

Predictability of Early Onset Atopic Dermatitis by Cord Blood IgE and Parental History

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Cord blood IgE and atopic family history have been used as predictors of atopic disease in infants for more than 20 years. In recent years, the value of cord blood IgE in predicting the development of atopic dermatitis has been questioned, while family history of atopy has consistently been regarded as a useful predictor for atopic dermatitis. A birth cohort was followed-up to 6 months of age to record the development of atopic dermatitis and to study its association with cord blood IgE levels and parental history of atopy. The cumulative incidence of atopic dermatitis over the 1st, 3rd and 6th months of life amounted to 5.0%, 8.2% and 14.0%, respectively. When the cutoff value for cord blood IgE was set at 0.5 kU/L, there was a significant association between elevated cord blood IgE level and atopic dermatitis at 1, 3 and 6 months of age; when the cutoff value was set at 0.9 kU/L, the association was only found at 3 months of age. There was a significant association with atopic history of the mother. The effect of maternal atopic history on atopic dermatitis seen only at 1 month was lost by 3 months of age. There was no correlation between paternal history and atopic dermatitis. In our study, the predictive capacity of maternal history and cord blood IgE was not high enough to recommend them as screening factors. (Acta Paediatr Tw 2005; 46:272-7)

Key words: cord blood, IgE, parental history, atopic dermatitis

INTRODUCTION

Atopic dermatitis (AD), also called atopic eczema, is a common chronic skin disease, affecting 12% to 40% of infants in different studies from different countries.¹⁻³ Early identification of healthy individuals at risk is needed for selective primary prevention of atopic dermatitis. However, effective screening remains a challenge.

A number of environmental and genetic factors have been implicated. Cord blood IgE and family history have been used as predictors of atopic disease in infants for more than 20 years and proposed as easily accessible and valuable markers to screen infant for atopy risk.⁴ Cord blood IgE was considered as a good predictor for atopic disease in the past.⁵⁻¹³ Since 1988, the value of cord blood IgE in predicting the development of atopic disease has been questioned,¹⁴⁻¹⁷ while parental atopic history has consistently been regarded as an useful

predictor for atopic disease of the infant and child.^{6,18,19}

A birth cohort was followed-up at ages 1, 3, and 6 months to record the development of atopic dermatitis and to study the influence of cord blood IgE levels and parental history of atopy. The purpose of this study was to determine whether cord blood IgE and atopic parental history predict the development of early-onset atopic dermatitis.

MATERIALS AND METHODS

MATERIALS

A cohort of 411 (90%) cord blood values was obtained from the 456 newborns born in three Taichung obstetric departments during the period from January 1 to December 31, 2002. Cord blood was collected immediately after birth and total IgE levels were determined using the CAP system (Pharmacia, Uppsala,

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Sweden). The standard calibration curve had an upper limit of 100 kU/L and a detection limit of 0.35 kU/L. Parental history of atopy was also taken and defined by personal questionnaire reports of asthma, rhinitis, or atopic dermatitis (including typical atopic dermatitis, urticaria and food allergy) appearing before puberty and verified at least once by a physician.

Assessment of the infants for atopic dermatitis was done at 1, 3, and 6 months of age. The definition of atopic dermatitis has great variation. In our study, we adopted the criteria modified for diagnosis of atopic dermatitis in infants of Sampson,²⁰ and the diagnosis of atopic dermatitis was based on a combination from three different sources of information: the diagnosis made by the examining doctor, the examining doctor's opinion on reported relevant symptoms, and the reported diagnosis by the another physician.

At the beginning of this study, prematures and newborns with major health problems were excluded. Finally, 379 (83%) infants had complete the data after 6 months.

Statistical methods

Cord blood IgE was evaluated as a risk factor for atopic dermatitis by computing odds ratios (ORs) as a measure of association between the outcome variables and the dichotomized cord blood IgE at different cut-off points (0.5 and 0.9 kU/L). Approximate Cornfield's 95% confidence intervals (95% CI) for the odds ratios were computed.

For the evaluation of cord blood IgE as predictor of atopic dermatitis, the dichotomized cord blood IgE was regarded as a diagnostic screening test for the outcome variables. Specificity was the proportion of healthy patients who were correctly classified as negative. Sensitivity was the proportion of patients with disease

who were correctly classified as positive. Positive predictive value was the proportion of true test-positive patients among all test positive results.

For statistical computations, we used SPSS for Windows, Version 12.0.

RESULTS

Occurrence of atopic dermatitis

Of the 456 families potentially eligible for inclusion in the study, cord blood was obtained and tested from 411 newborns (90%). At the end of follow up, 379 infants (83%) had complete data for evaluation. The demographic characteristics of study subjects are listed in Table 1. The cumulative incidence of atopic dermatitis over the 1st, 3rd and 6th months of life amounted to 5.0%, 8.2% and 14.0%, respectively.

