Complement Components (C3, C4), C-Reactive Protein As Inflammatory Markers In Chidhood Asthma

Najat Bashir Alghazal[1]; Enass Kilani Ghwarsha[2]; Farj Ali Ahamed Elshaari[3] and Rabea Alghazal[4]

[1]Consultant pediatrician in Children's hospital, Benghazi, Libya. MBBS, DCH, CABA
[2]Faculty of Science, Department of Biochemistry, University of Benghazi.
[3]Faculty of Medicine, Benghazi University.Head of Medical technology department Perth, Australia
[4]Head of immunology and Virology lab in the Children's hospital, Benghazi, Libya
Najatg@yahoo.com, rabeaalghazal@yahoo.com

Abstract: Objective: To assess the involvement of C3-C4 and CRP in the pathophysiology of childhood bronchial asthma. **Method:** Selection of the patients (n=40) was made according to the recommended international criteria for diagnosis of asthma. Serum levels of C3, C4 and CRP were measured by radio immunodiffusion technique in 40 Libyan, non obese, children between (4-12 years), sex: 26 males, 14 females, with mild to moderately severe asthma, all patients were in active disease and on preventive therapy. Age matched comparisons were made with 28 healthy non obese children between (4-12years), sex: 13 males and 15 females. **Results:** Mean C3 level and C4 level were not significantly changed in non obese asthmatic children as compared to controls (p>0.05). The level of C-reactive protein was higher in asthmatic children than normal children (P>0.05) in all age groups. The serum level of C3, C4 are non significantly changed in non obese asthmatic children with positive correlation between C3, C4 levels. The level of C3-C4 was not significantly changed, possibly due to all asthmatic non obese patients being in inactive disease possibly to lack of induction of pro inflammatory cytokins and interlukin 1 (IL-1). CRP may be a potential indirect marker of asthma severity and control, as so can be used to assess the grade of inflammation in asthmatic patient (11) as inflammation is one of the major characteristics of respiratory allergy diseases.
[Najat Bashir Alghazal; Enass Kilani Ghwarsha; Farj Ali Ahamed Elshaari and Rabea Alghazal. **Complement Components (C3, C4), C-Reactive Protein As Inflammatory Markers In Chidhood Asthma.** *Life Sci J* 2016;13(8):66-69]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 11. doi:10.7537/marslsj130816.11.

Key words: Asthma, Children, Complement.

1. Introduction:

Asthma affects more than 300 million people worldwide (1) and is the most common chronic illness in childhood.

Asthma is defined as chronic inflammatory disease characterized by increased responsiveness of the tracheal bronchial tree to a variety of stimuli which may be spontaneous, allergen-related or drug induced, the primary pathophysiological abnormality being; bronchial wall inflammation leading to airway narrowing (2-4) manifesting clinically in the form of repeated episodes of wheezing, dyspnea, tight chest and coughing in particular at night and in the morning (5).

The complement system contains more than 30 plasma and cell surface proteins that interact with each other and with other immune system components. It's activity is highly regulated and it generates products that destroy infected cell or microorganisms. The product of complement system protein activation has a number of different biological effects. The anaphylatoxins and chemo-attractant processes recruit leukocytes, increase vascular permeability, stimulate bronchoconstriction and cause degranulation of mast cells (6-7).

C-reactive protein (CRP) is a well known inflammatory marker. CRP is known to be able to activate complement component (8).

Serum concentration of CRP is generally determined to assess systemic inflammation e.g. Pneumonia, rheumatic diseases and intestinal diseases etc. It has recently been observed that high sensitive C-reactive protein (hs CRP) can serve as a relevant prognostic marker in patients with cardiovascular disease or diabetes mellitus (9) hs CRP can be used to assess the grade of inflammation in asthmatic patients (10) as inflammation is one of the major characteristics of respiratory allergy diseases.

2. Material and Methods:

Patients and healthy controls; 40 children with bronchial asthma aged (4-12); sex: 26 males, 14 females (non obese), were obtained randomly from the pediatric allergy clinic at Benghazi children's hospital, all the patients are on inhaled corticosteroids [Beclomethasone inhaler, Fluctisone preparation and salmeterol (serotide discus), Buclensoid inhaler with femetorol (symtricort)]; all patients are in active disease.

