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Research Paper

C-Reactive Protein In Dental Infections – A Mini Review

[1)] Dr.Nirmala Chandrasekaran, M.D.S
Reader, Department of Conservative Dentistry & Endodontics, Ragas Dental College & Hospital
2/102, SH 49, Uthandi, Tamil Nadu 600119

[2)] Dr.Anil Kumar Ramachandran, M.D.S
Professor and Head of the Department,
Department of Conservative Dentistry & Endodontics, Ragas Dental College & Hospital

[3)] Dr.Anjana K S
3rd Year Post Graduate Student
Department of Conservative Dentistry & Endodontics, Ragas Dental College & Hospital
Corresponding Author: Dr.Nirmala Chandrasekaran

ABSTRACT
C-reactive protein (CRP) is an acute inflammatory protein found in Saliva and Gingival Crevicular Fluid (GCF). CRP is primarily produced by the liver hepatocytes and contributes to the inflammatory process through their pro-inflammatory properties. CRP plays a prominent role as an inflammatory biomarker in dental infections like periodontitis, dental caries, endodontic infections and systemic diseases. This article is a first-time effort done to describe in brief, the association of CRP in dental infections.
KEY WORDS*: CRP, C-Reactive Protein, Dental infection, Endodontic Infection, Periodontitis, Inflammation*

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I. INTRODUCTION:

C-Reactive Protein (CRP) is homo – pentameric plasma protein secreted largely by the hepatocytes[2]. C-reactive protein (CRP) increases up to 1,000-fold during infection or inflammation. They are also synthesized in smooth muscle cells, endothelial cells, lymphocytes, macrophages, and adipocytes[3]. CRP might be elevated even if ESR is normal. CRP is quicker than ESR to return to normal after therapy. Few cytokines especially, IL-6 and IL-1 regulate CRP at transcriptional level. Pankow et al observed that inter-individual variation in blood CRP levels is 35–40% heritable. Increased CRP levels are commonly associated with a disease, but liver failure impairs CRP production[4,5].

It is said to be first sensitive acute phase proteins because it has been released acutely at infection and inflammation sites. Generally, plasma rich proteins (PRP) are clear, protein-rich fluid found in the blood plasma which is left behind when platelets, red blood cells, and white blood cells are removed from the blood. It is around 7% of the total blood volume. The function of plasma proteins are transport of vitamins, minerals, hormones and enzymes all over the body and mainly acts in immune system[1]. It undergoes a rapid change in serum concentration during the response to a specific event or reaction in the body and the response is called the acute-phase response or the acute-phase reaction. (TABLE 1)

(Figure 1). Acute phase proteins are classified into following types:1)positive acute phase proteins 2)Negative acute phase proteins.

