

Review Article

C-Reactive Protein: Significance of a Non-Specific Biomarker: A Review

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ABSTRACT

C-reactive protein (CRP) is a non-specific acute phase reactant that increases in response to infection or inflammation. Higher levels suggest a more severe infection and have been used to predict the severity of COVID-19 disease. CRP, an acute phase protein, is one of several downstream indicators of inflammation. CRP improves cell-mediated immunity by increasing phagocytosis, hastening chemotaxis, and activating platelets. Here, in this review, we will discuss more about historical background, pathophysiology involved, normal ranges and interpretation of raised levels and significance of CRP in various pathologies. This will further enhance our knowledge related to clinical significance of CRP in day-to-day practice.

Keywords: Atherosclerosis, Cancer, Cardiovascular Disease, COVID-19, C-Reactive Protein

INTRODUCTION

C-reactive protein (CRP) responds to infection or inflammation and was found while investigating Streptococcus pneumoniae patients.^[1,2] It plays a vital role in inflammation and increases cell-mediated immunity by accelerating phagocytosis and chemotaxis, and activates platelets.^[3]

HISTORICAL BACKGROUND

CRP was discovered by Tillet and Francis as it has the capacity to precipitate and interact with phosphorylcholine residues of the C polysaccharide that is produced from teichoic acid within the cell wall of Streptococcus pneumoniae. It plays a significant role in innate immunity and its level rises in inflammatory diseases such as rheumatoid arthritis, cancer and cardiovascular disease.^[4]

PATHOPHYSIOLOGY OF CRP

CRP, like serum amyloid P (SAP) component, has undergone extensive evolutionary conservation.^[5] Pentraxins have an unusual structure having five non-glycosylated globular components arranged in a symmetrical cyclic pattern, resulting in a pentameric, discoidal and flattened form.^[6] It is formed by liver during proinflammatory cytokine activity.^[7] It increases de novo CRP production by upregulating Deoxyribonucleic acid (DNA) damage-inducible transcript 3 cytosine-cytosine-adenosine-adenosine-thymidine (CCAAT)/enhancer binding proteins (C/EBP) that are critical transcription factors in this pathway.^[8,9] It is seen in adipocytes cell indicating that obesity and chronic inflammation are related in yet another way.^[10,11]

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INTERPRETATION OF LEVELS OF CRP

Less than 0.3 mg/L: Normal

0.3 to 1.0 mg/L: Minor rise

1.0 to 10.0 mg/L: Moderate rise

More than 10.0 mg/L: Marked rise

More than 50.0 mg/L: Severe rise.^[12]

SIGNIFICANCE IN VARIOUS PATHOLOGIES

➤ In systemic lupus erythematosus

During active disease, many persons with active systemic lupus erythematosus (SLE) have CRP values that are just slightly elevated or even normal. A large increase in level in an SLE patient indicates the presence of many concurrent infections.^[13]

➤ In diabetes:

Increased levels can predict the onset of diabetes, and it was observed in research, conducted in an American Indian population having diabetes that CRP elevations were seen in cardiovascular disease in non-diabetic women, but it was not seen in diabetic women or men, indicating that the CRP elevations can act as a predictive marker for diabetes.^[14]

➤ In cancer:

Assessment of its level during cancer can guide the doctor to evaluate the severity of the disease and can act as a reference in deciding the treatment and thus overall survival can be improved. It can also indicate the aggressiveness of the tumor in the body.^[15]

➤ In inflammation:

It is largely present at sites where inflammation or injury has occurred.^[16] CRP localisation in neutrophil infiltrates has been linked to vasculitis and allergic encephalomyelitis lesions.^[17]

➤ In infection:

It is an inflammatory marker that rises in bacterial infection,^[18] and it has the ability to fight infection.^[19]

➤ In COVID-19:

The excessive inflammation seen in COVID-19 patients is the primary cause for increased mortality and disease progression. During acute inflammation, severe insults or coronary heart disease, serum CRP levels are clearly raised. As the inflammation goes away, it becomes normal. It has the ability to enhance phagocytosis via a specific CRP receptor and destroy a wide range of pathogenic microorganisms.^[20]

➤ In chronic periodontitis:

According to some experts, periodontal diseases are induced by the interaction of particular gram-negative

bacterial species with the host defense in disease-sensitive individuals. The host responds to the microbial challenge with a significant inflammatory response that includes increased levels of inflammatory mediators. These mediators enhance acute phase reactant activation, resulting in elevated serum levels of CRP.

CONCLUSION

CRP appears to be more than just a marker of inflammation or infection; it appears to be a crucial regulator of inflammatory processes. More study is required to expand on these unique findings and completely understand the particular functions that each CRP variation plays at locations of local inflammation and infection.

Declaration of patients consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of Artificial Intelligence (AI)-Assisted Technology for manuscript preparation

The authors confirm that there was no use of Artificial Intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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