

# The inverse association between serum anti-streptolysin-O titers and the frequency of exacerbations of asthma in childhood

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## SUMMARY

**Background:** the decline in infections in childhood may contribute to the rising severity and prevalence of atopic disorders in developed countries. Support for this hypothesis has been obtained from findings of an inverse association between tuberculin responses and atopy and from findings of high prevalence of asthma in certain islands with low prevalence of respiratory infections. With this regard, we investigated the association between serum anti-streptolysin-O (ASO) titers and the frequency of exacerbations of asthma in childhood.

**Methods:** thirty atopic asthmatic children who has no sign of upper respiratory tract infection at the time of presentation or during the previous two months were included in the study. Serum ASO titer was measured as an indicator of past streptococcal upper respiratory tract infections. ASO titer  $\geq$  200 Todd units was accepted as positive.

**Results:** a statistically significant association is found between high anti-streptolysin-O titers and decreased number of exacerbations in those children.

**Conclusions:** our data suggests that streptococcal infections might be a factor attenuating asthma in childhood.

**Key words:** Asthma. Children. ASO.

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## INTRODUCTION

The prevalence of atopic diseases has been increasing in many parts of the world over the last several decades (1). The decline in infections in childhood are thought to contribute to the rising severity and prevalence of these disorders in developed countries (2). Support for this hypothesis has been obtained from findings of an inverse relationship between occurrence of atopy and the number of siblings (3), from findings of an inverse association between delayed type hypersensitivity to mycobacterium tuberculosis and atopy (4) and from findings of a very high prevalence of asthma in certain islands with low prevalence of respiratory infections (5).

Streptococcal infections are still prevalent in many parts of the world. We had an observation that asthmatic children followed in our outpatients clinic do not experience an exacerbation of their disease while having an streptococcal upper respiratory tract infection. Acting from this point, we aimed to investigate if there is any association between anti-streptolysin-O titers (ASO) and the frequency of exacerbations of asthma in childhood.

## METHODOLOGY

The study is prospectively designed to examine the possible inverse association between streptococcal infections and the frequency of exacerbations of atopic asthma in childhood. All patients met the

**Table I**  
**The characteristics of the ASO [+] and the ASO [-]  
asthmatic groups**

	ASO [+] Asthmatics	ASO [-] Asthmatics	p Value
Mean Age (years) ± SD	9.70 ± 2.90	7.84 ± 2.58	0.0542
Gender (Boy/Girl)	11/6	6/7	0.4601
Elevated Immunoglobulin E Rate (%)	82	92	0.6129
Inhaled Steroid Prophylaxis Rate (%)	59	84	0.2293
Median Exacerbation Number/ Last 12 Months	0.00	1.00	0.0218

American Thoracic Society criteria for asthma (6). Acute exacerbation of asthma is defined as the disease period in which reversible (either spontaneously or with treatment) symptoms like cough, wheezing and/or dispnea had been present.

Thirty atopic asthmatic children who had no sign of upper respiratory tract infection at the time of study and during the previous two months were included in the study. The ages, gender, immunoglobulin level, present asthma therapy (having inhaled steroid prophylaxis or not) and the number of acute exacerbations of asthma that had been experienced during the previous 12 months was recorded for each patient. Serum ASO titer was measured in every patient with agglutination method (RapiTex ASL, Behring) as an indicator of past streptococcal upper respiratory tract infections. The patients having ASO titer greater than or equal to 200 Todd units were accepted as ASO positive.

The patients were then divided into two groups, as ASO [-] and ASO [+] asthmatics. These two groups were compared with Mann Whitney U Test for their ages and the number of acute exacerbations. The ratio with respect to gender and inhaled steroid prophylaxis were compared with Fisher's Exact Test.

## RESULTS

The median age for ASO (+) asthmatic children was 10.00 years (Mean ± Standard Deviation (SD): 9.70 ± 2.90, Range: 4.83-14.58). There were 11 boys, 6 girls. Fifty nine percent of children were having inhaled steroid prophylaxis. The median number of acute exacerbations experienced in the last 12 months was 0 (Mean ± SD: 0.76 ± 1.20, Range: 0-4) (table I).

