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Pediatrics

A Study on Complement Components (C3, C4) as Inflammatory Markers in Asthma in a Tertiary Care Centre in Eastern Bihar.

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ABSTRACT

Objective: To analyze the serum levels of complement factors C3 and C4 in in a tertiary care centre in asthmatic children in Eastern Bihar.

Methods: In a Case Control Study, Serum levels of the C3 and C4 complement components were assayed in 120 children aged from 2 to 12 years with the diagnosis of bronchial asthma (not in acute attack) and 120 age-and sex-matched healthy controls. All children were subjected to a thorough clinical study, complete blood counts, absolute eosinophil count and serum complements (C3, C4).

Results: In the present study it was found that Serum C3 was significantly higher in asthmatics when compared to controls (140.60 ± 38.80 mg/dl vs 107.70 ± 45.00 mg/dl respectively, (p = 0.01). However, differences in serum C4 levels were not significant (41.30±48.80 mg/dl vs 44.60 ± 39.70 mg/dl respectively, p = 0.69). A significant positive correlation was found between severity of asthma and serum C3 (p=0.02) but not with serum C4.

Conclusions: We observed that Serum levels of C3 are elevated in children with stable asthma in majority of children but not with C4 and there was also a positive correlation between serum C3 and severity of asthma.

KEYWORDS : Children; Complement; Asthma.

INTRODUCTION

Asthma is defined as a chronic inflammatory disease characterized by hyperreactivity of the lower respiratory tract and by variable limitation to airflow, reversible spontaneously or with treatment and manifesting clinically in the form of repeated episodes of wheezing, dyspnea, tight chest and coughing, in particular at night and in the morning on waking.[1] Asthma affects more than 300 million people worldwide [2]and is the most common chronic disease in childhood.

The complement system consists of more than 30 plasma and cell surface proteins that interact with each other and with other immune system components. Its activity is highly regulated and it generates products that destroy infected cells or microorganisms. The products of complement system protein activation have a number of different biological effects. The anaphylatoxins and chemoattractant components C3a, C4a and C5a can contribute to inflammatory processes, recruiting leukocytes, increasing vascular permeability, stimulating bronchoconstriction and causing degranulation of mast cells. Complement system plays an integral role in immune responses of the host. The role of the complement system in asthma has been suggested, possibly through initiation and/or amplification of the inflammatory response in the airways through the complement activation cascade.[3] Some studies have reported increased plasma complement levels especially C3,[4] whereas others have demonstrated no significant changes.[5]

The objective of the present study was to assess the serum levels of two complement factors (C3, C4), in asthmatic children of Eastern Bihar and compare them with those of healthy controls.

MATERIAL AND METHODS

The present case-controlled study was conducted in a tertiary care centre in Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar from June 2008 to January 2017. This study included 120 asthmatic children and 120, age and sex matched healthy controls. Patients aged between 2 to 16yr and diagnosed according to Global Initiative for Asthma Guidelines 2007,[6] were included. Patients who had acute chest infection or other acute inflammations and those who refused to participate in the study were excluded.

Before enrollment in the study, an informed consent was taken from parents/guardians of the children included in the study. The study design conformed to the Revised Helsinki Declaration of Bioethics [7] and was approved by the Scientific Ethical Committee of Department of Pediatrics, Jawaharlal Nehru Medical College and Hospital, Bhagalpur

The investigations performed were: Complete blood counts (CBC), absolute eosinophil count and serum complement factors (C3, C4) using commercial immunokits. Statistical analysis included frequency distributions, percentage distributions, mean ± standard deviation, unpaired student's t test and Spearman's rank coefficients (rho). Calculation of 95% confidence intervals (95% CI) was performed when appropriate. P values less than 0.05 were considered significant.

Table 1. Basic Characteristics of Cases.

