



RESEARCH ARTICLE

ROLE OF hs-CRP IN ASTHMA AND CORONARY ARTERY DISEASE

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ABSTRACT

Serum high sensitive – C reactive protein is a non specific inflammatory marker. Asthma and Coronary artery disease are associated with inflammation. In condition of asthma, oxygen level in the body decreases so heart pressure would increase to supply oxygen to all over the body. This heart pressure can lead to create heart disease. In this phenomenon, IL-6 releases which stimulate the production of hs-CRP. Thus this review discusses the Role of hs-CRP in Asthma and Coronary artery disease – a non-specific inflammatory marker.

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INTRODUCTION

Asthma is serious global health problem. It is one of the burning problems of our society which is seen in all age group. According to WHO promoted organization GINA (Global initiation for Asthma, [www.gina.com](http://www.gina.com)) "Asthma is one of the most common chronic diseases in the world. It is estimated that around 300 million people in the world and accounts for about 1 in every 250 death worldwide. The global prevalence of asthma is anticipated to be approximately 4.5 per cent (Masoli et al., 2004; To et al., 2012). There are about 334 million patients with asthma affecting all age groups across the world (The Global Asthma Report 2014). The prevalence of asthma has increased over time and an additional 100 million people worldwide are expected to develop asthma by the year 2025 (The Global Asthma Report 2014). In the Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis in adults (INSEARCH), a survey conducted in two phases across 16 centres in India, the prevalence of asthma in adults was 2.05 per cent, with an estimated burden of 17.23 million (Aggarwal et al., 2006). A recent analysis using three different estimate models (INSEARCH, GINA and WHO survey) suggest that the prevalence of asthma in India varies between 2.05 to 3.5 per cent (17-30 million patients) (Agarwal et al., 2014).

Asthma and Coronary artery disease

"Chest discomfort or pain will mislead us about the symptoms of asthma. Asthma is directly proportional to coronary artery disease and treatment for both the diseases are totally different. So the patients should take the symptoms seriously and get the treatment." said Young J. Juhn, M.D., M.P.H., senior author of the Olmstead County study and professor of paediatrics and adolescent medicine at the Mayo Clinic in Rochester, Minnesota. Coronary artery disease makes the arteries harden and inflamed. Similarly, airway swelling occurs in asthma. Leftwich notes it's possible for inflammation in one part of the body to spread. Asthma has been associated with increased coronary artery disease. Adult asthma, especially among women, is an independent predictor of increased risk for coronary artery disease. Lipid accumulation and inflammation are the two common characteristics of the coronary artery disease (Hansson, 2005; Packard and Libby, 2008; Davies, 1983).

History

The C-reactive protein is precipitated by the somatic C-polysaccharide antigen of streptococcus pneumonia. So it is given the name CRP. First it was separated by the serum of patient with acute inflammation (Pepys and Batz, 1983). It is discovered by Tillet and Francis in 1930 (Tillet and Francis, 1930). Initially it was considered as pathogenic secretion because it increased in various diseases and later found that it is

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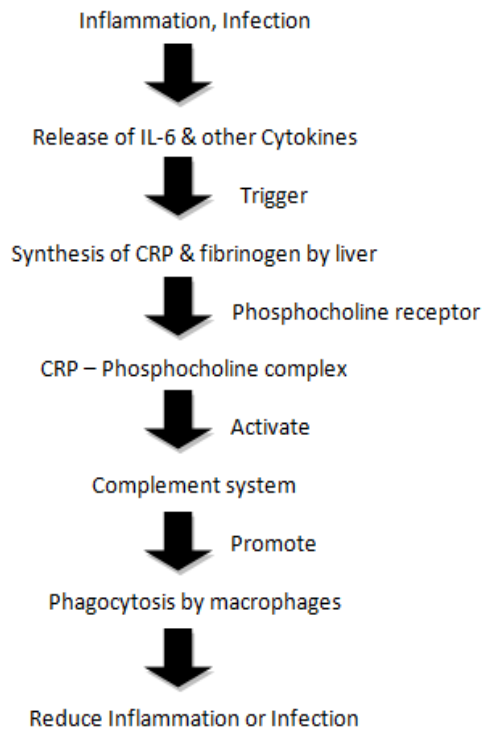
a native protein of hepatic origin (Kennelly *et al.*, 2009; Pincus *et al.*, 2007; Ratey *et al.*, 2008).

### Structure

C-reactive protein is a ring shaped pentameric protein which consists of five identical non-glycosylated polypeptide subunits, each 23 KDA in mass, held together by non-covalent bonds. It is a member of pentraxin (penta = five, ragos = berries) family of proteins (Pepys and Hirschfield, 2003; Pepys and Batz, 1983; Anderson, 2006). It is an acute phase protein which is present in blood plasma (Thompson *et al.*, ?). Gene for C-reactive protein is situated on chromosome 1 (1q23.2) (<https://www.ncbi.nlm.nih.gov/gene/1401>). It is made up of 224 amino acids (NCBI Entrez Protein #CAA39671).

### Synthesis and function

It is synthesized by the hepatocytes in the liver and is regulated by pro-inflammatory cytokines, tumour necrosis factor-alpha and IL-6 which are secreted by macrophages, T – cells and adipocytes (Devaraj *et al.*, 2009; Lau *et al.*, 2005). Figure 1 shows the acute phase response phenomena. It plays a role in innate immunity as an early defence system against infection (Pepys and Hirschfield, 2003; Lau *et al.*, 2005).



