



Original research article

Risk factors for and expression of immune and inflammatory factors in atopic dermatitis in Chinese population: A birth cohort study

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ABSTRACT

Objective: To explore the risk factors for atopic dermatitis (AD) and disclose the relationship between immune inflammatory factors (Immunoglobulin E (IgE), interleukin (IL)-4, IL-18) and the prevalence of AD in a Chinese population.

Methods: To evaluate the risk factors for infant AD, a total of 921 mother-newborn pairs were recruited through a questionnaire survey conducted during 2009–2011. Venous blood was collected from the mothers during birth hospitalization and umbilical cord blood was collected during delivery. Thirty-five infants with AD paired with their mothers served as the patient group. Thirty-five non-AD pairs were selected randomly and were used as the control group. Enzyme-linked immunosorbent assay (ELISA) was performed to detect the levels of IgE, IL-4, and IL-18. The relationship between the prevalence of AD and the levels of IgE, IL-4, and IL-18 was analyzed. The risk factors for allergy were assessed in IgE positive cases.

Results: Family income, parental history of atopy, age of menarche, performing housing renovation before pregnancy, instance of a virus infection during pregnancy, and calcium supplementation during pregnancy were potential factors determining the incidence rate of infant AD. Compared with the control group, the AD patient group showed higher levels of IgE and IL-4 in both the maternal serum and umbilical cord blood ($P < 0.01$). In the cases with AD, IL-8 was increased only in the maternal serum ($P < 0.01$). In addition, the allergens dust mite, mugwort pollen, and mycete spores were risk factors for the incidence of IgE-positive AD.

Conclusion: IgE and IL-4 levels in the maternal serum and umbilical cord blood as well as IL-18 level in the maternal serum are related to the occurrence of childhood AD. Potential factors for infant AD include family income, parental history of atopy, age of menarche, housing renovation before pregnancy, virus infection, and calcium supplementation during pregnancy.

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1. Introduction

Atopic dermatitis (AD), also known as atopic eczema, is a type of skin inflammation, characterized by itchy, red, swollen, and cracked skin. Typically, AD initiates in childhood and progresses with varying degrees of severity over the years [1,2]. In children under one year of age, much of the body may be affected. Scratching worsens symptoms, and the patients have an increased risk of skin infections. AD patients also have complications, such as asthma,

allergic rhinitis, and hay fever.

The causes of AD are not completely clear but are believed to involve genetic factors, immune system dysfunction, environmental exposures, and difficulties with the permeability of the skin [1,2]. From a genetic point of view, when one twin is reported to have AD, the other twin has a high chance of developing AD [3]. Environmental factors also affect the development of AD [4]. Persons who live in cities and dry climates are more commonly affected by the disease [5]. The contact with allergens, such as pollen, dust, etc., is also related to AD incidence [6]. Additionally, emotional stress may also exert an impact on the development of AD [7]. Therefore, a systematic analysis of risk factors for AD occurrence is urgently required.

The diagnosis of AD is commonly based on the signs and

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symptoms manifested. Other diseases that need to be excluded before making a diagnosis are contact dermatitis, psoriasis, and seborrheic dermatitis [2]. Reportedly, the levels of immune and inflammatory factors are considerably altered in the serum of AD patients. The results of a study showed that the concentration of IgE in neonatal umbilical cord blood can be used to predict the occurrence of AD [3]. Furthermore, the levels of IgE, IL-4, and IL-18 were identified as risk factors for AD [8]. However, there are no publications elucidating whether those immune inflammatory factors are associated with AD incidence in a Chinese population. Herein, a birth cohort study is reported that was carried out in a Chinese population to evaluate the risk factors for AD and establish the association between AD and the levels of IgE, IL-4, and IL-18 in both maternal serum and neonatal umbilical cord blood serum.

