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CLINICAL REPORT

Atopic Dermatitis in Young Children: Diagnostic Criteria for Use in Epidemiological Studies Based on Telephone Interviews

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The aim of the study was to establish diagnostic criteria for atopic dermatitis in 1.5-year-old children that could be employed in epidemiological studies of atopic dermatitis based on telephone interviews. In a Danish cohort of 100,000 pregnant women, 4 computer-assisted telephone interviews were carried out. In the last interview, conducted when the child was 1.5 years old, mothers were asked about their child's skin condition. Eighty-one women who had answered that their child suffered from either an itchy rash or atopic dermatitis were invited to participate in the study. Of these, 60 took part in the study and had their child examined by a dermatologist. Affirmative answers to 1) itchy rash or doctor-verified atopic dermatitis and 2) recurrent rash or rash for at least 4 consecutive 0.5-month periods, and 3) localization in elbow creases, behind the knees, wrists/hands, face or generalized rash resulted in the highest sensitivity and specificity for atopic dermatitis as diagnosed by the dermatologist, who found 37 of 60 children (62%) suffering from atopic dermatitis. Using this algorithm, telephone interviews can be used to diagnose atopic dermatitis in young children in large-scale epidemiological investigations. ***Key words: itchy rash; localization; self-reported atopic dermatitis; time pattern.***

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Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease that usually becomes clinically recognizable within the first 2 years of life. Even among dermatologists, the diagnosis can be difficult to establish in young children for whom the period of clinical symptoms may have been short and the localization not always typical. Furthermore, the course of the disease fluctuates in affected children, and may sometimes be completely quiescent.

Several sets of diagnostic criteria for AD have been suggested for epidemiological studies based on clinical examination and questionnaires (1–3). The aim of this study was to establish diagnostic criteria for present and previous AD in 1.5-year-old children; criteria which could be employed in epidemiological studies of AD based on telephone interviews.

MATERIAL AND METHODS

In Denmark, a cohort of 100,000 pregnant women was established to study the effects of exposures *in utero* and early life (4). Four computer-assisted telephone interviews were conducted. In the last interview, conducted when the child was 1.5 years old, mothers were asked about their child's skin condition. The questions are presented in Fig. 1. Each woman was asked if her child suffered from itchy rash (Main Question A). If she answered no, she was asked if her child had AD (Main Question B). If she answered yes to question A, she was asked if it was recurrent (A1) or lasted more than 2 weeks (A2). If she answered no to the subsequent questions A1 and A2, she was asked question B. If she answered yes to one or both of A1 and A2, she was later asked if the rash was AD (A3). If she answered no to A3, she was asked question B. Thus, all women were asked question A. Women who answered no to question A, and women who answered yes to question A but subsequently no to both A1 and A2, or no to A3 were all asked question B. This way, question B functioned as an extra possibility of detecting AD in difficult cases when the mothers did not perceive the rash as itchy, when the rash was of limited duration, or when the child had several types of itchy rash.

The women participating in the present study were selected among women living in greater Copenhagen and participating in the last interview between 1 October 2001 and 10 January 2002. Women who answered affirmatively to either question A or question B were invited to participate. Those who agreed to participate were subsequently scheduled for examination by a dermatologist appointed as validator (EB). The validator was unaware of the answers given in the telephone interview. At the examination a detailed history regarding earlier and present skin conditions of the child was recorded. The child's skin was examined. Based on the answers and the examination, the validator determined whether the child had present AD, previous AD, another skin disease or no skin disease. The study was approved by the local Ethics Committees ((KF) 11-019/01).

Statistical methods

The comparability between participants and non-participants with regard to their answers in the interview was tested by chi-square tests. The association between an answer and AD as

