Original Research Paper

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Association of Atopy and Allergic Diseases with Idiopathic Nephrotic Syndrome

Medical Science

KEYWORDS : atopy, allergic diseases, skin prick test, idiopathic nephrotic syndrome

Ika Citra Dewi Tanjung	Department of Child Health, Faculty of Medicine, University of Sumatera Utara/ Haji Adam Malik Hospital, North Sumatera, Indonesia
Lily Irsa	Department of Child Health, Faculty of Medicine, University of Sumatera Utara/ Haji Adam Malik Hospital, North Sumatera, Indonesia
Muhammad Ali	Department of Child Health, Faculty of Medicine, University of Sumatera Utara/ Haji Adam Malik Hospital, North Sumatera, Indonesia
Rita Evalina	Department of Child Health, Faculty of Medicine, University of Sumatera Utara/ Haji Adam Malik Hospital, North Sumatera, Indonesia
Oke Rina Ramayani	Department of Child Health, Faculty of Medicine, University of Sumatera Utara/ Haji Adam Malik Hospital, North Sumatera, Indonesia

ABSTRACT

Background *Allergic diseases such as atopic dermatitis, allergic rhinitis and bronchial asthma is a hypersensitivity reaction and its related with atopy. Idiopathic nephrotic syndrome can be precipitated by allergic reactions either aeroallergens or food allergens.*

Objective *This study was performed to determine the association between atopy and allergic diseases with idiopathic nephrotic syndrome in Eastern countries, Indonesia.*

Methods *A cross sectional study has been conducted on 27 children with idiopathic nephrotic syndrome between September 2012 and May 2014 in Haji Adam Malik Hospital, North Sumatera, Indonesia. Atopy was diagnosed based on trace card Indonesian Pediatric Society Allergy Immunology working group and positive skin prick test, and allergic diseases was diagnosed based on ISAAC phase I questionnaires. The diagnostic criteria for idiopathic nephrotic syndrome based on the International Study of Kidney Diseases in Children. Associaton of atopy and allergic diseases with idiopathic nephrotic syndrome were analyzed using Fisher's exact test.*

Results *Of the 27 children in our study, 20 were males with mean age 8.9 years old. Atopy was found in 19 children and allergic diseases was found in one children. The most common allergen that found in idiopathic nephrotic syndrome was house dust mites. Atopy and allergic diseases were not associated with idiopathic nephrotic syndrome (P= 1.000 and P= 0.370, respectively).*

Conclusion *There was no association between atopy and allergic diseases with idiopathic nephrotic syndrome. Further research is needed to confirm the association between atopy and allergic diseases with INS in developing countries.*

Introduction

Idiopathic nephrotic syndrome is the most frequent glomerular disease in children. It has a well-recognized association with atopy for the last 60 years and subsequently, various studies have described a higher incidence of allergic disorders such as asthma, allergic rhinitis, and atopic eczema in children with INS.[1]

Idiopathic nephrotic syndrome can be precipitated by allergic reactions, either aeroallergens (pollens, mold and dust) or food allergies.1 Other study reported that children with steroid sensitive INS had asthma and allergic rhinitis about three times more often and atopic dermatitis ten times more often than the general population.2

These findings have raised the possibility that atopy may have a role in the pathogenesis of INS and allergens could be the triggering factor in the development of

proteinuria. However, the exact frequency of atopy and allergic diseases related to INS has varied in many countries. There is ample evidence that the pattern of atopy and allergic disease related to INS in Eastern countries such as Indonesia is different from that in Western countries. The aim of the study was to determine the association between atopy and allergic diseases with INS children (infrequent and frequent relaps) in North Sumatera, Indonesia.

Methods

A cross sectional study was conducted in the Pediatric Allergy Immunology and Nephrology Outpatient Unit and Inpatient Unit Haji Adam Malik General Hospital Medan, between September 2012 and May 2014.

Subjects in this study were children aged under 18 years old that diagnosed with INS in remission phase. Not taking medications containing steroids orally or applied to the skin prick test (SPT) area for 24 hours and antihistamine for three days before SPT examination. The subjects excluded if found dermatographism, refuse performed SPT and the questionnaire data are not filled completely.

