Review Article

C-REACTIVE PROTEIN

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ABSTRACT

C-reactive protein (CRP) is synthesized in the liver after macrophages and T-lymphocytes secrete interleukins. It is an acute phase protein, and the normal concentration ranges from 0.8 mg/L to 3 mg/L. It is used as a marker of inflammation. CRP levels are increased in infection,trauma, necrosis, malignancy, and allergic reactions. Patients having elevated CRP are at risk of suffering from diabetes, hypertension, and cardiovascular disease. CRP levels are reduced after exercise. COVID-19 positive patients also had increased CRP levels in Wuhan, China.

Key Words: C-reactive protein, Necrosis, CVID-19, Hypertension

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INTRODUCTION

C-reactive protein (CRP) is an inflammatory biomarker formed in the liver in reaction to interleukin secretion by macrophages and T-lymphocytes. Its normal serum CRP level is 0.8 – 3 mg/L; its level increases in patients having inflammation infection, necrosis, malignancy, and allergic conditions. Patients with higher CRP levels have an increased risk of developing diabetes, hypertension, and cardiovascular disease. Its levels are reduced after exercise.

History and genetic

In the plasma, the c-reactive protein is present as an annular pentameric protein.[1]Its discovery was made in 1939 by Tillet and Francis.[2] It is formed in the liver following the secretion of interleukin by macrophages and T cells.[3] It was first detected in patients' serum with acute inflammation,which reacted to pneumococcal cell membrane polysacrharide.

[4]The chromosome 1 (1Q 23.2)[5] contains the CRP gene. Its structure is composed of 5 monomers. Each has 224 amino acids.[6]Its molecular mass is 2.5106 da.[7]

Functions

The complement system is activated by binding CRP with bacterial cell membrane polysaccharides leading to the removal of recrotex, apoptive cells, bacteria, and phagocytosis by macrophages.[8]Secretion of IL-6 from macrophages[9] and adipocytes[10]causes the acute phase response in response to a number of acute and chronic inflammatory conditions,including bacterial, fungal, and viral infections, rheumatic fever, tissue injury, and necrosis.[11]Normal CRP levels is 0.8 – 3.0 mg/dL. CRP levels increase with age.[12]TNF-α and TGF-β can increase CRP. The highly suggestive level of serum CRP for inflammation due to bacterial infection is 100 – 500 mg/dL. When the inflammation subsides, serum CRP levels fall rapidly.[13]Secretion of CRP

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from liver cells is inhibited by interferon alpha and liver failure.[14,15]

Important Uses

For Diagnosis

Serum CRP acts as a marker of inflammation. Measurement of serum CRP is a useful indication of the disease progress and effectiveness of treatment.[16,17]As compared to erythrocyte sedimentation rate (ESR),serum CRP is a more accurate and sensitive indicator of the acute phase response.[18,19]

Cardiovascular disease

Individuals with higher levels of serum CRP have a higher risk of developing diabetes., hypertension, and cardiovascular disease.[20,21]Statins are useful in patients having increased CRP.[22,23]Exercise reduces CRP levels in patients with coronary artery disease.[24]It is a nonspecific indicator in patients having coronary artery disease.[25,26]

Fibrosis and inflammation

In patients with scleroderma, polymyositis, and systemic lupus erythematosus, serum CRP levels are not raised.[27,28]CRP levels are raised in Crohn's disease and inflammatory bowel disease (IBD). and ulcerative colitis.[29]Low risk of colon cancer is associated with low-grade inflammation.[30]

Obstructive sleep apnea

Obstructive sleep apnea (OSA) patients have increased IL-6 and OSAserum CRP levels, an effect thatis reduced by continuous positive airway pressure.[31]

Rheumatoid arthritis

Higher levels of CRP are associated with the severity of rheumatoid arthritis and its common comorbidities, such as metabolic syndrome, diabetes, cardiovascular disease,and interstitial lung disease.[32,33]

Viral infection

In patients of avian flu H7N9, serum CRP levels are higher than in patients with H1N1 influenza.[34]In Wuhan, China,patients had higher CRP levels during the COVID-19 epidemic.[35-37]

CONCLUSION

Measurement of serum CRP is useful in determining the disease progress or effectiveness of treatment.