The median age for ASO (-) asthmatic children was 7.67 years (Mean ± SD: 7.84 ± 2.58, Range: 4.75-13.92). There were 6 boys, 7 girls. Eighty four percent of children were having inhaled steroid prophylaxis. The median number of acute exacerbations experienced in the last 12 months was 1 (Mean ± SD: 1.61 ± 1.21, Range: 0-4) (table I).

There was no significant difference between ASO (+) and ASO (-) asthmatics with respect to age, gender and inhaled steroid prophylaxis ( $p = 0.0542$ , 0.4601 [Odd's Ratio: 2.139], 0.2293 [Odd's Ratio: 3.850] respectively). However as they were compared for the number of acute exacerbations of asthma during the last 12 months, the ASO (-) asthmatics were found to experience significantly more acute exacerbations than the ASO (+) asthmatics ( $p = 0.0218$ ) (table I).

## DISCUSSION

Several findings support the concept that atopic diseases result from TH2 dominated responses to environmental allergens (7). The hypothesis that infections may inhibit development of atopy postulates that infectious agents such as viruses and intracellular bacteria preferentially stimulate the development of TH1 type immunity (8). Interferon-gamma which is an important part of the TH1 response can suppress the TH2 responses characteristic of atopy. With this regard an inverse association has been shown between atopy and Mycobacterium tuberculosis (4), hepatitis A infection (9), measles (8).

It has been shown that purified group A streptococcal super antigens are potent inducers of inflammatory (TH1) cytokines (10). Streptococcal pyrogenic exotoxin type C (SPE-C) is a member of the bacterial super antigens that are potent stimulants of T cells (11). In 1996, in an *in vitro* study, Ohara et al showed that SPE-C raised the messenger-RNA (m-RNA) level of type 1 helper T cells related cytokines, such as Interferon-gamma, IL-2 and TNF. Consistent with the mRNA accumulation, protein concentrations of Interferon-gamma, IL-2 and TNF were increased in SPE-C stimulated peripheral blood mononuclear cells but IL-4 was not (11).

After our clinical observation that asthmatic children experiencing a group A streptococcal upper respiratory tract infection generally do not present with acute asthma attack simultaneously, we decided to investigate the possible inverse association that may exist between serum ASO titers and number of asthma exacerbations experienced in the past. We demonstrated a statistically significant

association between high ASO titers and less acute exacerbations in children with asthma.

We can speculate that by stimulating T-helper 2 type cytokines such as interferon-gamma and interleukin-2, streptococcal antigens could protect against development of exacerbations in asthma. The results of this preliminary report warrants other studies with a larger number of children along with the measurements of relevant cytokines in order to improve the understanding the mechanism of a probable protective role of streptococcal antigens.

## RESUMEN

**Fundamento:** la disminución de las infecciones en la infancia puede contribuir a aumentar la gravedad y prevalencia de los trastornos atópicos en los países desarrollados. Esta hipótesis ha sido respaldada a partir de los hallazgos de una asociación inversa entre las respuestas a la tuberculina y la atopía y a partir de los hallazgos de una alta prevalencia de asma en algunas islas con una baja prevalencia de infecciones respiratorias. Partiendo de esta base, investigamos la asociación entre los títulos séricos de antiestrepolisina O (ASO) y la frecuencia de exacerbaciones de asma en la infancia.

**Método:** fueron incluidos en el presente estudio 30 niños con asma atópica sin signos de infección de vías respiratorias altas en el momento de la presentación o durante los dos meses previos. Se determinó el título ASO en suero como indicador de infecciones estreptocócicas previas de las vías respiratorias altas. Se aceptó como positivo un título ASO  $> 0 = 200$  unidades Todd.

**Resultados:** se identificó una asociación estadísticamente significativa entre unos títulos antiestrepolisina O altos y una disminución del número de exacerbaciones en estos niños.

**Conclusiones:** los datos del presente estudio sugieren que las infecciones estreptocócicas pueden ser un factor atenuante del asma en la infancia.

**Palabras clave:** Asma. Niños. ASO.

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