Original research article

Assessment of Serum High Sensitivity CRP in Bronchial Asthma

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Abstract

Background: Chronic airway inflammation is a hallmark of asthma, but the usefulness of high-sensitivity C-reactive protein tests (hs-CRP), which are known to be sensitive markers of low-grade systemic inflammation, has not been thoroughly investigated in asthma. Estimation of blood hs-CRP levels in asthma patients and their correlation with clinical traits and levels of airway inflammation are the objectives of this study.

Methods: Based on the inclusion and exclusion criteria n=40 cases were included in the study. The demographic profile data was collected using a pretested and structured questionnaire. A detailed history of asthma was obtained along with a complete clinical examination of the patient. The investigations included Pulmonary function tests, Complete blood count, estimation of serum hs-CRP, IgE levels, and Absolute eosinophil count.

Results: The atopic asthma group had the mean value of serum IgE 924.53 ± 205.63 IU/ml compared to the mean value of 198.17± 59.36 IU/ml. The difference was found to be statistically significant. The comparison between mild intermittent and mild persistent cases showed p values were 0.0141 hence it was significant. Comparison between mild persistent and moderate persistent showed p values 0.236 hence insignificant. The intergroup comparison between three groups with ANOVA showed p values of 0.0136 hence it was considered significant

Conclusion: In the current study it was found that there is a possibility to use hs-CRP as a marker of ongoing inflammatory activity as well as the effectiveness of treatment because patients with recent asthma attacks have elevated hs-CRP levels. The absolute eosinophil counts are much greater in the allergic asthma group, and the levels of AEC are correlated with illness severity.

Keywords: High sensitive C reactive protein (hs-CRP), Bronchial Asthma, serum IgE

Introduction

Asthma is a chronic inflammatory disorder of the airways in which many cells play a role in particular mast cells, eosinophils, and T lymphocytes. [1] People who are sensitive to this inflammation experience frequent episodes of coughing, wheezing, dyspnea, and chest tightness, especially at night or in the morning. The majority of the time, these symptoms are linked to a widespread but varied airflow restriction that is at least somewhat reversible, either

naturally or with therapy. An increase in the airways' hyperresponsiveness to various stimuli is also brought on by the inflammation. Previous research has demonstrated that asthma patients' airway mucosa has enhanced local and systemic inflammatory activity. [2] The complement pathways are activated by high-sensitivity C-reactive protein, a sign of inflammation, infection, and tissue damage that helps the host fight off infection. [3] The pace of synthesis drives the increase in high-sensitive c-reactive protein, which then declines fast after around 19 hours. [3, 4] High sensitivity c-reactive protein is made in the hepatocytes under the transcriptional control of the proinflammatory cytokine interleukin (IL-6), however adipose tissue plays a key role in the metabolism of hs-CRP by generating 30% interleukin-6 (IL-6). [3, 5, 6] Hepatocytes and Browicz-Kupffer cells produce the majority of C-reactive protein. CRP can also be produced by lymphocytes and monocytes. [7, 8] The mechanisms of CRP production activation are currently poorly known. It has been demonstrated that IL-1, IL-6, and TNF-α cytokines, which are known to play a significant role in the pathophysiology of asthma, are the primary stimulators of this process. T-cell activation, proliferation, and differentiation are influenced by IL-6, which also has impacts on many other cells that regulate growth. Through phosphorylation of the transcription factor, it also activates the gene in charge of CRP production. [8, 9] CRP serves a variety of crucial roles in humans, albeit some of these roles are yet unclear. The capacity of CRP to detect bacteria and injured human cells and to facilitate their removal through complement and the activation of phagocytic cells is its primary biological function. Healthy individuals' serum contains CRP, and inflammatory and malignant processes can lead to an increase in CRP production and release. [10, 11] A recent population-based study found associations between elevated serum levels of hs-CRP and a high frequency of airway hyperresponsiveness and low forced expiratory volume in one second (FEV1). [12] suggesting that systemic inflammation may be linked to respiratory impairment. Another recent epidemiological investigation revealed a strong correlation between higher hs-CRP levels and the incidence of nonallergic asthma as well as respiratory symptoms. [13]

Material and methods

This cross-sectional study was conducted in the Department of General Medicine, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Telangana State. Institutional Ethical committee approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the local language. Those willing to participate in the study voluntarily were only included.