(Figure 1. showing acute phase response)

### Diagnostic relevance: inflammatory marker

Asthma and coronary artery disease is associated with inflammation and can be diagnosed by using various inflammatory markers. These markers can be divided into three groups as follows (a) cytokines and chemokines (b) soluble adhesion molecules and (c) acute phase reactants (Roberts, 2004). Among them C- reactive protein is an acute phase reactant and very sensitive to systemic inflammation, infection and tissue destruction (Pepys and Hirschfield, 2003). In the

asthma airway inflammation as well as systemic inflammation occurs. There are few methods like ELISA, immunoturbidimetry, nephelometry, rapid immunodiffusion and immunoluminometry which are used to measure C-reactive protein level (Roberts, 2004). The level of hs-CRP is increasing with age (Thomas *et al.*, 2008). The normal level of CRP is 0-6 mg/L (Pearson *et al.*, 2003). It is raised in pregnant women, inflammations, infections and burn cases (Keng Sheng Chew, 2012). The value of CRP rises from about 6 hours and reaches at peak level within 48 hours. The half life of CRP is 19 hours approximately (Hirschfield and Pepys, 2003). Research shows that the level of hs-CRP remains unchanged during the trial (Glynn *et al.*, 2009).

### High sensitive C - reactive protein and Coronary artery disease

In condition of coronary artery disease, the level of LDL increases and plaque is deposited around the arteries. This can lead to heart attack or stroke. The plaque of LDL cholesterol can damage the wall of artery and causes inflammation. To prevent the inflammation some proteins released by the cells called acute phase reactants. C-reactive protein is one of them (Source internet).

### Factors affecting concentration of hs-CRP

There are so many factors which can affect the level of hs-CRP. Higher level of hs-CRP is due to blood pressure, inflammation, infection, smoking, diabetes mellitus, heart diseases, metabolic syndrome, medication, non-steroidal anti-inflammatory drugs, alcohol consumption and weight loss can lowers the level of CRP. Some external factors also influence the level of hs-CRP like environmental factors, seasonal variation, age, gender and race (Pearson *et al.*, 2003).

### DISCUSSION

The overall conclusion of this study, the asthmatic patients have higher serum hs-CRP level in comparison to healthy controls because airway swelling occurs in asthma resulting release of high sensitive C-reactive protein in blood circulation. Besides the airway inflammation, systemic inflammation may exist in asthma (Jousilahti *et al.*, 2002; Buyukozturk *et al.*, 2004; Enright *et al.*, 1996). Except that increased hs-CRP level has been associated with many non-communicable diseases like CAD (Sarwar *et al.*, 2009), ischemic stroke (Rost *et al.*, 2001), diabetes mellitus (Festa *et al.*, 2000), metabolic syndrome (Ford, 2003), and peripheral artery disease (Ridker *et al.*, 1998). Monadi M *et al.* found that higher serum hs-CRP level in asthmatic patients than healthy controls, so it indicate positive correlation between asthma and hs-CRP and negative correlation between patients taking inhaled corticosteroid therapy and hs-CRP level (Ridker *et al.*, 1998). As well as elevated serum hs-CRP is not only indicates lung inflammation but also an important marker of future development of cardiovascular diseases (Monadi *et al.*, 2016). Some other factors like infection by bacteria, obesity, pollution and smoking increases production of IL-6 which stimulate CRP production. Damaged tissues itself may be a source for synthesis of CRP (Anderson, 2006). R. C. Sahoo *et al* studied on asthmatic and non-asthmatic patients. A weak but significant positive correlation observed between hs-CRP level and age of atopic asthmatic patients. No statistical difference found between sex and hs-CRP level. Gender difference is also

controversial (Sahoo *et al.* 2009). Broad area prospective studies have explained that hs-CRP is a strong independent marker of future myocardial infarction, stroke, peripheral arterial disease and sudden cardiac death in healthy subjects and repeating events and death in patients with acute or stable coronary syndromes (Bassuk *et al.*, 2004). Some old studies found that the level of hs-CRP is related to smoking which is independent factor for increased hs-CRP (Ridker, 2001). Cigarette smoke induced the production of IL-6 in the lung tissues (Anderson, 2006). Takemura *et al.* suggest that the level of hs-CRP in steroid-naive and steroid-inhaling adult non-smoker patients with asthma and healthy subjects. Serum hs-CRP level was significantly increased in steroid-naive patients as compared to controls but not in patients on inhaled corticosteroids. Among steroid-naive patients, serum hs-CRP level was negatively correlated with indices of pulmonary function and positively with sputum eosinophil count. Among patients on inhaled corticosteroids the hs-CRP levels were not correlated with any of the indices (Takemura *et al.*, 2006). Kilic *et al.* also found positive relationship between hs-CRP level and asthma severity and negative correlation between hs-CRP level and asthma control test but no correlation was found between the parameters of pulmonary function test and hs-CRP level in asthmatic patients (Kilic *et al.*, 2012). Razi E *et al.* were investigated that elevated serum hs-CRP level may be associated with airway obstruction in acute asthma and a confounding marker and diagnostic tool for detecting and monitoring airway inflammation in asthma patients (Razi *et al.*, 2012).

## Conclusion

The overall finding shows that the systemic inflammation is a cause of respiratory dysfunction (Kony *et al.*, 2004). The hs-CRP is surrogate marker of inflammatory diseases. Inflammation occurs in asthma, cardiovascular disease and diabetes mellitus. So it can establish the relationship between asthma, cardiovascular disease and diabetes mellitus.

## Limitations

It is not a longitudinal study. So we can't note the periodic changes in serum hs-CRP level with clinical features over the course of asthma treatment. Sample size should be more for this study.

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