Original Research Paper

Volume - 11 | Issue - 10 | October - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Biochemistry

SERUM HIGH SENSITIVITY C-REACTIVE PROTEIN AS NON SPECIFIC MARKER IN BRONCHIAL ASTHMA PATIENTS

Dr Shailendra Singh Bhadauria* Associate Professor Department of Biochemistry Government Medical College, Banda (210001) INDIA. *Corresponding Author

Dr Archana Kushwah Assistant Professor Department of Nutrition Government PG College, Beenaganj (473118) INDIA.

ABSTRACT

Background: Asthma is characterized as chronic airway inflammation along with respiratory manifestations like, shortness of breath, wheezing, chest tightness and variable expiratory airflow limitation. In bronchial asthma significance of highly sensitive C-reactive protein (hs-CRP) has not been fully studied as an acute phase reactant protein and a sensitive marker of low-grade systemic inflammation.

Aims and Objectives: The study was aimed to find out the relationship between serum level of hs-CRP and bronchial asthma.

Materials and Methods: Present study was designed to measure the hs-CRP in 60 (sixty) patients with bronchial asthma (case) and 40 (forty) healthy control subjects. In the all asthmatic patients, 39 patients had partially controlled and uncontrolled and 21 patients had asthma during exacerbation.

Results: Highly sensitive CRP was significantly higher ($p<0.0001$) in asthmatic patients as compared to the control group. In asthmatic with exacerbation, serum hs-CRP was significantly higher than in partially controlled and uncontrolled asthmatic patients ($p<0.0001$) and control subjects ($p<0.0001$).

Conclusion: Serum hs-CRP may be a non specific marker of asthma and its exacerbation.

KEYWORDS : Atopic asthma, non atopic asthma, hs-CRP

INTRODUCTION:-

Asthma is a heterogeneous disease characterized by chronic airway inflammation with dominant physiological features of systemic inflammation and reversible airflow narrowing. The clinical symptoms include wheezing, breathlessness, chest tightness and cough that may vary over the time and in intensity, with variable expiratory air flow limitation.[1] The prevalence of asthma increased gradually worldwide over the last several decades. Present estimates suggest that asthma affects more than 300 million people worldwide, with a predicted additional 100 million people to be affected by 2025 and approximately 25000-35000 people die per year from the disease. Bronchial asthma is classified pathophysiologically into two types, atopic and non atopic asthma.[2] According to the level of control, asthma is classified into three types, well controlled asthma, partially controlled asthma and uncontrolled asthma.[26]

C-reactive protein (CRP) is an inflammation sensitive plasma protein which is synthesized by the liver and is regulated to a large extent by the pro-inflammatory cytokine interleukin 6 (IL-6).[1] The measurement of CRP level in the blood is simple and has been used for decades in clinical practice to follow the progression of inflammatory processes.[2] Reduced lung function has been associated with various inflammation sensitive plasma proteins.[3,4]

Standard biochemical assays for CRP lack the sensitivity needed to determine the levels of inflammation and thus, clinical utility of standard CRP evaluation is extremely limited. Recent improvements have resulted in a new generation of highly sensitive assays that can detect the CRP at levels 100-fold lower than the earlier assays.[5] Determination of CRP using a highly sensitive assay is referred to as highly sensitive CRP (hs-CRP). Now, using hs-CRP, assessment of conditions indicative of chronic, low-grade inflammation is possible. A positive correlation has been observed between raised hs-CRP levels and risk of asthma, respiratory impairment and bronchial hyper-reactivity in several studies.[3,6] There is a strong relationship between hs-CRP and non-atopic asthma even when adjusted for body weight but not so between hs-CRP and atopic asthma.[7] An association has been reported between elevated hs-CRP levels and respiratory symptoms, such as wheeze, attack of breathlessness and nocturnal cough.[8] The present study was aimed to evaluate the significance of hs-CRP in asthma cases.

MATERIALS AND METHODS:-

The study was carried out in the Department of Biochemistry, Government Medical College, Banda (U.P.) from January 2019 to December 2019 with all ethical norms to evaluate the association of hs-CRP in asthmatic patients. A written consent was obtained from all participating subjects, who were then explained the study design and purpose of the study. In the present study hs-CRP was estimated in 60 (sixty) patients with asthma and 40 (forty) healthy controls. In the all asthmatic patients, 39 had partially controlled asthma, and 21 had asthma with exacerbation, 16 patients had atopic asthma and 44 patients had non atopic asthma, 09 patients were on regular inhaled corticosteroids and 51 patients were not on inhaled corticosteroids (ICS). The subjects included in the study were the patients from outdoor and indoor of Associated Hospital of Government Medical College, Banda (U.P.).