CASES (120)	
Age (years)	5.39 ± 3.27
Sex (male/female)	72/48
Residence (urban/rural)	88/32
Onset (years)	1.59 ± 1.12
Duration (years)	3.86 ± 2.85
Atopic manifestations (yes/no)	56/64
Seasonal variation (yes/no)	48/72
Passive smoking (yes/no)	16/104
Family History of Asthma (yes/no)	64/56
SEVERITY OF ASTHMA	
Intermittent	72 (60%)
Mild persistent	40 (33.33%)
Moderate persistent	8 (6.66%)
Severe persistent	0 (0.00%)

Table 2. Comparison of Laboratory Data between Cases and Controls.

	{1}*Cases	{1}*Conrols	{2}*95% CI	p
Total leucocytic count (103 cells/ ml)	6.33 ± 2.41	5.72 ± 1.98	-0.19 to 1.40	0.13
Absolute eosinophilic count (cells/ml)	385 ± 236	221 ± 133	94.06 to 232.80	0.01*
Serum C3 (mg/dl)	140.60 ± 38.80	107.70 ± 45.00	17.73 to 48.10	0.01*
Serum C4 (mg/dl)	41.30 ± 48.80	44.60 ± 39.70	-19.30 to 12.86	0.69

1*: Mean ± standard deviation, 2*: confidence intervals, 0.01:Significant

RESULTS

Table 1 describes the demographic and clinical data of cases. **Table 2** shows a statistically higher absolute eosinophil count in asthmatics. Serum C3 was significantly higher in asthmatics when compared to controls (140.60 ± 38.80 mg/dl vs 107.70 ± 45.00 mg/dl respectively, p = 0.01). However, differences in serum C4 levels were not significant

(41.30 ± 48.80 mg/dl vs 44.60 ± 39.70 mg/dl respectively, p = 0.69). There was a significant positive correlation between severity of asthma and serum C3 (p = 0.02) but not with serum C4.

DISCUSSION

It was detected that there is a significant increase in serum C3 levels in stable asthmatic children when compared to controls. This agrees with previously published works that reported increased C3 levels in asthmatics.[8] This finding suggests a relation between C3 and asthmatic inflammatory process, which might be causal in nature. Anaphylatoxin C3a is generated as a byproduct of complement activation or via breakdown of C3 by β tryptase of mast cells.[9] It has shown to activate mast cells, basophiles and eosinophils and to cause smooth muscle contraction. Following allergen challenge, C3a is generated in the lungs of subjects with asthma but not in healthy subjects.[9] C3a stimulates robust mast cell degranulation, that is greatly enhanced following cell-cell contact with airway smooth muscle (ASM) cells. Therefore, C3a likely plays an important role in asthma primarily by regulating mast cell-ASM cell interaction.[10]

In our study, patients with increasing severity of asthma had higher C3 levels (p =0.02), which is almost similar to the study results of Solomon et al, who reported a positive correlation between plasma C3a and severity of asthma (p = 0.03).[11] With increasing severity of the disease, systemic inflammatory mediators of asthma like tumor necrosis factor-α and interleukin-1 might be exerting a stimulatory effect on the liver to produce larger amounts of C3, which in turn might have augmented the severity of asthma.[12]

Our study did not find a significant difference between serum C4 levels in asthmatic children and the control group (41.30 ± 48.80 mg/dl vs 44.60 ± 39.70 mg/dl respectively, p = 0.69). There was no correlation between C4 levels and severity of asthma. Lack of sufficient studies in the literature, regarding the relation between peripheral C4 levels and asthma, makes it important to recommend larger-scale studies at this point. The limitation of our study is that it is a hospital-based study, so the findings may differ from a community setting.

CONCLUSIONS

We concluded in our study that serum levels of C3 are elevated in children with stable asthma, and there is a positive correlation between serum C3 and severity of asthma. There were no similar observations as regards serum C4. However, further research in this area is still needed. Considering the importance of asthma and its mortality and morbidity, more studies are needed that investigate the role that the complement system plays in the pathology of this disease.

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