2. Materials and methods

2.1. Patients

Pregnant women who had their antenatal examinations and deliveries in Tianjin First Central Hospital (Nankai, Tianjin, China) and Tianjin Center of Obstetrics and Gynecology Hospital between January 2009 and January 2011 were recruited to establish a birth cohort. Questionnaires were distributed to those pregnant women. All participants in this study signed informed consent, and all experiments were conducted after the approval of the Ethics Committee of the Tianjin First Central Hospital and Tianjin Center of Obstetrics and Gynecology Hospital.

2.2. Questionnaires

Questionnaire content included children's gender, family information of the children, family income, etc. The analyzed data of the questionnaires are presented in Table 1. Housing renovation was defined by referring to the literature [9]. Venous blood (2 mL) was collected from the pregnant women, and umbilical cord blood (2 mL) was collected during the infant delivery. Telephone follow-ups to the parents were made at the two time points: 12 and 24 months after the baby's birth.

The children who had itches or a skin rash in an itchy area were invited to the clinic and examined by dermatologists. The levels of IgE, IL-4, and IL-18 in the maternal serum and neonatal umbilical cord blood were determined by ELISA method. Non-AD mother-newborn pairs served as the control group.

2.3. AD diagnostic criteria

During the follow-up at the 12th and 24th months, AD was confirmed by the Williams diagnostic criteria [10] with a minor modification. The child was diagnosed with AD when both the first item and any one item within the range 2–5 were fitted (Table 1). The revised diagnostic criteria were more suitable to the population in China [11]. Venous blood was collected from the mothers during birth hospitalization, and umbilical cord blood was collected from the newborns at birth. Thirty-five infants with AD paired with their

mothers served as the patient group, while 35 infants without AD paired with the mothers were selected randomly and served as the control group. All patients and matched controls were from the Han Chinese population.

2.4. Measurement of total IgE level

Total IgE was detected by ELISA following the instruction of the kit manufacturer (Diacclone Research Company, French). A wavelength of 450 nm was used for determination of IgE level. Values higher than 165 IU/mL were considered IgE-positive.

2.5. Measurement of specific IgE level

We used Western blot to detect serum IgE levels. Ingested and inhaled allergens were analyzed. The inhaled allergens included dust mites, house dust, ragweed pollen, Artemisia pollen, mold, poplar pollen, willow, elm, cat hair, dog dander, cockroaches, and *Humulus scandens*. Crab, shrimp, marine and freshwater fish, egg, peanut, soybean, beef, and mutton constituted the ingested allergens. The measurement of IgE was based on the instructions detailed on the assay kit. A sample was regarded as allergen-positive at an IgE concentration higher than 0.35 IU/mL.

2.6. Determination of IL-4 and IL-18 levels

The levels of IL-4 and IL-18 were detected via ELISA at a wavelength of 450 nm following the instructions of the kit manufacturer (DiaccloneResearch Company, French).

2.7. Statistical analysis

Statistical analyses were performed using SPSS version 19. The prevalence of AD was calculated using the chi-square test. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by logistic analysis. Data are presented as the mean \pm standard deviation. The *t*-test was utilized to analyze the difference between the two groups. A *P* value less than 0.05 was considered statistically significant.

3. Results

3.1. Risk factors for atopic dermatitis

A total of 1215 questionnaires were distributed to the pregnant women, and 1208 effective questionnaires were collected, accounting for a response rate of 99.42%. A small number of the cases ($n = 287$) were excluded due to delivery in other hospitals, delivery after less than 32 completed weeks of gestation, and loss of follow-up. Finally, a total of 921 cases completed the study. According to Williams's diagnostic criteria of AD, 35 children were diagnosed with AD 24 months after birth. Among them, 19 cases were male and 16 cases were female. The prevalence of AD was 3.80%. Five of the 35 AD mothers had AD history, three had asthma history, and five had allergic rhinitis history. Among them, AD prevalence rate

Table 1
Questions for the diagnosis of AD.

Questions for the follow-up:	
1.	Whether pruritus often appears on child skin?
2.	Whether itchy skin disease often occurs in the back of neck, bilateral elbow, and knee?
3.	Whether children and parents have any other history of allergic disease?
4.	Is there a rash in your child's back of neck, bilateral elbow, and knee?
5.	Has the child's skin been dry ever?

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