AUTHOR'S CONTRIBUTION

NH: Conception of work and supervision
MSA: Drafting article and critical review

REFERENCES

1. Thompson D, Pepys MB, Wood SP. The physiological structure of human C-reactive protein and its complex with phosphocholine. Structure. 1999 Feb 15;7(2):169-77. doi:10.1016/S0969-2126(99)80023-9. PMID 10368284.
2. Rodwell VW, Bender DA, Botham KM, Kennelly PJ, Weil A. Illustrated Biochemistry. New York: McGraw-Hill; 2015.
3. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest 2003 Jun 15;111(12):1805-12. doi:10.1172/JCI18921.
4. Pathak A, Agrawal A. Evolution of C-reactive protein. Frontiers in immunology. 2019 Apr 30;10:943.
5. Yang M, Derbyshire MK, Yamashita RA, Marchler-Bauer A. NCBI's conserved domain database and tools for protein domain analysis. Current protocols in bioinformatics. 2020 Mar;69(1):e90.
6. Mateescu AL, Mincu NB, Vasilca S, Apetrei R, Stan D, Zorilă B, Stan D. The influence of sugar–protein complexes on the thermostability of C-reactive protein (CRP). Scientific Reports. 2021 Jun 21;11(1):13017.
7. Enocsson H, Karlsson J, Li HY, Wu Y, Kushner I, Wetterö J, Sjöwall C. The

complex role of C-reactive protein in systemic lupus erythematosus. J Clin Med. 2021 Dec 13;10(24):5837. doi:10.3390/jcm10245837.
8. Hart PC, Rajab IM, Alebraheem M, Potempa LA. C-reactive protein and cancer—diagnostic and therapeutic insights. Frontiers in immunology. 2020 Nov 19;11:595835.
9. Lau DC, Dhillon B, Yan H, Szmitko PE, Verma S. Adipokines: molecular links between obesity and atheroslcerosis. Am J Physiol Heart Circ Physiol. 2005 May;288(5):H2031-41. doi:10.1152/ajpheart.01058.2004.
10. Mantovani A, Garlanda C, Doni A, Bottazzi B. Pentraxins in innate immunity: from C-reactive protein to the long pentraxin PTX3. J Clin Immunol. 2008 Jan;28:1-3. doi:10.1007/s10875-007-9126-7.
11. Mold CA, Nakayama SH, Holzer TJ, Gewurz H, Du Clos TW. C-reactive protein is protective against Streptococcus pneumoniae infection in mice. J Exp Med. 1981 Nov 1;154(5):1703-8. doi:10.1084/jem.154.5.1703.
12. Enocsson H, Gullstrand B, Eloranta ML, Wetterö J, Leonard D, Rönnblom L, et al. C-reactive protein levels in systemic lupus erythematosus are modulated by the interferon gene signature and CRP gene polymorphism rs1205. Front Immunol . 2021 Jan 28;11:622326. doi:10.3389/fimmu.2020.622326.
13. Grützmeier S, Von Schenck H. Four immunochemical methods for measuring C-reactive protein in plasma compared. Clin Chem. 1989 Mar 1;35(3):461-3. doi:10.1093/clinchem/35.3.461.
14. Helal I, Zerelli L, Krid M, ElYounsi F, Maiz HB, Zouari B, Adelmoula J, Kheder A. Comparison of C-reactive protein and high-sensitivity C-reactive protein levels in patients on hemodialysis. Saudi J Kidney Dis Transpl. 2012 May 1;23(3):477-83.
15. Zhou C, Yang X, Zhang C, Zhang S, Zhang P. Fluorescent CdSe/ZnS quantum dots incorporated poly (styrene-co-maleic anhydride) nanospheres for high-sensitive C-reaction protein detection. Surfaces and Interfaces. 2021 Jun 1;24:101057.
16. Dittrich S, Tadesse BT, Moussy F, Chua A, Zorzet A, Tängdén T, et al. Target product profile for a diagnostic assay to differentiate between bacterial and non-bacterial infections and reduce antimicrobial overuse in resource-limited settings: an expert consensus. PloS one. 2016 Aug 25;11(8):e0161721. 2016PLoSO.1161721D. doi:10.1371/journal.pone.0161721.
17. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA. 2001 Jul 18;286(3):327-34. doi:10.1001/jama.286.3.327.
18. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA. 2001 Jul 18;286(3):327-34.doi:10.2337/db06-0922.
19. Lopez-Garcia E, Schulze MB, Meigs JB, Manson JE, Rifai N, Stampfer MJ, Willett WC, Hu FB. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. J Nutr.2005 Mar 1;135(3):562-6. doi:10.1093/jn/135.3.562.
20. Sindhu S, Singh HK, Salman MT, Fatima J, Verma VK. Effects of atorvastatin and rosuvastatin on high-sensitivity C-reactive protein and lipid profile in obese type 2 diabetes mellitus patients. J PharmacolPharmacother.

