

Complement Factor (C3) Level as Marker of Inflammation in Paediatric Asthma

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Abstract

Aim: To assess the serum levels of a complement factors C3 in Indian asthmatic children and compare them with those of healthy controls in order to establish a relationship between the levels of these factors and asthma disease process.

Method: Serum c3 levels of 44 children with acute asthma and 44 controls of the age group of 6-16 years was determined and statistically compared. Lung function tests (FEV1%) was done and correlated with serum c3 levels using Pearson's comparison coefficient.

Results: The mean serum c3 value of cases (138±32.99) is higher than the controls (112.82±14.6), with 32% cases showing higher than normal level of serum C3. Pearson's correlation coefficient reveals negative correlation between FEV1% with serum C3 levels.

Conclusion: This study reveals that serum levels of complement c3 are statistically higher in subjects with asthma as compared to healthy subjects. Further, serum levels of c3 reflect the severity of the disease, with its levels being higher when disease is more severe.

Introduction

Asthma a chronic inflammatory disease of the airway has a complex pathogenesis involving various immune cells, immune mediators and pathways. Amongst them, innate response has been increasingly appreciated in the pathogenesis of asthma, in particular, the involvement of complement in asthma¹⁻³.

Complement is an assembly of proteins found in the blood and body fluids and on cell surfaces. Soluble complement components form the proteolytic cascade, whose activation leads to the generation of complement effectors that target various cells involved in the immune response⁴. It plays an integral role in immune responses of the host and is the innate response of the host to pathogens. Now it has been established that not only does it play a role in innate immunity, it also bridges innate and acquired immunity. However, excess of complement, like the deficiency of it, is deleterious to the host and contributes to the development of disease⁴.

The level of complements such as C3 and C4 is often found to be elevated in many chronic inflammatory diseases such as chronic spontaneous urticarial⁵. 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 cascade⁶. However studies conducted to establish the possible relationship have produced conflicting results.

Hence it becomes important to establish the role of altered c3 levels in asthmatics to enable the use of the same as a diagnostic tool and a parameter to assess asthma control. This study explores the correlation between compliment C3 levels and severity of asthma, measured by FEV1 level.

Aims and Objectives

The aim of the present study was to assess the serum levels of a complement factors C3 in Indian asthmatic children and compare them with those of healthy controls in order to establish a relationship between the levels of these factors and asthma disease process.

Materials and Methods

The case control study was conducted over a period of 6 months (July 2018- December 2018) in Ramaiah teaching hospital on a sample of 88 children aged between 6 to 16 years, 44 cases and 44 controls.

Inclusion criteria- The cases were children with established asthma visiting the outpatient department and the controls were healthy age and sex matched children.

Exclusion criteria- Children with co-existing cardio-pulmonary co morbidities and nutritional deficiencies were excluded from the study.

The high production of C3a fragments results in an increase in total components C3⁶. It is also considered that the quantification of subfractions of complement C3 is expensive, making it difficult applicability in view of the possibility of biomarkers in asthma. For these reasons, serum C3 levels have been chosen for this work.

Informed consent was taken from all the care givers of the patients. Pulmonary function tests to determine FEV1 was performed to determine asthma control status. 3ml of a random sample of blood was collected into a plain vacutainer using all aseptic precautions in the phlebotomy section. It was centrifuged at 4000 rpm for 8-10 minutes. After separation serum samples were stored at -20^o C. c3 and were estimated using immune-electric method.

Frequency distribution, percentage distribution, mean +/-SD, Pearson's comparison co-efficient was calculated with 95% confidence intervals for the comparison of the findings of case and control groups.

Results

The data hence collected was systematically tabulated and analyzed with SPSS software.

The descriptive statistics for the case and control group is as shown in the table 1

The over all levels of serum complement c3 is higher in the case group, with the mean of 138±32.99 among the

Table 1. Descriptive statistics.

	Mean ± SD	
	Controls	Cases
Age (kg)	8.12 ± 2.862	7.41±2.28
BMI (kgm ⁻²)	15.67 ± 1.2	15.66 ± 1.8
Serum C3	112.82 ± 14.6	138.24 ± 32.99
Albumin(mg/dl)	4.292±0.51	4.068±0.45
FEV1%	92.304±7.33	77.884±6.59
FEV1/FVC%	75.49±6.37	69.588±9.98

cases and 112.82±14.6 among the controls. Further, 30% of the cases had above normal values of c3.

On calculation of Pearson's correlation coefficient, the FEV1% of the cases were found to have a negative correlation with c3, r= -0.877, P<0.001. This implies that with rise in FEV1%, the serum c3 levels fall.

Discussion

The data observed in this study show that most patients with atopic intermittent asthma had higher values of complement c3 when compared to the values of healthy children without asthma of the same age group. Further, 32% of the patients with asthma had c3 levels higher than normal range. Even though the mean for the group of children with asthma (cases) is within the normal range, it is higher than the mean amongst the healthy individuals. Furthermore, based on the understanding of the mechanism due to which c3 levels are higher in asthmatics, it can be hypothesized that the level of serum c3 can reflect the extent of inflammation and the severity of the disease. To explore the same Pearson's correlation coefficient was calculated. It revealed that there is a negative correlation between serum c3 levels and FEV1%, r= -0.877, P<0.001. This reflects that with worsening of the disease, causing lower FEV1%, serum c3 levels were higher.

The study is limited by the small sample size, a larger sample size would help draw more statistically accurate conclusion. Further, this study doesn't explore the pathophysiology of altered serum complement levels and the disease process of asthma. Even though serial testing of serum complement C3 levels may be useful to monitor and demonstrate asthma control improvement, it's economic viability in a clinical setting hasn't been explored in this study.

Najam et al. analyzing 64 patients with severe moderate asthma, aged 1-12 years found elevated serum levels of C3 determined by radial immune-diffusion in most patients, similar to the observation in this study⁸. It is possible that the high value of C3 is due to the action of cytokines involved in the pathogenesis of asthma as noted in the study conducted by Nakano Y et al⁹. Hasegawa et al. found an association between complement proteins and the development of asthma: polymorphisms in the C3 gene,

C5 and receptors for C3a and C5a are associated with high levels of IgE and the development of asthma in children and adults¹⁰. Many other studies in concordance to the present study have reported increased plasma complement levels especially C3^{11,12}. Abdul F et al demonstrated that the levels of c3 has also been shown to give a clue about the severity of the disease process in the individual, similar to the finding in the current study¹⁰.

Hence it can be concluded that serum c3 level is a possible bio marker for the inflammatory process of asthma and reflects the severity of the disease. Any individual with symptoms of reactive airway disease and abnormal pulmonary function test results can be screened for increased serum C3 levels. Further, serial serum C3 levels can be measured to assess asthma control since a relationship between serum C3 levels and disease severity has been established. However the demonstration of the above utility of serum C3 levels is beyond the scope of this research study.

Since this study is limited by the relatively small sample size, a study with larger group could be undertaken in the future to produce statistically more accurate results. Future studies can also be aimed at demonstrating the pathophysiology of complement alteration in asthma. Furthermore, studies that explore the utility and economic viability of complement C3 in monitoring asthma control can be performed to clinically apply the findings of this study in asthma control management.

Conclusion

At the end of this study it is observed that serum levels of complement c3 are statistically higher in subjects with asthma as compared to healthy subjects.

Furthermore, the serum levels of c3 refelects the severity of the disease as evidenced by the negative correlation between serum c3 levels and pulmonary function test FEV1%.

Hence, Serum levels of C3 can serve as a marker for inflammation and possibaly severity of asthma.

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