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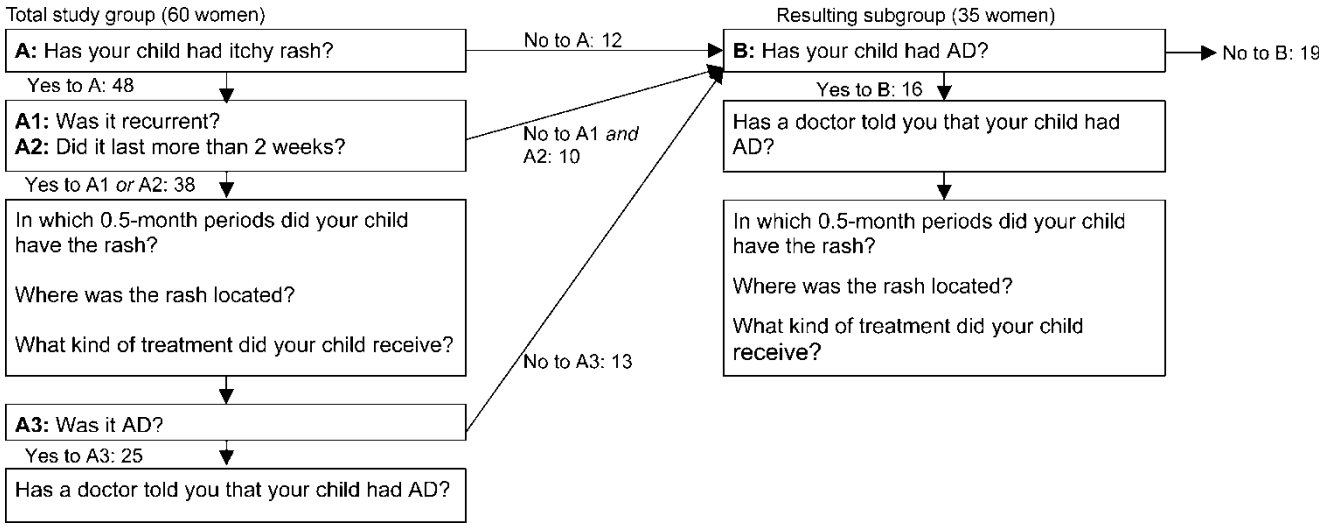

Fig. 1. Questions asked in the telephone interview about atopic dermatitis (AD) and the number of yes/no answers.

diagnosed by the validator was investigated by chi-square tests. Furthermore, we employed an overall measure of relative value derived by adding the sensitivity and specificity together and subtracting 100 (Youden's J statistic) (5). To investigate which combination of answers to the questions best matched the diagnosis made by the validator, the responses were divided into three groups of features which are characteristic for AD: 1) itchy skin rash and/or self-reported AD, 2) time pattern (relapsing eczema and/or rash of a certain duration, calculated by summing up the 0.5-month periods with rash), and 3) localization (Table I). A variable for each combination of answers was designed within each group. Subsequently, evaluation was made of all combinations containing one variable from each of the three groups. The sensitivity and specificity of each of these combinations were computed, and the combination resulting in the highest relative value (see above) was chosen as the algorithm for AD. All analyses were performed in SAS 8.0. It should be noted that had we used the kappa coefficient, we would have obtained the same optimal algorithm for AD. However, we found the kappa coefficient less relevant in the present situation owing to the lack of symmetry between AD as verified by the validator and based on the interview.

Table I. *Percentages of affirmative answers to the questions in the telephone interview according to the diagnosis atopic dermatitis made by the validator*

Answers in telephone interviews	Atopic dermatitis according to the validator: Yes ($n=37$) (%)	Atopic dermatitis according to the validator: No ($n=23$) (%)	*p*-value	Relative value*
Itchy rash/self-reported AD				
Itchy skin rash	86	70	0.11	16.9
AD according to mother	81	48	0.007	33.3
AD according to doctor	76	35	0.002	40.9
Family history of atopic disease	76	52	0.06	23.5
Time pattern				
Recurrent itchy skin rash	76	26	0.0002	49.6
2 or more 0.5-month periods	76	70	0.60	6.1
3 or more 0.5-month periods	54	52	0.89	1.9
4 or more 0.5-month periods	49	35	0.29	13.9
5 or more 0.5-month periods	49	30	0.16	18.2
Localization				
Face	16	0	0.04	16.2
Arm, extensor side	19	13	0.55	5.9
Elbow creases	38	13	0.04	24.8
Wrists/hands	41	4	0.002	36.2
Leg, extensor side	24	26	0.88	−1.8
Behind knees	51	17	0.009	34.0
Ankles/feet	3	0	0.43	2.7
Generalized/4 or more localizations	24	9	0.13	15.6

*Relative value = (sensitivity + specificity) − 100.

RESULTS

The children were between 18 and 22 months old when the telephone interview was conducted. Of 81 invited women, 9 (11%) declined participation and 12 (15%) agreed to participate but were unable to find a suitable time to do so. Sixty children whose mothers had reported either an itchy rash or AD were therefore examined by the validator. There were no major differences between the women who participated and those who did not, irrespective of cause, in the answers to questions about itchy rash, self-reported or doctor-verified AD, recurrent AD, duration, localization in flexures, or family history of allergic diseases (data not shown, all p-values >0.15). The median time between the interview and the clinical examination was 25 days (range 10–43 days).

According to the validator, 37 (62%) of 60 children had AD; 27 (71%) had present AD and 10 (29%) previous AD (Table I). Among the 23 children who did not have AD, 3 had nummulate eczema, 4 xerosis, 2 urticaria, 1 sequelae after a viral infection, 1 dermatitis without specification, 1 napkin dermatitis and 1 a convincing history of seborrhoeic dermatitis, while 10 children had no skin disease.