Patients were excluded if they were smokers, obese, had respiratory infection within the month preceding the study, a rheumatologic illness, malignancy, diabetes, heart failure, history of venous thrombo embolism , coronary heart disease and liver or kidney disease. Normal volunteers were also enrolled in the study as controls without any previous history of lung or allergic diseases and were not using any medication. At the time of enrolment, full clinical examination, pulmonary function test, and blood sampling were conducted. Normal volunteers had normal lung function tests (FEV1>80%) and normal IgE level. Subjects with high IgE were considered as atopic asthma. Partially controlled asthma, uncontrolled asthma and exacerbation of asthma were defined according to guidelines.

Determination of serum hs-CRP:- Serum hs-CRP was determined using an immuno-fluorescence assay(hs-CRP Fast test Kit) by Gentin Biotech, Inc, U.K.

STATISTICAL ANALYSIS:-

All the results were statistically analyzed by using the SPSS version 20.0 for Windows. All data were processed to compute mean and standard deviation and expressed as Mean±SD. Differences of Mean among two groups were compared with unpaired Student's t-test. The significance test was done at 95% confidence level.

RESULTS:-

Table 1 showed that significantly higher serum hs-CRP (in mg/L) was found ($p<0.0001$) in asthmatic patients (Mean±SD=11.64±1.16, Median=7.75) when compared to the control group (Mean± SD=1.51±1.31, Median=1.00). In asthmatic with exacerbation, serum hs-CRP was significantly higher (Mean± SD=19.16±1.30, Median=18.00) than control subjects (Mean±SD=1.51±1.31, Median=1.00). In asthmatics on regular ICS, serum hs-CRP was significantly higher (Mean±SD=2.96±2.94, Median=2.00) than control subjects (Mean±SD=1.51±1.31, Median=1.00). In asthmatics without regular ICS, serum hs-CRP was significantly higher (Mean±SD=13.24±1.19, Median=9.00) than asthmatics on regular

ICS (Mean±SD=2.96±2.94, Median=2.00). In atopic asthma patients serum hs-CRP was significantly higher (Mean±SD=3.53±2.37, Median=2.70) than control (Mean±SD=1.51±1.31, Median=1.00). In non atopic asthma hs-CRP level was significantly higher (Mean± SD=14.63±1.22, Median=11.10) than atopic patients (Mean± SD=3.53±2.37, Median=2.70). In acute severe asthma patients hs-CRP was significantly higher (Mean±SD=19.16±1.30, Median= 18.00) than inadequately controlled asthma (Mean±SD=7.10±7.62, Median=6.00).

Table 1 Distribution and comparison of hs-CRP level between different groups

Study Group	Mean±SD	Median	p value
Asthmatic (n=60)	11.64±1.16	7.75	0.0001
Control (n=40)	1.51±1.31	1.00	
Acute Asthma (n=21)	19.16±1.30	18.00	0.0001
Control (n=40)	1.51±1.31	1.00	
Asthmatic on ICS (n=09)	2.96±2.94	2.00	0.0001
Control (n=40)	1.51±1.31	1.00	
Asthmatic on ICS (n=09)	2.96±2.94	2.00	0.0001
Asthmatic not on ICS (n=51)	13.24±1.19	9.00	
Atopic (n=16)	3.53±2.37	2.70	0.0001
Non Atopic (n=44)	14.63±1.22	11.10	
Atopic (n=16)	3.53±2.37	2.70	0.0001
Control (n=40)	1.51±1.31	1.00	
Partially Controlled (n=39)	7.10±7.62	6.00	0.0001
Acute Asthma (n=21)	19.16±1.30	18.00	

DISCUSSION:-

C-reactive protein (CRP) is a β globulin increased in production in acute illness contributing to the activation of complement system; it is termed C because it causes precipitation of somatic C-polysaccharide of Streptococcus pneumonia is an elegantly sensitive though non-specific marker of acute inflammation and tissue damage.[9] Structurally CRP is composed of five identical non-glycosylated polypeptide subunits, each 23 kDA in mass, held together by non-covalent bonds to form a disc-like pentagonal ring.[10,11] The CRP is predominantly synthesized in the liver and is regulated by pro-inflammatory cytokines, primarily the tumor necrosis factor-alpha and interleukin-6. There is a rapid increase in the production of CRP (10000 fold) during acute phase response, resulting in the release of elevated quantities into the circulation. Although its functional mechanism is still unclear, the CRP may serve as a general scavenger protein and play an important role in opsonisation, phagocytosis, and cell-mediate cytotoxicity.[11,12]