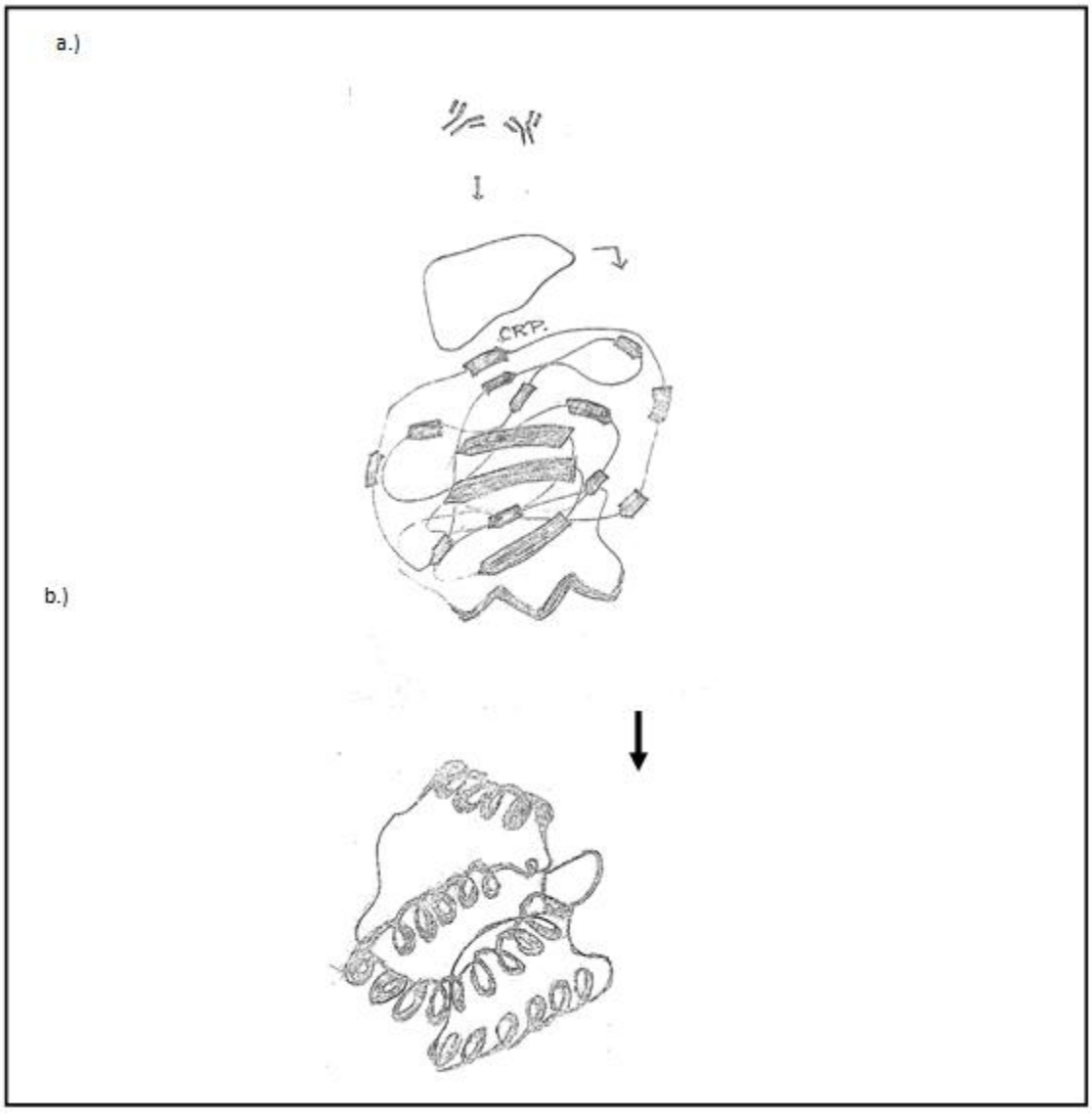

FIGURE 1: a) CRP molecules get released from the liver cells by stimuli of antibodyproduction.
b)ultrastructure of CRP molecule

TABLE1: classification of acute phase proteins

Positive acute phase proteins	Negative acute phase proteins
The plasma protein concentration increases in response to the stimuli	The plasma protein concentration decreases in inflammation.
It serves as part of the innate immune system under different physiological functions within the immune system.	Some examples include Transferrin, Albumin, Antithrombin and Retinol-binding protein. This decrease can be useful markers of inflammation.
Some act to destroy or inhibit growth of microbes, some give negative feedback on the inflammatory response (e.g., serpins), some products of the coagulation system increases vascular permeability and act as chemotactic agents for phagocytic cells(e.g., C-reactive protein, Serum amyloid P component, Serum amyloid A & Complement factors)	Decrease in synthesis is considered to increase "positive" acute-phase proteins more effectively.

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CRP IN DENTAL INFECTIONS:

CRP IN DENTAL CARIES:

Dental caries is a multifactorial disease. Generally, our oral cavity consists of many symbiotic microbial communities such as Streptococcus species and Saprophytic bacteria which are harmless to our body. Due to some denaturing environmental conditions, an increase in the oral pathogenic content occurs which

causes decreases in pH by the release of acid and increases demineralization of enamel. Due to this, bacteria and its products enter into the enamel and causes destruction of organic substances and demineralization of inorganic substance of the tooth. Salivary contents like calcium, phosphate, bicarbonates and fluorides help in the remineralization of enamel in the area of demineralization. If the defense mechanisms succeed, then defective enamel gets remodeled. If there is failure of the defensive mechanisms , the bacteria proliferate largely and dominate the entire dentin. The CRP in the saliva then increases due to the presence of enamel caries, since immune cells are not present in enamel itself to stimulate the hepatocytes to produce the CRP. The proliferation and metabolic activity of these microorganisms leads to the release of bacterial components into dentinal tubules which diffuse towards the pulp, whereas the dentin demineralization enables the bioactive molecules to be released from the dentin matrix. Recognition of bacterial components by host cells at dentin – pulp interface, triggers host protective events such as inflammatory and immune responses[6,7].

