

Plasma ^1H NMR profiling of β -thalassemia patients with liver fibrosis

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Thalassemias are amongst the most common genetic diseases worldwide with a complex phenotype ranging from clinically asymptomatic individuals to hemolytic anemia. α - and β - thalassemia, the two forms of these autosomal recessive disorders, are characterized by the decreased or absent production of either the alpha-like or the beta-like globin chains, respectively. Ineffective erythropoiesis and deregulation of iron homeostasis constitute complications of the disease affecting most of organs including liver. The metabolic profile is related to phenotype and biochemical activity. Therefore, this relatively new and promising field, is considered regarding a noninvasive method for the assessment of liver fibrosis severity, on different stages of the disease.

Plasma samples, collected from healthy individuals (n=10) and thalassemia patients with low (F0-1, n=10) and high fibrosis index (F4, n=11), were profiled using ^1H -NMR. Applying specialized pulse sequences, both small molecules-metabolites and lipoproteins information were acquired. Statistical analysis was performed based on univariate and multivariate methods aiming to relate hepatic fibrosis stages/severity with certain metabolite and/or macromolecule profiles.

Our analysis revealed the advantageous profiling of plasma macromolecular entities and more precisely, higher cholesterol was characteristic of healthy samples, while thalassemic patients F0-1 showed increased signals related to lipids methylene signals. Liver fibrotic samples were of lower metabolite and lipid content compared both with healthy and F0-1 samples. Phenylalanine as well as organic acids (lactic, formic and pyruvic acid) were found to be significantly increased in thalassemic samples in contrast to 3-hydroxybutyric acid that was higher in healthy subjects.

Proton-NMR profiling of plasma is a powerful, noninvasive, and holistic method that offers wealth of information from metabolites to lipoprotein entities and shows promises for clinical diagnostics.

Key notes: Thalassemia, Metabolomics, NMR, Plasma, Statistics