C-reactive protein (CRP) is a highly sensitive marker for many inflammatory and infectious problem, and it is nonspecific but a sensitive test for acute illness; moreover, the level of CRP is rapidly changeable with the change of clinical symptoms. A positive associationship has been observed between raised CRP levels and asthma, respiratory impairment, and bronchial responsiveness.[3,8,13-17] However, in some studies there is no relationship between CRP levels and spirometry indices such as FEV1 or IgE in asthma patients.[18,19]

In our study hs-CRP levels was observed much higher in asthmatics than normal healthy controls similar to that of the studies by many researchers who found that hs-CRP is a useful marker in bronchial asthma.[8,12,20] Highly sensitive CRP has been demonstrated by Obaidi et al to be higher in asthmatics as opposed to controls.[21] The majority of patients with reduced FEV1 have asthma, chronic obstructive pulmonary disease (COPD), or fibrotic lung disease.[16] In these conditions, cytokines are over expressed in lung tissues, potentially resulting in systemic low-grade inflammation.[16,22,23] Our findings support the hypothesis that in bronchial asthma not only local but also systemic inflammation exits.

Several studies have demonstrated that patients with atopic and non atopic bronchial asthma differ in many aspects which includes response to cold air, levels of nitrogen oxide, response to adenosine monophosphate (AMP) in expired air and the level of inflammation in the airways.[24-26] Our study shows a strong association between elevated hs-CRP and non atopic asthma, than between hs-CRP and atopic asthma which further emphasizes the difference between these two sub groups of asthma. This finding is similar to that of Sahoo et al Olafsdottir et al.[7,8] The elevated hs-CRP levels in non atopic bronchial asthma patients support the hypothesis that in non atopic asthma, there is not only a local but also an ongoing systemic inflammatory process. Our study also showed that the patients with bronchial asthma not on ICS has increased serum hs-CRP levels compared to those on ICS while in patients on ICS treatment, serum hs-CRP levels are more than healthy controls. It is presumably that asthmatics on ICS, which has anti-inflammatory properties, used in these patients might have reduced serum hs-CRP.[12]

A study concluded that significant positive association of hs-CRP with exacerbation rates and significant negative association of hs-CRP and FEV1 are seen during remission.[27] Thus hs-CRP levels during revocation may be used as a marker for predicting future exacerbation in asthmatic patients. A positive correlation of increased levels of serum hs-CRP with a high frequency of airway hyper responsiveness and FEV1 among subjects without heart disease observed and concluded that CRP levels were significantly higher during exacerbations than in stable asthmatic patients.[3] A study demonstrated that asthma increased gradually with increasing hs-CRP.[6] In the present study, asthma exacerbation was strongly related to higher hs-CRP levels, whereas partially controlled, uncontrolled asthma and control subjects had lower levels of hs-CRP supporting the findings of studies on 235 cases that hs-CRP rises and falls with the severity of asthma.[21,29]

CONCLUSION:-

hs-CRP can be considered as a good biomarker for judging the severity and stability of asthma, and future studies for the impact on the long-term outcome may be fruitful in minimizing the unwanted and irreversible changes of asthma.

