Biochemical and hematologic laboratory studies in a cohort of patients with Barth Syndrome

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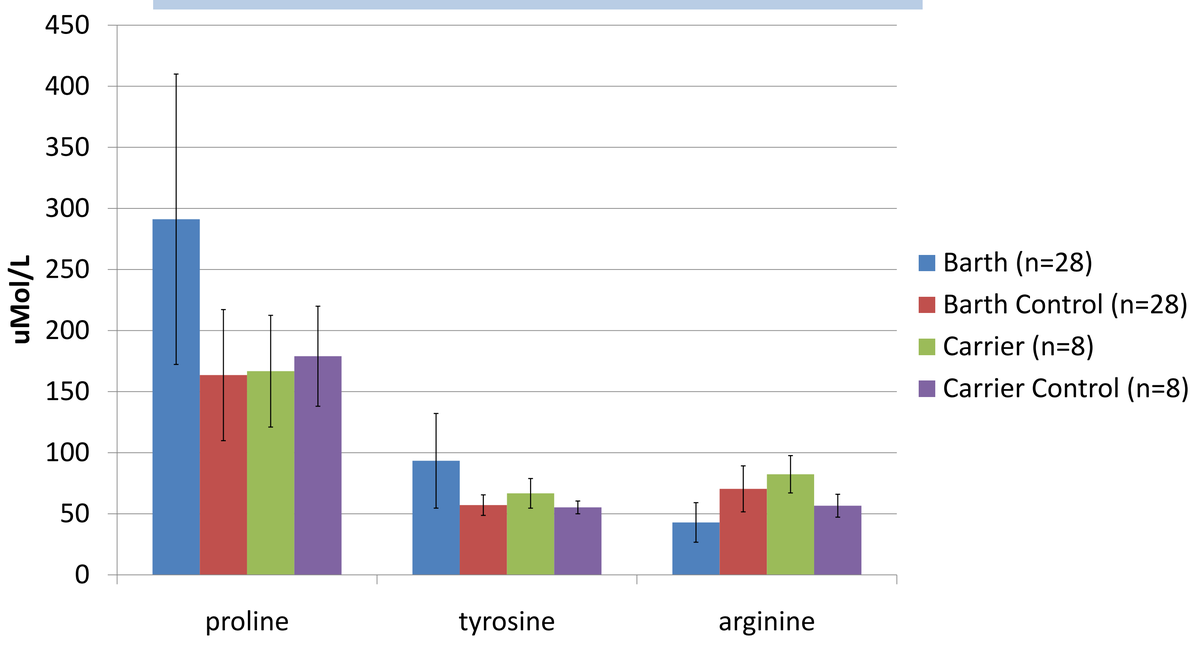
Barth Syndrome (BTHS, MGC type II) is a rare X-linked disorder characterized by dilated cardiomyopathy, skeletal myopathy and neuropenia, caused by defects in Tafazzin. This results in abnormal cardiolipin, a main component of the mitochondrial inner membrane. In order to gain a better understanding of typical clinical laboratory values, we measured hematologic and biochemical values in cohorts of patients and carrier females.

Lab value (normal)	Patients (n)	Value (SD)	Carriers (n)	Value (SD)
MGC plasma (162+/- 68 (SD) nmol/L)	28	1087.5 +/- 435	8	198.2 +/-113
Cholesterol (110-199 mg/dL)	28	137.6 +/- 26	8	202.2 +/- 43
Prealbumin (20-40 mg/dL)	18	16.9 +/-4	n/a	n/a

Prealbumin was low in the majority of BTHS patients, possibly indicating suboptimal liver synthetic ability or specific amino acid deficiencies. Of 55 fatty acids measured in red blood cells, only C16:1 trans fatty acid was different in Barth patients than controls (0.312 ug/mL +/-0.08 vs. 0.820 ug/mL +/- 0.2), indicating that fatty acid composition is not affected by cardiolipin abnormalities.