A total of 28 normal, non obese children without a family history of asthma, atopy and any other serious

illness, aged (4-12 years), sex: 13 males, 15 females were recruited from the polyclinic over period of one year [2013-2014].

All participant underwent height and body weight measurements, hence BMI was calculated as body weight in Kg/(height in m)².

BMI was considered normal if it was more than 18 and less 25 [18< BMI <25].

The examination of patients was carried out in the allergy clinic. Blood specimens were drawn after obtaining consent, blood was extracted from the antecubital vein of each subject and collected.

Complement [C3, C4, CRP] serum levels were estimated.

Table (1): C3, C4 and CRP in Normal Control and Patients (non-obese asthmatic child).

	Normal children (N=30)		Asthmatic children (N=40)		
	Mean	±SD	Mean	±SD	*P* values
C3 g/l	1.257	0.263	1.178	0.196	0.154
C4 g/l	0.313	0.0973	0.293	0.1185	0.436
CRP mg/l	1.5	1.776	7.0924	7.0924	0.322

N=Number of sample *P* values shown only if statistically significant: **P*<0.05 significant
P*<0.01 highly significant*P*<0.001 very highly significant
C3, complement C3C4, complement C4CRP, C reactive protein

Table(2): Correlations Between Serum C3, C4, CRP in Normal Children and non-Obese asthmatic children.

Correlations				
CRP	**C4**	**C3**	**AGE**	**N=70**
0.334	**0.00		0.083	**C3**
0.103		**0.00	0.248	**C4**
	0.103	0.334	0.115	**CRP**

**Correlation is significant at the 0.01 level (2-tailed).

Table(3): Correlations Between Serum C3, C4, CRP in Normal Children

Correlations			
CRP	**C4**	**C3**	**N=30**
0.954	*0.042		C3
0.834		*0.042	C4
	0.834	0.954	CRP

**Correlation is significant at the 0.01 level (2-tailed).

Table (4): Correlations Between Serum C3, C4, CRP in Normal Children and non-Obese asthmatic children

Correlations			
CRP	**C4**	**C3**	**N=40**
0.166	*0.004		C3
0.108		*0.004	C4
	0.108	0.166	CRP

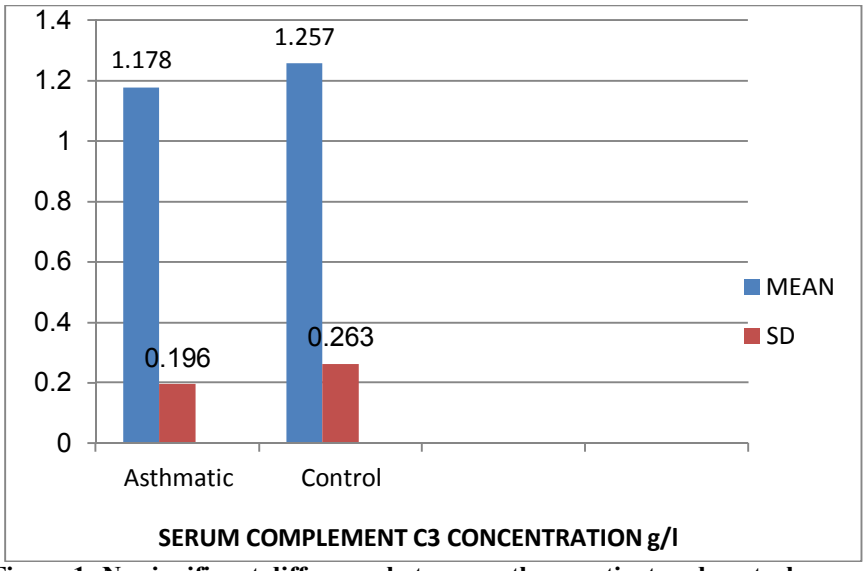


Figure 1: No significant difference between asthma patient and control group.