Inclusion criteria

1. Aged above 18 years
2. Males and females
3. Cases diagnosed as Bronchial Asthma according to the Global Initiative for Asthma (GINA), if they have a clinical diagnosis of asthma and spirometric values showing reversibility of more than and/or equal to 12% in forced expiratory volume in 1 s (FEV1), or at least 200 mL from baseline after inhalation of salbutamol (4×100 mcg) given by metered dose inhaler using a spacer device. [reference]
4. Voluntarily willing to participate in the study.

Exclusion criteria

1. Patients with upper or lower respiratory tract infection,
2. collagen vascular disease,
3. malignancy,
4. Ischemic heart disease,
5. Diabetes Mellitus, hypertension,

6. COPD
7. Body-mass index (BMI) is more than 30
8. H/o Smoking

Based on the inclusion and exclusion criteria n=40 cases were included in the study. The demographic profile data was collected using a pretested and structured questionnaire. A detailed history of asthma was obtained along with a complete clinical examination of the patient. The investigations included Pulmonary function tests, Complete blood count, estimation of serum hs-CRP, IgE levels, and Absolute eosinophil count. Patients were divided into allergic and non-allergic groups based on Serum IgE levels and allergic symptoms and also based on symptoms frequency, short-acting beta-agonists (SABA) use, and nighttime awakenings, patients were also divided into three groups.

Table 1: Assessment of Asthma severity based on the symptoms

Components of Severity	*Asthma Severity*		
	Mild Intermittent	*Mild Persistent*	*Moderate Persistent*
Symptoms (Days/Week)	<2	> 2, but not daily	daily
Night Time Awakenings (Monthly)	0-2	2-4	weekly
Saba use for Symptom Control (Weekly)	<2	>2 but not daily	daily

*Statistical Methods***:** Data was entered into Microsoft excel and analyses were done using SPSS version 19 in windows format. Continuous variables were represented as mean and standard deviations and the categorical variable was determined using the chi-square test, and ANOVA and p values of <0.05 were considered significant.

Results

A total of n=40 cases were included in the study out of which n=24(60%) were males and n=16(40%) were females. The male to female ratio was 3:2. The age range of the patients included in the study was from 18 years to 74 years. The most common age group involved in the study was 21 – 30 years with 42.5% of cases in the study followed by age of 31 – 40 years with 17.5% of cases. The mean age of the patients in the study was 28.96 ± 12.84 years. The detailed age-wise distribution of the cases in the study is given in table 1.

Table 1: Agewise distribution of bronchial asthma

Age Categories	*Frequency*	*Percentage*
18 – 20	4	10.00
21 – 30	17	42.50
31 – 40	7	17.50
41 – 50	6	15.00
51 – 60	4	10.00
61 – 70	2	5.00
Total	40	100.0

The categorization of cases based on allergic history revealed n=28 cases with allergic dermatitis out of which n=26(92.85%) cases were with symptoms and n=2(7.14%) cases were

without symptoms. A history of allergic rhinitis was found in n=21 cases out of which n=19(90.47%) cases were with symptoms and n=2(9.25%) cases were without symptoms. Allergy to foods was reported by n=20cases out of which n=17(85%) cases were with allergic symptoms and n=3(15%) were cases without symptoms. Allergy to drugs was found in n=30 cases out of which n=29(96.66%) cases were without symptoms and n=1(3.33%) case was showing allergic symptoms. Allergic conjunctivitis was found in n=32 cases out of which n=6(18.75%) had symptoms and n=26(81.25%) cases were without symptoms. Note that some of the cases were having more than one history of allergies present with them.

Out of n=40 cases, n=29 cases were with atopic asthma and n=11 cases were with non-atopic asthma. The serum IgE levels in both groups are depicted in table 2. The atopic asthma group had the mean value of serum IgE 924.53 ± 205.63 IU/ml compared to the mean value of 198.17± 59.36 IU/ml. The difference was found to be statistically significant.

Table 2: Comparison of serum IgE levels in atopic and nonatopic asthma

Serum IgE level	*Group*	*Number*	*Mean*	*Std. Deviation*	*Z*
	Atopic asthma	29	924.53	205.63	5.793
	Non-Atopic asthma	11	198.17	59.36	P=0.01

The assessment of hs-CRP with serum IgE levels in allergic and non-allergic cases was compared. Those cases with >1.0 mg/L hs-CRP were considered positive and those below <1.0 mg/L were considered negative depicted in table 3. The comparison of values between these groups was found to be 0.134 hence it was insignificant.