Subjects were collected with consecutive sampling. Informed consent was obtained from all parents and from older children (adolescents). The history and physical examinations were obtained for each patient to evidence an infections or allergic illness immediately preceding or accompanying the diagnosis of INS.

The clinical criterias of INS was based on the International Study of Kidney Diseases in Children (ISKDC). Relapse was defined as increased urinary protein excretion (Albustix ≥2+ for at least 3 consecutive days or > 40 mg/m2 per hour) and serum albumin ≤25 g/l. Remission was defined as serum albumin ≥35 g/l and normal protein excretion (Albustix trace or negative for at least 3 consecutive days or <5 mg/m^2

per hour). Infrequent relapses was defined as relapses less than two times within six months after initial response or less than four times within one year. Frequent relapses was defined as two or more relapses within six months after initial response or four or more relapses within one year.[3,4]

Allergic diseases were diagnosed based on The International Study of Asthma and Allergies in Childhood (ISAAC) phase I questionnaires. The core questionnaires were used to obtain atopic dermatitis, allergic rhinitis and bronchial asthma.5 Atopy was diagnosed based on trace card of Indonesian Pediatric Society Allergy Immunology working group and positive SPT. The trace card of Indonesian Pediatric Society Allergy Immunology working group was used to assess risk factors for allergies in the family based on the presence or absence of allergic symptoms in one or more family members. Family members are father, mother or siblings. Low risk factors for allergies when family values was zero, moderate when family values one to three and high when family values four to six.

The skin prick test (SPT) extracts was manufactured by Pharmaceutical Installation of General Hospital Center dr.Soetomo,Surabaya Indonesia for the following two categories of allergens: two inhaled allergens (house dust mites and chicken dander) and eight food allergens (vistin, crabs, shrimps, cow's milk, chicken, chocolate, peanuts and white eggs). A histamine 1% solution was used as positive control and a coca filtra solution was used as negative control.

Skin prick test was done by introduction of a very small of allergens extracts on the epidermis volar forearm. A positive SPT was defined as a wheal diameter at least 3 mm or greater than negative control (coca filtra) after 15-20 minutes. Adrenalin (1:1 000) was available when we performed SPT in anticipation of anaphylaxis reactions.

The implementation and assessment of SPT were performed by doctors that blind about patient's clinical history. Informed consent was obtained from the parents prior to SPT, and this study was approved by the Ethics Committee of Medical Faculty University of North Sumatera, Indonesia.

The data were analyzed with SPSS for Windows program 17.0 version. Statistically significant at $P < 0.05$, means and SDs of age, body weight and body height were analyzed. Fisher's exact test was used to determine the association between atopy and allergic diseases with INS.

Results

The study was conducted in 27 children with INS that fulfill the inclusion and exclusion criterias. Frequent relapses idiopathic nephrotic syndrome was more common than infrequent relapses. Aged range of samples was from three years old until 18 years old (median eight years old) and mean age was 8.9 years old. There were 20 boys and seven girls. Mean body weight was 26.1 kg and mean body height was 122.1 cm. Atopy was found in 19 children, whereas allergic diseases was found in one children.(**Table 1**)

Table 1. Samples characteristics

Characteristics	N=27
Diagnose of INS	
Frequent relapses	17
Infrequent relapses	10
Age, mean (SD), years	8.9 (4.02)
Sex, n	
Male	20
Female	7
Body weight, mean (SD), kg	26.1 (11.08)
Body height, mean (SD), cm	122.1 (19.37)
Atopy	
Yes	19
No	8
Allergic diseases	
Yes	1
No	26
Risk factors for allergy	
Low	15
Moderate	12
High	0

In our study, the most common positive allergen sensitization to house dust mites was found in 13 children, and chocolate was found in 11 children (**Figure 1**).

