

## C-reactive Protein Interpretation May Be Compromised in Paediatric Patients with Plethora

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**Introduction.** C-reactive protein (CRP) is an acute-phase reactant that serves as an early marker of inflammation or infection. Human CRP is composed of five identical nonglycosylated polypeptide subunits, each composed of 206 amino acid residues. The protein is synthesised in the liver and is normally found in the blood at concentrations of less than 5 mg/L. CRP levels rise rapidly within the first six to eight hours during infectious or inflammatory disease states, making it an excellent clinical marker for diagnosis and monitoring. Since patients' management relies heavily on CRP status, all factors that could potentially influence CRP levels are of particular interest.

**Aim, Materials and Methods.** The aim of the study was to explore the relationship between plethora and CRP in paediatric patients in a bulk cohort. 90,739 parallel blood tests (Advia 2120i, Siemens) and turbidimetric CRP tests (Cobas 60000, Roche) performed in Riga Children's Clinical University Hospital Laboratory in 2008–2013 were retrospectively analysed. The anonymised results were obtained from Riga Children's Clinical University Hospital Laboratory LIS ("Dialab"). Patients with anemia and haematooncological patients were excluded. Plethora was defined as haematocrit (HCT) above age and gender specific normal range. CRP > 5 mg/L was considered elevated. Genders were analysed separately; the patients were assigned to six age groups: birth to 28 days, 1–11 months, 1–2 years, 3–6 years, 7–12 years and 13 to < 18 years. Statistics were performed by MS Excel and IBM SPSS v23 (custom tables for medians, Mann-Whitney U for differences and Spearman rho for correlations).

**Results.** Plethora was found in 879 cases (9.7%). Preliminary screening revealed that CRP in patients with plethora was significantly lower (median 1.2 vs. 2.4 mg/L,  $p < 0.001$ ); frequency of CRP > 5 mg/L was lower, too (27.1 vs. 38.6%,  $p < 0.001$ ). On the other hand, the plethoric and non-plethoric cohorts were not directly comparable both by gender (M:F for the former 1.87 vs. 1.14 for the latter) and by age (123 vs. 45 months),  $p < 0.001$  for both. At the same time, CRP level and CRP > 5 mg/L rate highly significantly correlated with age and gender ( $p < 0.001$  for all), making it necessary to cross-section the cohort. The difference remained when the genders were analysed separately. In girls, CRP was 1.20 mg/L in plethora vs. 2.21 mg/L in non-plethoric samples and the rate of CRP > 5 mg/L 20.9 vs. 37.9%; in boys – 1.20 vs. 2.50 mg/L, elevated CRP rate 30.4 vs. 39.3,  $p < 0.001$  for all. Analysis of the age groups revealed significant differences for CRP level in groups 1–11 months (1.59 vs. 1.70 mg/L,  $p = 0.003$ ), 1–2 years (1.47 vs. 3.63 mg/L,  $p < 0.001$ ), 3–6 years (1.30 vs. 3.67 mg/L,  $p = 0.001$ ) and 13–17 years (1.00 vs. 1.5 mg/L,  $p = 0.001$ ). Frequency of elevated CRP was lower in plethora in groups 0–28 days (5.9 vs. 23.0%,  $p = 0.035$ ), 1–2 years (25.7 vs. 44.4%,  $p < 0.001$ ), 3–6 years (33.1 vs. 45.0%,  $p = 0.008$ ) and 13–17 years (22.0 vs. 34.4%,  $p < 0.001$ ). After the cohort was normalised by age and gender, the difference became particularly striking:  $p = 8.4E-97$  for CRP level and  $p = 2.9E-179$  for CRP < 5 mg/L.

**Conclusions.** The study demonstrated that CRP level is significantly lower in paediatric patients with plethora when compared to patients with normal HCT. The phenomenon was observed in both genders, throughout the age groups and in many patients' profiles. Thus, the phenomenon is probably an artefact related to dehydration and could cause significant clinical misinterpretation.

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