The antimicrobial action is exerted by causing pores in the cell wall of bacteria which causes leakage of the contents and kills bacteria. If the defensive mechanisms succeed, the microorganisms are inhibited and the pathway of microorganisms gets repaired and regenerated by the formation of reactionary dentin by pre-existing odontoblasts. Reparative dentin is formed by the new odontoblastlike cells. If the defensive mechanism fails, the bacteria enter into the pulp, and causes activation of immune cells resulting in release of pro-inflammatory cytokines and an increase in CRP concentration by increasing vascular dilation and vascular permeability. Pulpal necrosis occurs leading to peri-radicular lesions. CRP concentration increases in saliva in case of enamel and dentin carious conditions but in case of pulpal inflammation, CRP is increased in plasma and Gingival Crevicular Fluid (GCF) (FIGURE 2) [8-13].

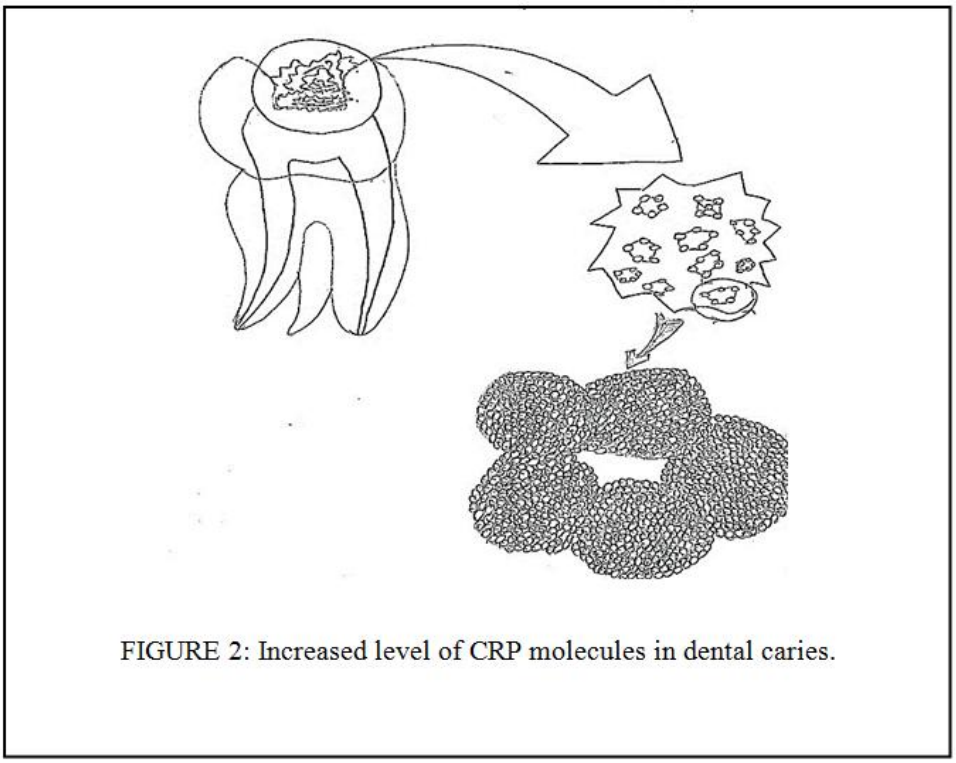

FIGURE 2: Increased level of CRP molecules in dental caries.

CRP IN PERIODONTAL INFECTIONS:

When the bacteria and their toxins enter into the peri-radicular area from the pulp (through peri-apical foramen) and GCF, it tends to causes infection and inflammation of that particular site.This activates the monocytes, macrophages, lymphocytes, neutrophils and dendritic cells resulting in the production of anti-inflammatory cytokines by the activation of humoral and cell- mediated immunity and certain antibodies like Ig G and Ig M. Thus, whenever the bacteria come in contact with the host immune cells in periapical areas, the immune cells bind with the bacteria through their Pathogen Recognizing Receptor (PRR).