Cord blood IgE as a risk factor and predictor

When the cutoff value for cord blood IgE was set at 0.5 kU/L, there was a significant association between elevated cord blood IgE level and atopic dermatitis at 1, 3 and 6 months of age (odds ratio [OR]: 2.70, 95% confidence interval [CI]: 1.06-6.85; OR: 2.95, CI: 1.40-6.21; OR: 3.04, CI: 1.67-5.53); when the cutoff value was set at 0.9 kU/L, the association was only found at 3 months of age (OR: 2.32, CI: 1.01-5.30) (Table 2). Also, elevated cord blood IgE was shown to be a relatively specific, but non-sensitive predictor of atopic dermatitis in infant (Table 5). The maximum positive predictive value of 25% was achieved with the cut-off point set to 0.5 kU/L at the age of 6 months.

Parental atopic history as a risk factor and predictor

Table 3 shows that there was only a significant

Table 1. Demographic Characteristics of Study Subjects

	Number	Percentage (%)
Total subjects*	379	
Male gender	196	51.7
Weeks of gestation, mean $\pm$ SD	39.4 $\pm$ 1.7	
Birth weight (grams), mean $\pm$ SD	3384 $\pm$ 425	
Maternal age (yr), mean $\pm$ SD	28.6 $\pm$ 4.2	
Cord IgE $\geq$ 0.5kU/L	99	26.1
Cord IgE $\geq$ 0.9kU/L	51	13.5
Positive maternal atopic history	107	28.2
Positive paternal atopic history	61	16.1

*A cohort of 411 cord blood values was obtained at the beginning, and 379 infants completed the study after 6 months.

Table 2. Cumulative Incidence of Atopic Dermatitis at Different Ages by Different Cut-off Value of Cord IgE

	Atopic Dermatitis			
	Number	%	OR	95CI
1 m/o				
Cord IgE ≥ 0.5 kU/L	9	2.4	2.70	1.06-6.85
Cord IgE ≥ 0.9 kU/L	5	1.3	2.44	0.84-7.09
Total subjects	19	5.0		
3 m/o				
Cord IgE ≥ 0.5 kU/L	15	4.0	2.95	1.40-6.21
Cord IgE ≥ 0.9 kU/L	9	2.4	2.98	1.29-6.90
Total subjects	31	8.2		
6 m/o				
Cord IgE ≥ 0.5 kU/L	25	6.6	3.04	1.67-5.53
Cord IgE ≥ 0.9 kU/L	9	2.4	1.38	0.63-3.04
Total subjects	53	14.0		

OR: odds ratio; 95CI: 95% confidence interval.

Table 3. The Association between Cumulative Incidence of Atopic Dermatitis and Parental Atopic History

	Atopic Dermatitis			
	Number	%	OR	95CI
1 m/o				
Maternal atopic history	10	2.6	3.01	1.19-7.64
Paternal atopic history	4	1.1	1.42	0.45-4.43
Total subjects	19	5.0		
3 m/o				
Maternal atopic history	12	3.2	1.68	0.79-3.60
Paternal atopic history	6	1.6	1.28	0.50-3.26
Total subjects	31	8.2		
6 m/o				
Maternal atopic history	20	5.3	1.67	0.91-3.06
Paternal atopic history	8	2.1	0.92	0.41-2.05
Total subjects	53	14.0		

OR: odds ratio; 95CI: 95% confidence interval.

association with atopic history of the mother at 1 month (OR: 3.01, CI: 1.19-7.64). This provided a specificity of 73% and a sensitivity of 53% for prediction of atopic dermatitis (Table 5). There was no correlation between paternal history and atopic dermatitis. Therefore an evaluation of the predictive capability of paternal history with regard to atopic dermatitis could be omitted.

Cord blood IgE >0.5 kU/L and maternal atopic history as a risk factor and predictor

The preceding analyses showed that elevated cord

blood IgE was a better predictor of atopic dermatitis when the cut-off point was set at 0.5 kU/L. Only maternal history of atopy was positively associated with atopic dermatitis. Combining these two risk factors substantially increased the association with atopic dermatitis (Table 4). This also provided a higher specificity but a lower sensitivity for prediction of early onset atopic dermatitis (Table 5). The positive predictive value increased slightly and its maximum value reached 30% at 6 months of age.