REFERENCES:-

1. Gillman B, Papachristodoulou DK, Thomas JH. Will's Biochemical Basis of Medicine. Oxford: Butterworth Heineman; 2000.
2. Burtis CA, Ashwood ER. Tietz Textbook of Clinical Chemistry. 3rded Philedelphia: Saunders Co; 1999:617-721.
3. Kony S, Zureik M, Driss F, Neeukirch C, Leynaert B, Neukirch F. Association of Bronchial Hyperresponsiveness and Lung Function with C-reactive Protein (CRP): population based study. Thorax. 2004;59:892-96.
4. Mendall MA, Strachan DP, Butland BK, Ballam L, Morris J, Sweetnam PM et al. C-reeactive protein: Relation to total mortality, Cardiovascular mortality and Cardiovascular rik factors in men. Eur Heart J. 2000;21:1584-90.
5. Aziz N, Fahey JL, Detels R, Butch AW. Analytical performance of a highly sensitive C-reactive protein-based immunoassay and the effects of laboratory variables on levels of protein in blood. ClinDiagn Lab Immunol. 2003;10:652-57.
6. Jousilahti P, Salomaa V, Hakala K, Vantera E, Palosuo T. The association of sensitive inflammation markers with bronchial asthma. Ann Allergy Asthma Immunol. 2002;89:381-85.
7. Sahoo RC, Acharya PR, Noushad TH, Anand R, Acharya VK, Sahu KR. A study of high sensitivity C-reactive protein in bronchial asthma. Indian J Chest Dis Allied Sci. 2009;51:213-16.
8. Olafsdottir IS, Gislason T, Thjodleifsson B, Olaffson I, Gislason D, Jogi R et al. C reactive protein levels are increased in non-allergic but not allergic asthma: A multicentre epidemiological study. Thorax. 2005;60:451-54.
9. Pepys MB, Batz MI. Acute phase protein with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid a protein. Adv Immunol. 1983;34:141-212.
10. Thmpson D, Pepys MB, Wood SP. The physiological structure of human C-reactive protein and its complex with phosphocholine. Structure. 1999;7:169-77.
11. Anderson GP. COPD, asthma and C-reactive protein. EurRespir J. 2006;27:874-76.
12. Takemura M, Matsumoto H, Niimi A, Ueda T, Matsuoka H, Yamaguchi M et al. High sensitivity C-reactive protein in asthma. Eur Respir J. 2006;27:908-12.
13. Ford ES. The epidemiology of obesity and asthma. J Allergy Clin Immunol. 2005;115:897-909.
14. Cirilo DJ, Agarwal Y, Cassano PA. Lipids and pulmonary in the third health and nutrition examination survey. Ann J Epidemiol. 2002;55:842-48.
15. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eriksdottir G, Rumley A et al. C=reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. N Eng J Med. 2004;350:387-97.
16. Mannino DM, Ford SS, Redd SC. Obstruction and restrictive lung disease and markers of inflammation. Ann J Med. 2003;114:758-62.
17. Gann WQ, Man SFP, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: A systemic review and meta analysis. Thorax. 2004;59:574-80.
18. Ramirez D, Patel P, Casillas A, Cotelingam I, Bogas P, Bahna SL. Assessment of high sensitivity C-reactive protein as a marker of airway inflammation in asthma. Ann Allergy Asthma Immunol. 2010;104(6):483-89.
19. Ehrahim R, Hassan F, Hossain A, Vajihe C, Armin R. Evaluation of high sensitivity C-reactive protein in acute asthama. Tanaffos. 2012;11(1):32-37.
20. Mojtaba E, Somayeh B, Payman A, Davood K. A study of high sensitivity C-reactive protein in relation to respiratory symptoms in mild to moderate asthma. International Journal of Biosciences. 2011;1(5):83-88.
21. Obaidi AHA, Samarai AGMA, Jawad AKY, Janahi JMA. Association between C-reactive protein and asthma. Turkish Thoracic Journal. 2010;11:98-104.
22. Sin DD, Lacy P, York E, Man SF. Effects of fluticasone on systemic markers of inflammation in chronic obstructive pulmonary disease. Am J RespirCrit Care Med. 2004;170(7):760-65.
23. Sin DD, Man SF. Why are patients with chronic obstructive pulmonary disease ay increased risk of cardiovascular disease The potential role of systemic inflammation in chronic obstructive pulmonary disease. Circulation. 2003107(11)1514-19.
24. Ludviksdottir D, Janson C, Bjomsson E, Stalenheim G, Boman G, Hedenstrom H et al. Different airway responsiveness profiles in atopic asthma, non atopic asthma and sjogren's syndrome: BHR Study Group Bronchial Hyperresponsiveness. Allergy. 2000;55:259-65.
25. Ludviksdottir D, Janson C, Hogman M, Hedenstrim D, Bjomsson E. Exhaled nitric oxide and its relationship to airway responsiveness and atopy in asthma. BHR Group Respir Med. 1999;93:552-56.

26. Amin K, Ludviksdottir D, Janson C, Nettelbladi D, Bjornsson GM. Inflammation and structural changes in the airways of patients with atopic and non atopic asthma. BHR GROUP. Am J Respir Crit Care Med. 2000;162:2295-201.
27. Menon B, Nimal G, Dogra V, Kaur C. C-reactive protein as a marker of asthma control. Int J of Basic and Applied Medd Sci. 2013;3(3):114-19.
28. Menon B, Kaur C, Kaushik R. Evaluation of high sensitivity C-reactive protein in patients of bronchial asthma and its correlation with exacerbation rate and pulmonary function. European Respiratory Journal. 2008;32(52):195s.
29. Monadi M, Firozjahi A, Hosseini A, Javadian Y, Sarbatdran M, Haidari B. Serum C-reactive protein in asthma and its ability in predicting asthma control, a case control study. Caspian J Intern Med. 2016;7(1):37-42.