But the bacteria have a tendency to mutate themselves and escape from these receptors. Therefore, in case of innate immunity, the host cells contain receptors which recognize certain structures on microbes called Microbial Associated Molecular Pattern (MAMP) / Pathogen Associated Molecular Pattern (PAMP) – such as fimbriae, lipopolysaccharides, lipoproteins, outer membrane protein and heat shock proteins. Since, the MAMP'S/PAMP'S do not undergo any mutation, they can easily be identified and recognized.

CRP gets increased in plasma and activates the complement system through lectin pathway leading to activation of opsonization/ lysis/phagocytic processes, by vasodilation and increased vascular permeability activity. If defensive mechanisms succeed, the microorganisms are inactivated and pro-inflammatory cytokines gets reduced by anti-inflammatory cytokines leading to repair and regeneration of the tissue.

If defensive mechanisms fail, then the bacteria invade deeper into the periapical area resulting in death of aerobic microorganisms leading to liquefaction necrosis and an increase in pro-inflammatory cytokines. Finally, distension of PDL and extrusion of tooth results in tenderness, formation of cyst, abscess and granuloma. If irritant still persists, loss of alveolar bone occurs. With appropriate management, CRP can reduce. According to the severity and extension of periapical lesions, an increase in circulating CRP concentrations can occur (FIQURE 3)[14-17].

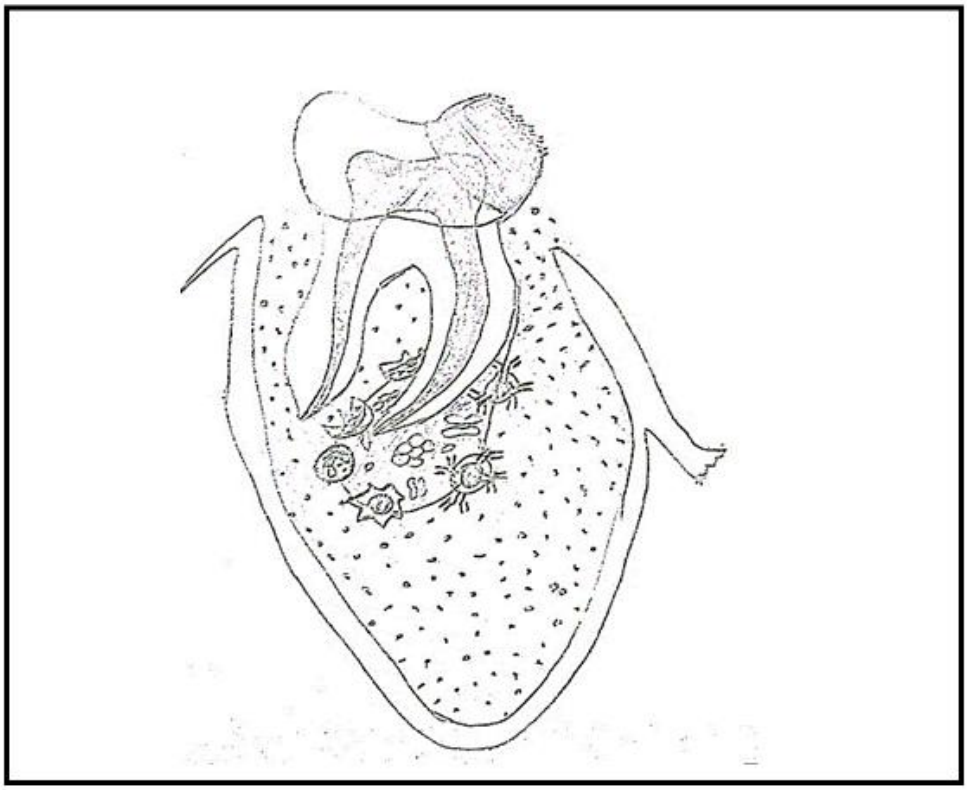

FIGURE 3: Increased levels of CRP in GCF and saliva in periodontal disease and alveolar bone loss.

CRP IN DENTAL EMERGENCY:

CRP levels increases in patients associated with infections secondary to mandibular fracture, post-operative complications followed by tooth extraction and odontogenic infections. Reduction of CRP levels occur following successful treatment. Persistent high serum CRP levels is a marker of underlying tissue damage in these patients. Quik Read CRP is a useful tool in assessing the serum CRP levels in patients with acute odontogenic infections.