Table 4. The Association between Cumulative Incidence of Atopic Dermatitis and Cord IgE ≥ 0.5 kU/L with Positive Maternal Atopic History

	Atopic Dermatitis			
	Number	%	OR	95CI
1 m/o				
Cord IgE ≥ 0.5 kU/L + Positive maternal atopic history	5	1.3	4.79	1.60-14.36
3 m/o				
Cord IgE ≥ 0.5 kU/L + Positive maternal atopic history	6	1.6	3.24	1.21-8.66
6 m/o				
Cord IgE ≥ 0.5 kU/L + Positive maternal atopic history	9	2.4	2.97	1.28-6.90

OR: odds ratio; 95CI: 95% confidence interval.

DISCUSSION

Hamburger et al. (1974) first observed that cord blood IgE was a risk factor and predictor of allergic disease in the infant.²¹ In previous studies, varying cutoff points for cord blood IgE have been used,^{13,22-25} and the optimal cutoff value is difficult to ascertain. The results of data from different studies are still controversial, but there is a general agreement that a high cord blood IgE level is associated with later atopic disease. Cord blood IgE ≥ 0.5 and 0.9 kU/L have been used as effective thresholds for atopic disease.²³⁻²⁵ In our studies, cord blood IgE ≥ 0.5 kU/L, as a risk factor of atopic dermatitis, was superior to cord blood IgE ≥ 0.9 kU/L. This may reflect our study being on a small subjects followed over a short period. Cord blood IgE ≥ 0.9 kU/L was less reliable because of the small number of infants (for example, IgE ≥ 0.9 kU/L and atopic dermatitis: $n = 5$). Furthermore, low positive predictive value (PPV) of elevated cord blood IgE makes cord blood IgE determinations unuseful for general screening test.

Many studies have reported that maternal, but not paternal, atopic history was positively associated with elevated cord blood IgE or atopic disease.^{11,26,27} We found a similar condition for atopic dermatitis at one month of age. Perhaps this apparent difference in the influence of maternal vs. paternal allergic disease history is that atopic mothers may transplacentally pass allergens or cytokines, which stimulate T-cell response in uterus and result in increasing rate of the prevalence of early-onset atopic dermatitis. Another possibility is that this may be an example of 'Carter effect'.²⁸ The Carter effect had been demonstrated for asthma and atopic dermatitis.²⁹ Affected mothers may have inherited more genes and therefore have a stronger transmission to their children.

Furthermore, the effect of maternal atopic history on atopic dermatitis seen only at 1 month was lost by 3 and 6 months of age in our study. We suggest that environmental factors play a more important role in the development of atopic dermatitis after 3 months of age. Method of feeding,^{10,19,30} passive smoking,^{22,31} and early exposure to air pollutants and indoor allergens,^{19,32} etc. can significantly affect the development of atopic dermatitis. Furthermore, the accuracy and reliability of parental atopy history should be of concern because the current standard for reporting parental atopic history is by self-report and inquires only about the presence of current or ever-doctor-diagnosed disease. Presumably, such imprecise classifications can result in biased estimates of prognosis and risk factors.

For the recommendation of prevention measures, the positive predictive value is especially important. Tariq et al. reported that cord IgE was better than family history for predicting allergen sensitization and the predictive capacity could be further increased by combining cord IgE with parental atopy.²⁵ Our analysis demonstrated a similar but much weaker result in predicting the development of atopic dermatitis. The predictive performance of the combination of cord blood IgE ≥ 0.5 kU/L and maternal atopic history was poor with regard to atopic dermatitis, although a positive association existed. Some factors can lead to predictive uncertainty of cord blood IgE and parental atopic history. Reporting biases and systematic misclassification of family history are frequently criticized. In our study the information was collected retrospectively and recall bias was suspected. Second, questionnaires used to assess parental atopy are usually by mothers and hence may misclassify paternal symptoms. Third, seborrheic dermatitis, vasomotor rhinitis, and intrinsic asthma are

often misinterpreted to be atopic diseases.

There is no doubt that elevated total IgE levels are positively associated with atopic disease, but both genetic and environmental risk factors play a role in determining the level of IgE in cord blood. The gestational age, month of birth, birth order and gender of infants, prenatal exposure, and maternal atopic history or IgE levels influence the fetal immune system and affect cord blood IgE levels.^{7,22,27,33-35} The influence of environmental factors such as method of feeding,^{10,19,30} exposure to household pets^{19,32} and passive smoking,^{22,31} is also associated with the development of atopic dermatitis and may contribute to the predictive uncertainty of cord IgE and parental history. These risk factors have been studied in some detail. However, the complex interaction of these and other genetic and environmental factors needs further research.

We conclude that the predictive capacity of maternal history and cord blood IgE was not high enough to recommend them as screening instruments for primary prevention, although a significant association exists. Decreasing allergic activities and avoiding allergens during pregnancy may be the most important means of preventing offspring from having atopic dermatitis.

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