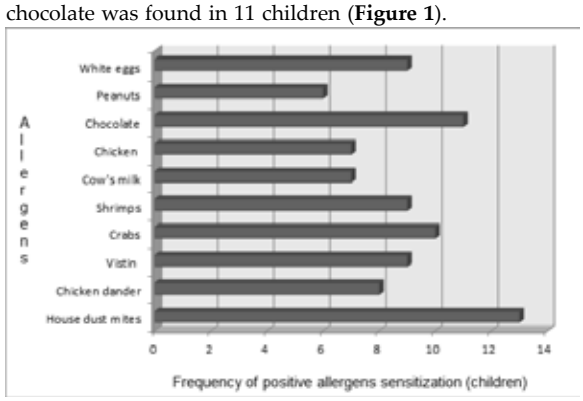

Figure 1. Frequency of positive allergen sensitization

Allergic diseases was found in one children, namely atopic dermatitis and allergic rhinitis. Statistical analysis showed there was no significant association between atopy and allergic diseases with INS (**Table 2**).

Table 2. Association between atopy and allergic diseases with INS

Variable Frequent relapses (n=17)		INS Infrequent relapses (n=10)		P
Atopy				
Yes		12	7	1.000
No		5	3	
Allergic diseases				
Yes	0		1	0.370
No	17		9	

Discussion

Idiopathic nephrotic syndrome is the most frequent glomerular disease in children with the immune system seems to play a critical role in the active phase, through disturbances involving several cell subsets, mainly T cells.6 Many previous study have focused on the relationship between NS and atopy in different populations.7,8 In our study, atopy was diagnosed based on trace card of Indonesian Pediatric Society Allergy Immunology working group and positive SPT in 27 children with steroid sensitive INS. We found the most common risk factors for allergy in this population was low (15/27), whereas the prevalence of atopy based on positive SPT was higher, affected more than half of subjects (19/27).

Atopy was most common found in children with frequent relapses NS compared with infrequent relapses. Our results was higher than previous studies. The prevalence of atopy related with INS was range between 42% and 48.6%.7,8 Atopy was more common found in steroid sensitive compared to steroid resistant.8 Higher prevalence in our study may caused by the differences of daily life.

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Previous study showed incidence of allergic diseases such as asthma, allergic rhinitis and atopic dermatitis was higher in steroid sensitive NS.9 Data from many studies showed that symptoms of allergic diseases such as atopic dermatitis, allergic rhinitis and bronchial asthma was higher in INS. Bronchial asthma, and allergic rhinitis were more often than atopic dermatitis.7,10,11 In our study, although the prevalence of atopy was higher, clinical signs of allergic diseases was found in one children based on ISAAC phase I questionnaire.

Inhaled allergens triggering relapses of MCNS have been suggested by anecdotal reports. The list of triggering aeroallergens includes tree and grass pollens, mold, house dust that identified by skin prick test. Food allergens as triggering factors in the pathogenesis of INS, also have been suggested based on case reports. These allergens identified by positive SPT or radioallergosorbent test (RAST) results for cow's milk, chicken, gliadin or ovalbumin.1 In this study, allergen sensitization using skin prick test with 10 allergens, consists of two inhaled allergens and eight food allergens. Of the 19 INS childhood with atopy, we found all of them sensitized with one or more allergens.

The most common positive allergen sensitization was house dust mites in 13 children and chocolate in 11 children. Our study results was similar with other studies. The most common specific IgE antibodies were directed against house dust mites, milk, and grass pollen mix. 8,12,13 This might occurs due to house dust mites was the most common aeroallergen that found in people daily activities.

Allergen-specific IgE was not done in this study, thus relation between SPT and specific IgE is unknown. However, SPT was used to diagnose atopy and this examination was cheap, minimally invasive and quickly results. We did not examine of serum IgE levels and immune mediators that involved with allergy or INS process, thus the association between atopy and allergic diseases with diseases activity of INS is unknown. However, the results of this study showed no association between atopy and allergic diseases with INS. It was similar with previous study.[4] This reflected that many immune mechanisms with various stimuli had influence INS, rather than a direct association with atopy or allergic diseases.