Table 3: Distribution of hs-CRP by Serum IgE levels

hs-CRP	*Serum IgE levels*					
	Non-Allergic (<300 IU/ml)			*Allergic (>300 IU/ml)*		
	N	%	Mean [hs-CRP]	N	%	Mean [hs-CRP]
Negative	7	63.63	0.25	20	68.96	0.18
Positive	4	36.36	1.91	9	31.03	1.79

The absolute eosinophil count in the cases of allergic asthma cases in the study mean value was 595.36/mm^3 as compared to non-allergic asthma was 235.67/mm^3 and the p-value was found to be 0.0458 hence considered significant. The parameters have been depicted in figure 1.

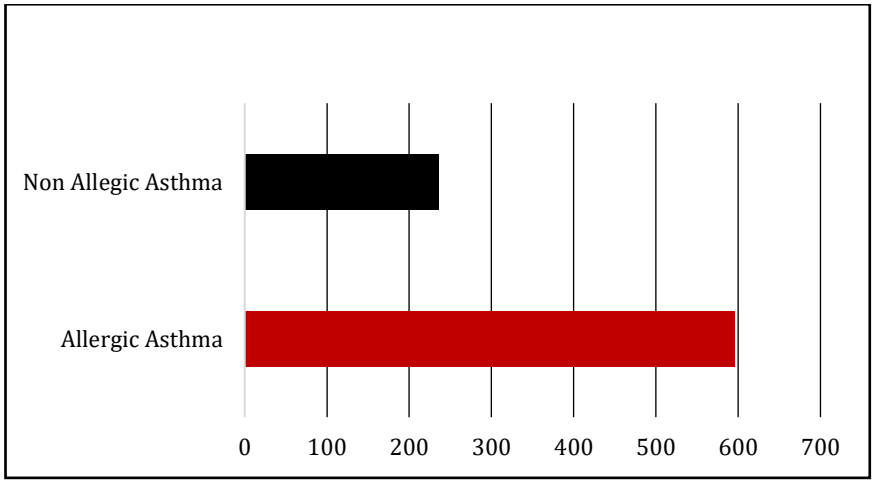

Figure 1: Absolute eosinophil count in both the cases of study

The assessment of absolute eosinophil count in cases of allergic and non-allergic asthma was estimated and found that those with high hs-CRP levels were not significantly associated with absolute eosinophil count the p values were 0.178 depicted in table 4.

Table 4: Distribution of hs-CRP by Absolute Eosinophil count levels

hs-CRP levels	**Absolute Eosinophil count (AEC)**					
	Non-Allergic			**Allergic**		
	N	%	Mean hs-CRP	N	%	Mean hs-CRP
Negative	8	72.72	0.21	20	68.96	0.17
Positive	3	27.27	1.85	9	31.03	1.83

Out of the n=40 cases in the study they were categorized as mild intermittent n=26 cases, mild persistent n=12 cases and moderate persistent n=2 cases the mean absolute eosinophil count was found to be highest in mild persistent cases followed by moderate persistent cases and least mean AEC counts were in mild intermittent cases given in table 5. The comparison between mild intermittent and mild persistent cases showed p values were 0.0141 hence it was significant. Comparison between mild persistent and moderate persistent showed p values 0.236 hence insignificant. The intergroup comparison between three groups with ANOVA showed a p-value of 0.0136 hence it was considered significant.

Table 5: Comparison of Absolute eosinophil count and category of asthma

Asthma type	Count of patients	Minimum AEC	Maximum AEC	Mean AEC	SD
Mild Intermittent	26	101.36	773.65	378.32	210.62
Mild persistent	12	190.72	840.81	544.36	182.05
Moderate Persistent	02	340.93	660.45	428.71	87.19

The comparison of hs-CRP levels based on the symptom frequency revealed 76.92% of cases of mild intermittent were negative for increased hs-CRP levels similarly, in the mild persistent levels 83.33% were negative for increased hs-CRP levels, and in moderate persistent no cases were negative of increased hs-CRP levels the inter-group ANOVA comparison of the values found p=0.756 hence not significant the details have been depicted in table 6.