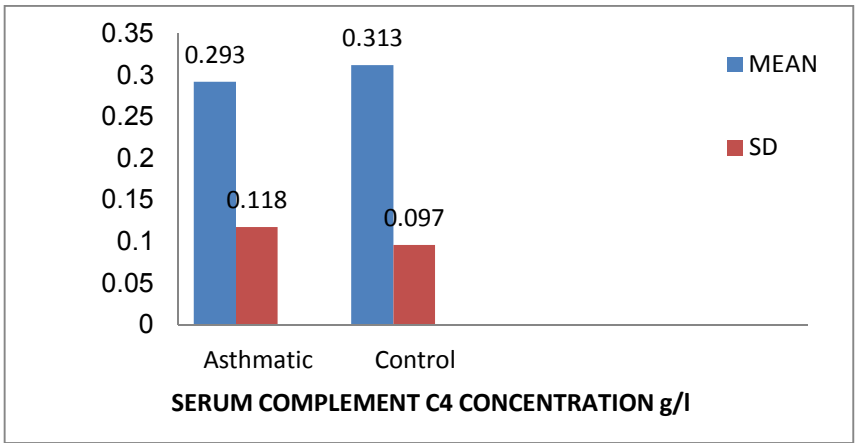
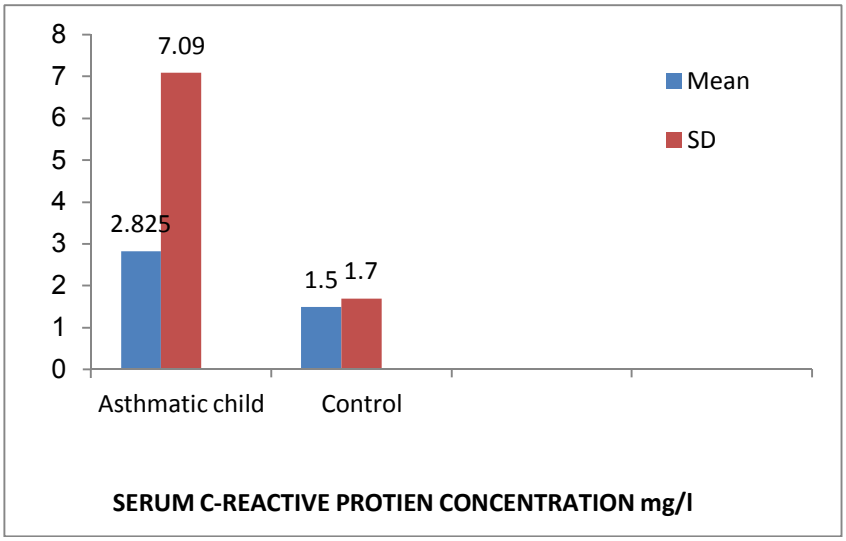


Figure 2: Serum level of C4 complement for children with asthma and 28 healthy children, both groups with age varying from (4-12 years)



4. Discussion:

The complements in asthma have since be studied to a great extent, although reports were conflicting, some studies have reported significantly increased serum C3 level where as other have demonstrates no change (11-13).

In our asthmatic patients the level of C3-C4 is not different compare to control, some reported studies were supported by the present finding that C3 level was increase in asthmatic patients with active disease only, while patients with non active disease had normal level of C3 (12-14). In 2005, it was studied in children with active asthma in Libya, and results showed elevated C3 levels and normal C4 levels. Elevated C3 may be due to induction of cytokines [Najam*et al.,* 2005].

Another study observed an increase in C3,C4 levels in patient with atopic asthma.[Mosca*et al.,* 2011].

Schiffer *et al.,* observedlower levels of C4 in asthmatic patients this suggests the greater involvement of classical pathway in comparison to the complement cascade.

CRP is known to be able to activate complement component, in this study all participants had higher levels of CRP, those findings are consistent with other studies (Jenes *et al.,* 2013).

Positivecorrelation has been reported between increase levels of CRP and current asthma (Jousilahti *et al.,* 2002).

Conclusion:

The primary site of biosynthesis of the majority of complements is in the liver, 90% of complements are derived from the liver (18).

Some of complements breakdown is known as anaphylatoxin(14,15).

Complement activation may be therefore considered as a possible contributor to bronchospasm and inflammation in asthma (18).

The present study's findings show normal level in C3,C4 levels in asthmatic, non obese patients with inactive disease (Najam *et al.,* 2005).

CRP was elevated in all patients and may be a potential indirect marker of asthma severity and control.

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8/25/2016