Although the pathogenesis of INS remains to be elucidated, immunological disturbance has been implicated in the disease.10 Abnormal T-cells response and Th_2 cytokines are strongly related to the pathogenesis of NS by alter the permeability of the glomerular capillary wall. The signals for IgE synthesis are delivered by IL-4 and IL-13. In relapse NS, activated T-cells increase the secretion of IL-4 and IL-13, which could induce isotype switching in IgE Interleukin 5 (IL-5) also promotes the production of IgE, whereas IFN-γ inhibits the secretion of IgE.[14]

Higher serum IgE levels associated with diseases activity of childhood INS, but did not linked to the pathogenesis.12 Allergic diseases were more common in childhood INS with higher serum IgE levels.14 The elevated serum IgE levels during relapses of steroid sensitive nephrotic syndrome, it might results from upregulation of interleukin 13 (IL-13).4 In addition, increased of serum IL-4 and IL-5 also found. Probably, cytokine activities related to the pathogenesis of INS.[14]

In this study, examination of cytokine and serum IgE levels related to allergy in INS patients was not done. However, we have to consider that other factors may be influential in association between atopy/allergic disease and INS.

Conclusion

There was no association between atopy and allergic diseases with INS. Further research is needed to confirm the association between atopy and allergic diseases with INS in developing countries.

References

1. Hafez MA, Shimada M, Lee PY, Johnson RJ, Garin EH. Idiopathic nephrotic syndrome and atopy : is there a common link? Am J Kidney Dis. 2009; 54:945-53
2. Kanai T, Shiraishi H, Yamagata T, Ito T, Odaka J, Saito T, et. al. Th2 cells predominate in idiopathic steroid-sensitive nephrotic syndrome. Clin Exp Nephrol. 2010; 14:578-83
3. The International Study of Kidney Disease in Children. Primary nephrotic syndrome in children: clinical significance of histopathologic variants of minimal change and of diffuse mesangial hypercellularity. Kidney Int. 1981; 20:765-71
4. Cheung W, Wei CL, Seah CC, Jordan SC, Yap HK. Atopy, serum IgE, and interleukin-13 in steroid-responsive nephrotic syndrome. Pediatr Nephrol. 2004; 19:627-32
5. Asher MI, Keil U, Anderson HR, Beasly R, Crane J, Martinez F, et. al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur Respir J. 1995; 8:483-91
6. Zhang SY, Audard V, Fan Q, Pawlak A, Lang P, Sahali D. Immunopathogenesis of idiopathic nephrotic syndrome. Nephrol. 2011; 169: 94-106
7. Tenbrock K, Schubert A, Stapenhorst L, Kemper MJ, Gellermann J, Timmermann K, et. al. Type I IgE receptor, interleukin-4 receptor and interleukin- 13 polymorphisms in children with nephrotic syndrome. Clin Sci. 2002; 102:507-12
8. Salsano ME, Graziano L, Luongo I, Pilla P, Giordano M, Lama G. Atopy in childhood idiopathic nephrothic syndrome. Acta Pediatr. 2007; 96:561-6
9. Asmaningsih N, Poernomo W, Noer MS. Serum immunoglobulin E levels in children with idiopathic nephrotic syndrome. Paediatr Indones. 2005; 45:55-9
10. Ikeuchi Y, Kobayashi Y, Arakawa H, Suzuki M, Tamra K, Morikawa A. Polymorphisms in interleukin-4 related genes in patients with minimal change nephrotic syndrome. Pediatr Nephrol. 2009; 24:489-95
11. Roy RR, Islam MR, Matin A, Khan R, Muinuddi G, Rahman MH, et. al. Relationship of childhood idiopathic nephrotic syndrome with asthma, hypertension, complement C3, urinalysis. Bangladesh J Child Health. 2011; 35:11-5
12. Tain YL, Chen TY, Yang KD. Implication of serum IgE in childhood nephrotic syndrome. Pediatr Nephrol. 2003; 18:1211-5
13. Toyabe S, Nakamizo M, Uchiyama M, Akazawa K. Circannual variation in the onset and relapse of steroid sensitive nephrothic syndrome. Pediatr Nephrol. 2005; 20:470-3
14. Youn YS, Lim HH, Lee JH. The clinical characteristics of steroid responsive nephrotic syndrome of children according to the serum immunoglobulin E levels and cytokines. Yonsei Med J. 2012; 53:715-22