Table 6: Comparison of IgE levels between the three groups of asthma.

hs-CRP	*Symptom frequency of asthma*								
	Mild intermittent			*Mild persistent*			*Moderate Persistent*		
	N	%	Mean hs-CRP	N	%	Mean hs-CRP	N	%	Mean hs-CRP
Negative	20	76.92	0.23	10	83.33	0.15	0	0.00	0.00
Positive	06	23.07	0.87	02	16.67	0.77	2	100.0	0.94

Discussion

To evaluate the significance of high sensitivity c-reactive protein (hs-CRP) in cases of bronchial asthma. There were n=40 cases of bronchial asthma included in the study. In the present study most of the patients 60% were in the 2nd to 4th decade of life. However, we found there was no correlation between hs-CRP and age in asthma patients. Hiyamashita et al., [14] found that aging is another confounding factor of elevated high sensitive c-reactive protein levels. Following Jousilatti et al., [15] and Sahoo et al., [16] who also reported data of a similar kind, our study found no statistically significant relationship between sex and high sensitivity c-reactive protein. D Dupler et al., [17] discovered two novel genes that contribute to atopic asthma. Patients develop a particular form of antibody that is meant to absorb and eliminate foreign substances when exposed to dust, animal proteins, fungus, or other potential allergens. The result is a change in the airway cells' sensitivity to specific substances. Additional exposure can quickly trigger an asthmatic reaction. It's been well recognized how important airway inflammation is. Asthma may also have systemic inflammation in addition to the inflammation of the airways. [18-20] According to one study, 20 individuals with silent asthma had considerably higher serum amyloid A levels than 20 healthy controls. [18] Acute phase proteins, such as plasma fibrinogen and serum amyloid A, were strongly correlated with the frequency of asthma in another cross-sectional population-based investigation. [19] Another recent multicentric epidemiological investigation revealed that nonallergic asthma was associated with higher serum levels of hs-CRP. [13] The extent of systemic inflammation and clinical indicators in asthma were not further examined in these trials, though. Our research is comparable to studies by Douglas et al., [17] and Tipirineni et al., [21] which found that the majority of asthmatics belonged to the atopic group. Our research revealed that patients with atopic asthma had higher total IgE levels. According to a study by Tipirineni et al., [21], and Sahoo et al., [16] patients with atopic asthma had higher total IgE levels. It is hypothesized that the IgE antibody to particular allergens, which is increased during acute infection and decreases during the convalescent phase, plays a pathogenic role in asthma exacerbations. In line with the findings of Razi et al., [22] and Halvani et al., [23] our investigation revealed higher absolute eosinophil counts in allergic asthma as well as in mild, moderate, and severe persistent asthma as compared to mild intermittent asthma. According to previous research, patients with allergic and non-allergic asthma differ in many ways, such as how they react to cold air, how they react to adenosine monophosphate (AMP), how much nitrogen oxide (NO) is present in exhaled air, and how much eosinophilic inflammation is present in their airways. [18, 24] However, the significance of high sensitive C-reactive protein tests (hs-CRP), which are known to be sensitive markers of low-grade systemic inflammation, has not been thoroughly researched in asthma. [25] Raised high sensitive c-reactive protein levels have been linked favorably to present asthma, respiratory impairment, and bronchial hyperresponsiveness. Additionally, our study has demonstrated a strong correlation between recent asthma flare-ups within the previous week and positive hs CRP ($p = 0.04$). However, it is far from apparent whether high sensitivity c-reactive protein and asthma are related (Olafsdottir). [26] Serum IgE levels are significantly greater in the mild persistent and moderate persistent groups, according to our findings. It supports earlier research by Naqvi et al., [26] that found an association between higher Serum IgE levels and worsening bronchial asthma. According to the results of our investigation, there is no correlation between blood levels of hs CRP and allergic or non-allergic asthma.

Conclusion

Within the limitations of the current study, it is found that there is a possibility to use hs-CRP as a marker of ongoing inflammatory activity as well as the effectiveness of treatment because patients with recent asthma attacks have elevated hs-CRP levels. The absolute eosinophil counts are much greater in the allergic asthma group, and the levels of AEC are correlated with

illness severity. Therefore, elevated AEC levels also indicate severe asthma. However, hs-CRP levels did not differ between allergic and non-allergic asthma.

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