With regard to itchy rash and/or self-reported AD, three combinations of answers were designed, namely itchy rash and AD according to the mother, itchy rash and AD according to a doctor, and itchy rash and AD according to the mother or a doctor. Five combinations of time pattern were designed: recurrent AD alone, and recurrent AD and/or rash for at least two, three, four or five consecutive 0.5-month periods. With regard to localization, 26 combinations were designed, combining 2 or more localizations in elbow creases/behind the knees, extensor sides, face, hands or generalized localization/four or more localizations. Thus, a total of $3 \times 5 \times 26$ (390) combinations of answers were tested with regard to largest obtainable relative value (sum of sensitivity and specificity−100). The combination resulting in the highest relative value (72.4) is presented in Table II. This combination correctly identified 30 of the 37 children with AD and 21 of the 23 without AD according to the validator, resulting in a sensitivity of 81% and a specificity of 91%.

Table II. *Criteria for atopic dermatitis resulting in the highest relative value (72.4) in this study*

Itchy rash ever *or* doctor-verified atopic dermatitis
and
recurrent rash *or* rash for at least 4 consecutive 0.5-month periods
and
localization in elbow creases, behind the knees, face, wrists/hands *or* generalized/4 or more localizations

DISCUSSION

The use of telephone interviews to diagnose AD with the purpose of studying risk factors for AD in young children provides several challenges and necessitates modifications of the currently used diagnostic criteria for use in epidemiological studies. First, the most commonly used diagnostic criteria presented by Hanifin & Rajka (6) and the UK Working Group's refinements of these criteria (1) include a clinical examination by a trained investigator to detect visible AD. However, it was recently reported that mothers can accurately report visible AD in their 1-year-old infants (7), and accordingly written questionnaires have been used with satisfactory results (2, 3). Thus, clinical examination, though of obvious value, does not seem to be absolutely necessary. Second, the most commonly used diagnostic criteria include a history of atopic disease in a first-degree relative. In studies of risk factors for AD this may confound interpretation of the results, since common environmental factors may affect both the index child and the relative(s). Furthermore, the probability of a positive family history increases with the number of siblings. Third, some existing diagnostic criteria attempt to diagnose present AD. However, in studies of risk factors for AD it is important to determine the lifetime prevalence, and thus to identify present as well as previous AD.

The detection of AD in young children implies further challenges as the localization is not always typical. However, we found that most of these 1.5-year-old children had the typical localization in elbow creases and/or behind the knees. Localization in the face was not very common, but was strongly associated with AD. As recently reported by others, many of these young children had hand eczema (Table I) (8).

From previous experience we are aware that some mothers of children with AD do not answer affirmatively when asked whether their child suffers from an itchy rash, since they use an emollient before it starts to itch. It has also been reported that parents of children with AD diagnosed by a doctor report itch to a lower extent, probably because itch-alleviating treatment has been initiated (9). We acknowledged this by allowing itchy rash not to be mandatory if the diagnosis AD had been made probable in other ways, i.e. by a doctor's diagnosis.

Taking these points into account, we established a set of diagnostic criteria for AD in 1.5-year-old children (see Table II). We find it likely that our criteria would be applicable within a larger age span; however, this would need to be evaluated. It should be noted that the diagnostic criteria to a large extent are data-driven, and therefore the sensitivity and specificity in the present subpopulation will tend to be larger than if the set of criteria were used on a different subpopulation. However, the diagnostic criteria defined in this study

are similar to those used by others and from a clinical perspective reasonable. Among the 20% of women who answered affirmatively to either itchy rash or AD, 62% had AD corresponding to a lifetime prevalence of AD at 1.5-years of age of 12% in the cohort, a figure in line with previous reports (10). We only invited women who reported either itchy rash or AD to ensure the best possible demarcation between AD and other skin conditions. Therefore calculations of true sensitivity and specificity at the population level cannot be done. However, had we invited all women, the sensitivity would very likely have been lower and the specificity even higher.

With no natural cut-off between children with and without AD, the choice of diagnostic criteria will always be a trade-off between sensitivity and specificity. Bearing this in mind, we consider the agreement between the diagnosis AD as made by a telephone interview and as made on a clinical examination to be satisfactory. In particular, it should be noted that the specificity is likely to be high, which is of particular interest when studying risk factors for AD. The modest sensitivity, however, indicates that potential risk factors can be overlooked. This may be compensated by increasing the size of the study population. Bearing the limitations in mind, telephone interviews can be used to diagnose AD in young children in large-scale epidemiological investigations.

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