

## C-Reactive protein vs. high - sensitivity C - reactive protein: What is the difference?

[C-Reaktif protein ve yüksek duyarlıklı CRP: Fark nerede?]

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C-reactive protein (CRP) is an acute phase reactant produced by liver under the control of cytokines, especially by interleukin-6. CRP is commonly measured as a non-specific acute phase protein in inflammatory, infectious and neoplastic cases and in tissue damage for a long time. CRP is present in plasma at a concentration <5 mg/L and concentrations >5 to 10 mg/L show the presence of overt infection or inflammation [1,2]. In healthy young adult volunteers the median CRP concentration is 0.8 mg/L, the 90<sup>th</sup> percentile is 3.0 mg/L, and the 99<sup>th</sup> percentile is 10 mg/L, and following an acute phase case, CRP concentrations may increase 10 000-fold [3].

CRP is measured by immunoassays, mostly by immunoturbidimetric and nephelometric techniques for routine monitoring of infectious or inflammatory processes, and detection limits of these assays are 3 to 5 mg/L [4]. In the mid-1990s, more sensitive CRP immunoassays than those previously used were developed by use of ultrasensitive ELISA or particle - enhanced techniques and these assays were named as “high-sensitivity” or “highly sensitive” CRP (hs-CRP). In general, detection limits of these assays are <0.3 mg/L and limits of quantification are in a concentration range of 0.11 to 0.31 mg/L [5]. Currently, within - laboratory analytical imprecision of hs-CRP assays are less than 10% [2].

It has been well established that inflammation is essential for cardiovascular disease pathogenesis [3]. In this connection, in the last 15 - 20 years, several prospective epidemiologic studies have demonstrated that hs-CRP is an indicator of upcoming vascular events such as acute myocardial infarction, stroke or peripheral vascular disease [6-10]. Hs-CRP is also associated with diabetes mellitus, metabolic syndrome, hypertension, and obesity [11-13]. Based on this information, hs-CRP is accepted as a biomarker for the assessment of cardiovascular risk and proposed as a component of Reynolds Risk Score for calculation of 10 years risk in addition to age, blood pressure, cholesterol concentration, smoking, and genetic susceptibility [14]. In summary, hs-CRP is a cardiovascular risk biomarker rather than an overt inflammatory biomarker. However, currently, use of hs-CRP for this aim is highly criticized because of high individual biological variability of CRP and relatively high assay imprecision [15-17]. Fortunately, the assay calibrators are traceable to WHO Reference Material 85-506, so there is not a harmonisation problem presently.

In this issue of Turkish Journal of Biochemistry, Günel *et al.* [18] present a study on some inflammatory markers and acute phase reactants such as neopterin, procalcitonin, erythrocyte sedimentation rate, and hs-CRP during

acute *Brucella* infection and extracellular bacterial infections. Although the study is well performed, there is concern because of hs-CRP measurement during an acute bacterial infection. As mentioned above, hs-CRP is used to measure lower CRP concentrations for risk assessment of cardiovascular events. On the other hand, it can be encountered with analytical problems like linearity and antigen excess or “hook effect” in hs-CRP assays when measuring sera of patients with acute bacterial infection. Thus the authors used an ELISA assay (DIASource, Belgium) in the study, and the linearity limit is given as 160 000 ng/mL (so 160 mg/L) in the kit insert. This linearity limit can be achieved by predilution and all the samples are prediluted in 1/20 ratio in the assay procedure.

In conclusion, although the authors used a hs-CRP ELISA kit for measurements in sera of patients with acute bacterial infection, they could assay the sera simply by traditional CRP kits and in this case they would not be encountered with linearity and hook effect problems. Traditional CRP and hs-CRP are the same entity, the difference between them are arisen essentially from different analytical sensitivities and assay ranges.

**Conflict of interest:** none

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