CRP IN LESIONS OF ENDODONTIC ORIGIN:

Apical periodontitis is a non - specific local inflammatory response to the bacteria in necrotic dental pulp. Research suggests that CRP and biomarkers such as IL-1, 2 and 6 are increased in apical periodontitis. A significant decrease in the CRP serum levels have been noticed after completion of root canal treatment. Symptomatic apical abscess has been associated with the high IL-6.

CRP IN COVID-19:

The main pathological changes of COVID-19 are through lung and immune system damage. Elevated levels of upto 86% of CRP are observed in severe COVID-19 patients. Mohammed Khaleel et al ., assessed the severity of symptoms in COVID-19 patients from different disease centers such as CDC and WHO and noticed a significant increase in symptoms in patients with poor oral health status(Figure 4)[30].

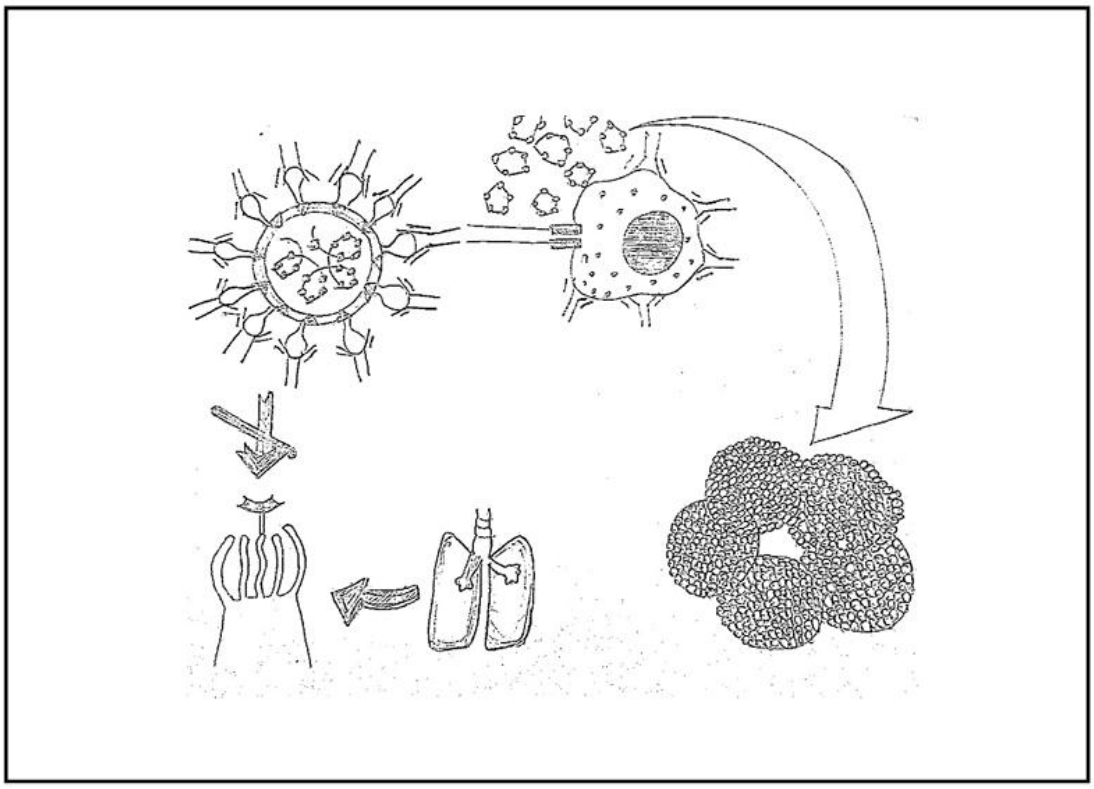

FIGURE 4: Increased levels of CRP in COVID-19 patients by inhibiting the ACE inhibitors followed by the production of antibodies.

II. CONCLUSION:

CRP levels are increased in dental infections like dental caries, periodontal infections, bone resorption, endodontic infections and oral malignancy. It can be easily measured and is very stable in serum or plasma with very marginal fluctuations. It is also more cost effective than the emerging risk markers. Thus, CRP evaluation may provide an inexpensive, reliable and simple method to detect or predict dental infection globally, enabling research for preventive approaches.

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