frequency for disease of family members on the other hand. This would lead to

a differential reporting bias and thereby lead to an apparently protective effect of this life event. We did not measure any family or marital interaction, thus this possible interrelation would have been missed, but as selection of life events was based on a commonly used life event scale and divorce as well as disease or death of a family member represented severe events (19, 31), that one would expect to be remembered reliably, reporting bias is considered unlikely. Furthermore, death of a family member similarly showed the same negative association with atopic eczema, even though it was not significant. Therefore, this explanation seems even more unlikely, as it is even harder to believe that someone would forget the death of a family member within the last 6 years. A Finnish study also investigated severe life events and the development of atopic diseases. Here, an association of preceding events and atopic disease could only be found for parental or personal conflicts, including parental divorce, but not for severe disease or death of a family member (13). In conclusion, all explanations for the protective effect of preceding disease of a family member seem speculative, and it might be a surrogate for one or more factors we did not measure in this study.

Parental unemployment did not seem to have any effect on the development of atopic eczema in the children, possibly because it might only cause stress for the parents but not for their children.

Characteristics of the study population were determined by the ongoing birth cohort study (LISA), where all participants were recruited from. The level of maternal school education as well as the number of parents with a history of atopy were very high, because of self selection

in the cohort study. Parents who are affected themselves, often show more interest in the topic and are more likely to participate (21). A higher educational level (32, 33) and parental history of atopy (34, 35) are both known risk factors for the development of atopic eczema in children. Adjustment for these potential confounders did not change the effect estimates for the life events, indicating that these were independent factors in the development of atopic eczema.

In the present study, for the first time, the effect of life events could be evaluated in a setting of a large birth cohort with prospective assessment of atopic eczema, a large number of participants and a fairly good response rate. The retrospective assessment of life events, which comprises the risk of recall bias, as discussed above, and the absence of objective verification of disease status in the participants need to be mentioned as limitations of this study.

In conclusion, the present epidemiologic data suggest that preceding divorce or separation of the parents may promote atopic eczema in their children, possibly by means of psychosocial stress induced by separation experiences or inadequate parenting, whereas severe disease of a family member acts as a protective factor, the reason for which is unclear.

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Appendix

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