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Metabolic profiles of adult survivors of severe acute malnutrition

Introduction
The increasing burden of heart disease and type 2 diabetes in lower middle income countries is likely related to exposure to western style diets; however, in many of these countries severe acute malnutrition (SAM) is also prevalent, resulting in a double burden of nutritional insults. While prenatal undernutrition has been associated with increased risk of later cardiovascular disease (1) the consequences of post-natal undernutrition are unknown. SAM can present as severe wasting or oedematous malnutrition; these phenotypes have distinct metabolic signatures. Children with oedematous malnutrition have lower rates of lipolysis (2) and protein turnover (3) than those with severe wasting. Studies using metabolomic analyses report that children with SAM had metabolic profiles that were different from controls even after recovery from SAM (4). Also, 31 metabolites had lower concentrations in children with oedematous malnutrition on admission (4). This study will investigate the long term risks of SAM by evaluating the cardio-metabolic profiles of adult SAM survivors.
Methods
Subjects: This retrospective analysis utilized a cohort of 1,336 Jamaican adults who were hospitalized as children with a diagnosis of SAM between 1963 and 1993 and age, sex and BMI-matched community controls.
Measurements: Birth weight and height and weight measurements were abstracted from hospital records. Anthropometry, blood pressure, glucose tolerance, insulin sensitivity, arterial stiffness, pulse wave velocity, indirect calorimetry and liver fat were measured in adult SAM survivors and controls. Muscle tissue was collected for epigenetic studies and fasting serum was collected for metabolomic analyses. A targeted metabolomics approach (direct injection flow-mass spectrometry) will be used to quantify acylcarnitines, amino acids, biogenic amines, phospholipids and sphingolipids. Fibroblast growth factors, TNF-α, vitamin D and IGF-I will be measured using ELISA.
Data Analysis: Skewed metabolic data were transformed towards a normal distribution and multiple linear regression analyses were used to assess differences between SAM survivors and controls, and between survivors of non-oedematous and oedematous malnutrition. Regression models were adjusted for age and sex and variably adjusted for height, BMI and birth weight. Metabolomic data will be analyzed using R Statistical Software using principal component analysis, partial least square discriminant analysis and lasso regression analyses.
Results
Children with severe wasting weighed 333g less at birth, and as adults, they had lower BMI and fat mass, greater glucose intolerance and differential gene methylation in metabolic, body composition and cardiovascular pathways compared to survivors of oedematous malnutrition. Survivors of severe wasting had more liver fat than oedematous malnutrition survivors after adjusting for age, sex and BW (β= -2.62, SE = 1.23; P = 0.03). In survivors of severe wasting, liver fat was associated with faster rates of catch-up growth during nutrition rehabilitation (r = 0.449, P = 0.004). Whole body fat oxidation was not associated with liver fat in this population. Metabolomic analyses are pending.
Conclusion
Our data indicate that survivors of severe wasting have higher cardio-metabolic risk than survivors of oedematous malnutrition as adults. Detailed metabolic profiling could provide mechanistic insight into the pathways involved.

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