2011 Dec;2(4):261-5. doi:10.4103/0976-500X.85954.
21. Jialal I, Stein D, Balis D, Grundy SM, Adams-Huet B, Devaraj S. Effect of hydroxymethyl glutaryl coenzyme a reductase inhibitor therapy on high sensitive C-reactive protein levels. Circulation. 2001 Apr 17;103(15):1933-5. doi:10.1161/01.CIR.103.15.1933.
22. Heart Protection Study Collaborative Group. C-reactive protein concentration and the vascular benefits of statin therapy: an analysis of 20 536 patients in the Heart Protection Study. The Lancet. 2011 Feb 5;377(9764):469-76. doi:10.1016/S0140-6736(10)62174-5.
23. Swardfager W, Herrmann N, Cornish S, Mazereeuw G, Marzolini S, Sham L, Lanctôt KL. Exercise intervention and inflammatory markers in coronary artery disease: a meta-analysis. Am Heart J. 2012 Apr 1;163(4):666-76. doi:10.1016/j.ahj.2011.12.017.
24. Lloyd-Jones DM, Liu K, Tian L, Greenland P. Narrative review: assessment of C-reactive protein in risk prediction for cardiovascular disease. Ann Intern Med. 2006 Jul 4;145(1):35-42. doi:10.7326/0003-4819-145-1-200607040-00129.
25. Bower JK, Lazo M, Juraschek SP, Selvin E. Within-person variability in high-sensitivity C-reactive protein. Arch Intern Med. 2012 Oct 22;172(19):1519-21. doi:10.1001/archinternmed.2012.3712.
26. Qi X, Tester RF. Fructose, galactose and glucose–In health and disease. Clinical nutrition ESPEN. 2019 Oct 1;33:18-28.
27. Clearfield MB. C-reactive protein: a new risk assessment tool for cardiovascular disease. Journal of Osteopathic Medicine. 2005 Sep 1;105(9):409-16.
28. Sidore C, Busonero F, Maschio A, Porcu E, Naitza S, Zoledziewska M, et al. Genome sequencing elucidates Sardinian genetic architecture and augments association analyses for lipid and blood inflammatory markers. Nat Genet. 2015 Nov;47(11):1272-81. doi:10.1038/ng.3368.
29. Lu H, Ouyang W, Huang C (April 2006). "Inflammation, a key event in cancer development". Mol Cancer Res. 4 (4): 221–33. doi:10.1158/1541-7786.
30. Allin KH, Nordestgaard BG. Elevated C-reactive protein in the diagnosis, prognosis, and cause of cancer. Crit Rev Clin Lab Sci. 2011 Aug 1;48(4):155-70. doi:10.3109/10408363.2011.599831.
31. Latina JM, Estes N3, Garlitski AC. The relationship between obstructive sleep apnea and atrial fibrillation: a complex interplay. Pulm Med. 2013 Oct;2013. doi:10.1155/2013/621736.
32. Pope JE, Choy EH. C-reactive protein and implications in rheumatoid arthritis and associated comorbidities. InSemin Arthritis Rheum2021 Feb 1 (Vol. 51, No. 1, pp. 219-229). WB Saunders. doi:10.1016/j.semarthrit.2020.11.005.
33. Ammitzbøll C, Steffensen R, Bøgsted M, Hørslev-Petersen K, Hetland ML, Junker P, et al. CRP genotype and haplotype associations with serum C-reactive protein level and DAS28 in untreated early rheumatoid arthritis patients. Arthritis Res Ther . 2014 Oct 31;16(1):475. doi:10.1186/s13075-014-0475-3.
34. Wu W, Shi D, Fang D, Guo F, Guo J, Huang F, Chen Y, Lv L, Li L. A new perspective on C-reactive protein in H7N9 infections. Int J Infect Dis. 2016 Mar 1;44:31-6.. doi:10.1016/j.ijid.2016.01.009.
35. Vasileva D, Badawi A. C-reactive protein as a biomarker of severe H1N1 influenza. Inflammation Research. 2019 Jan 15;68:39-46. . doi:10.1007/s00011-018-1188-x.

36. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Yu T. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet. 2020 Feb 15;395(10223):507-13. doi:10.1016/S01406736(20)302117.

37. Zhang J, Zhou L, Yang Y, Peng W, Wang W, Chen X. Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics. Lancet Respir Med. 2020 Mar 1;8(3):e11-2. . doi:10.1016/S2213-2600(20)30071-07159020.