Amino Acids in Patients and Carriers

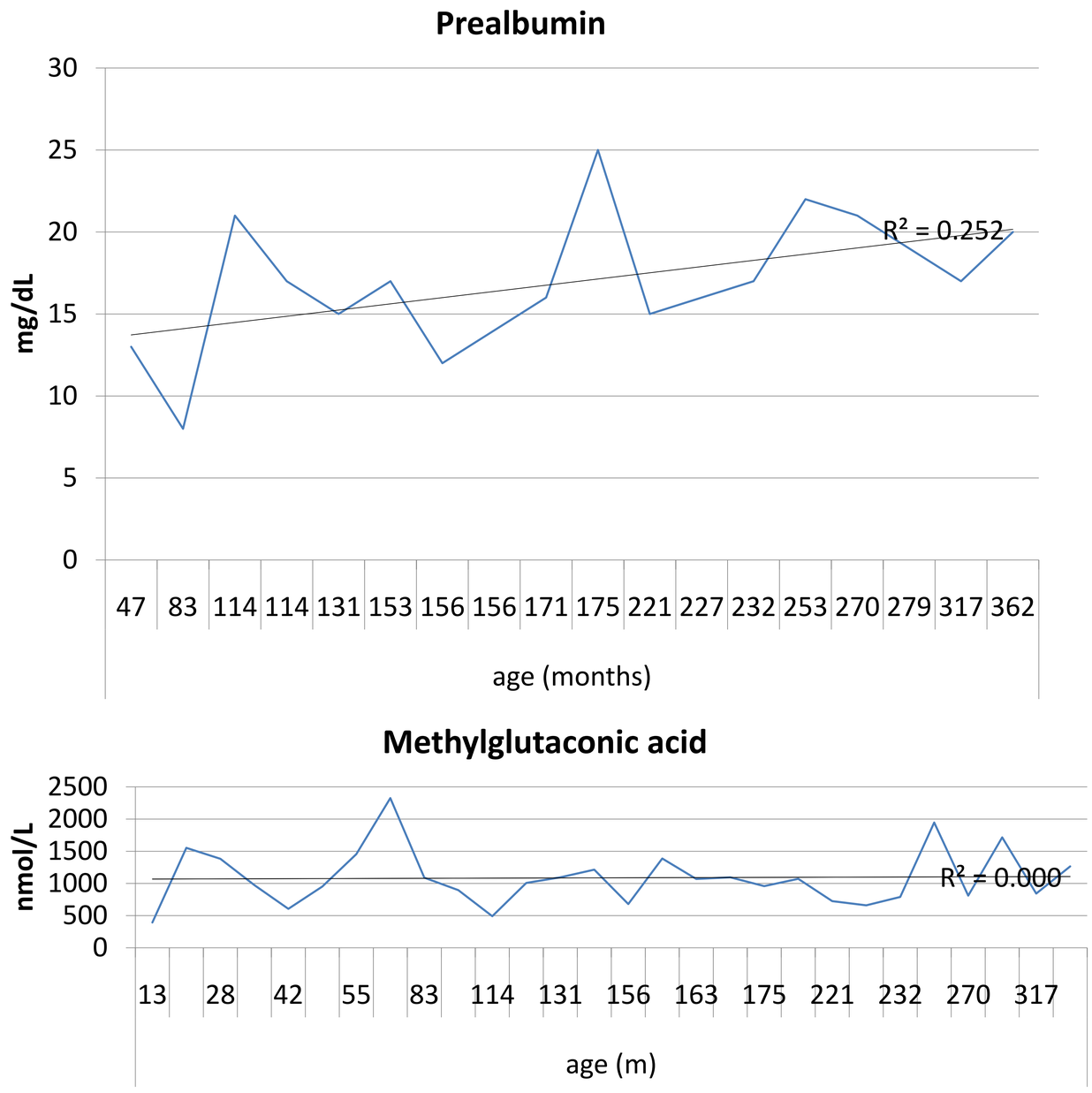


BTHS individuals had a unique amino acid profile, most notable for low arginine, elevated tyrosine and elevated proline. The elevated proline could be related to a chronic lactic acidemia or mislocalization of proline oxidase (a mitochondrial inner membrane (IMM) protein). The tyrosine is potentially indicative of liver dysfunction.

	BTHS Patients (n=17)
Hemoglobin	13.5 +/- 1.4 mg/dL
White blood cells	5664 +/- 1798 cells/mL
Absolute Neutrophil count	1935+/- 1224 cells/mL
Absolute Monocyte count	894+/- cells/mL
Platelets	304 +/- 103 K cells/mL

CBCs were measured in 17 affected individuals. The range for ANC was 300-4900 cells/mL, with 4/17 patients having neutrophil counts <1000 cells/mL. The range for AMC was 500-2400 cells/mL, with 5/17 patients having monocyte counts at or above 1000 cells/mL. R-squared analysis revealed no correlation between 3-MGC and ANC.

R-squared analysis revealed no correlation between age and any laboratory parameter, including amino acids, blood counts, prealbumin and MGC.



Our studies define a unique laboratory profile in individuals with Barth Syndrome, unrelated to age of the individual, which may reflect the pathophysiology caused by abnormal cardiolipin in the IMM. Additionally, we confirm the lack of a biochemical phenotype in female carriers.