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POSTER ABSTRACTS

113.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: BASIC AND TRANSLATIONAL

Assessment of Circulating Retinol Binding Protein-4 Levels in Patients with Compound Heterozygosity for Hb S and β-Thalassemia

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Background: Retinol Binding Protein-4 (RBP-4) is a member of the lipocalin family of proteins and the major transport protein of the hydrophobic molecule retinol, also known as vitamin A, in the circulation. Expression of RBP4 is highest in the liver, where most of the body's vitamin A reserves are stored as retinyl esters. For the mobilization of vitamin A from the liver, retinyl esters are hydrolyzed to retinol, which then binds to RBP-4 in the hepatocyte. After associating with transthyretin (TTR), the retinol/RBP-4/TTR complex is released into the bloodstream and delivers retinol to tissues via binding to specific membrane receptors. While, after its dissociation from TTR and retinol release, retinol-free apo-RBP4 in the circulation is filtrated by the kidney. More than 99% of that is reabsorbed by the proximal renal tubule, which renders urinary RBP-4 a highly sensitive marker for tubular dysfunction. We and other have shown previously that the patients with Sickle Cell Disease (SCD) have deficiencies or suboptimal levels of vitamin A, while recently (Br J Haematol. 2023;doi:10.1111/bjh.18862) higher urine RBP-4 in patients with SCD especially in those with persistent albuminuria but without an association of urine RBP-4 levels with estimated glomerular filtration rate (eGFR). In this context, we aimed to investigate the potential clinical significance of circulating plasma RBP-4 levels and its association with disease features in Caucasian patients with compound heterozygosity for HbS and β-thalassemia (HbS/β^{thal}).

Patients and Methods: Ninety Caucasian adult patients with HbS/β^{thal} at steady phase were included in the study, while 22 apparently healthy individuals of similar age and gender served as controls. None of the patients was diabetic and has received any transfusions at least 6-monthes before enrollment in the study. RBP-4 concentration was measured with an immunoturbidimetric assay applied in an automated chemistry analyzer, along with hematologic, and series of blood chemistry parameters reflecting renal, cardiac and endothelial dysfunction. eGFR values were calculated using the CKD-EPI (Cystatin C and/or Creatinine equations).

Results: We found that: a) Plasma RBP-4 levels were significantly lower in patients with HbS/β^{thal} compared to controls, 30.5±2.7mg/L (Confidence Intervals (CI): 28.8;32.2mg/mL) vs 36.3±3.6mg/L (CI: 32.7;39.9mg/mL), $p<0.003$. The patients with β^{+} genotypehave higher RBP-4 levels than those with β^{0} genotype ($p<0.05$), whereas patients treated with *hydroxycarbamide*(50/90) are more likely to express higher RBP-4 levels, p-trend=0.06; b) RBP-4 levels in patients with HbS/β^{thal} correlated positively with their age, body mass index (BMI) and Hb levels (r=0.264, p=0.012; r=0.334, p=0.001 and r=0.209, $p<0.05$, respectively; c) RBP-4 levels in patients with HbS/β^{thal} correlated with total bilirubin, total cholesterol, triglycerides and uric acid (r=-0.452, $p<0.001$; r=0.395, p=0.004; r=0.292, p=0.015 and r=0.435, $p<0.001$, respectively); d) RBP-4 levels in patients with HbS/β^{thal} correlated negatively with eGFR values rho=-0.360, p=0.003 and hs-CRP concentrations r=-0.309, p=0.004 and e) No correlations were found between RBP-4 levels with markers of cardiac and endothelial dysfunction such as High Sensitivity Troponin T, Growth Differentiation Factor-15, von Willebrand factor antigen, A Disintegrin and Metalloproteinase with Thrombospondin Type 1 Motif 13 antigen and P-Selectin, as well as with number of vaso-occlusive crisis and mean pulmonary arterial pressure in the patients.

Conclusions: These findings demonstrate a multifactorial role of RBP-4 in patients with HbS/β^{thal} as the circulating levels of the protein correlate significantly with markers of erythropoiesis, inflammation and renal function. It is unclear of this study if RBP-4 has any specific functions in patients with HbS/β^{thal}. However, RBP-4 should be more investigated in order to determine its clinical significance and in the case of sickle cell nephropathy both plasma and urine measurements should be considered.

Disclosures No relevant conflicts of interest to declare.

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