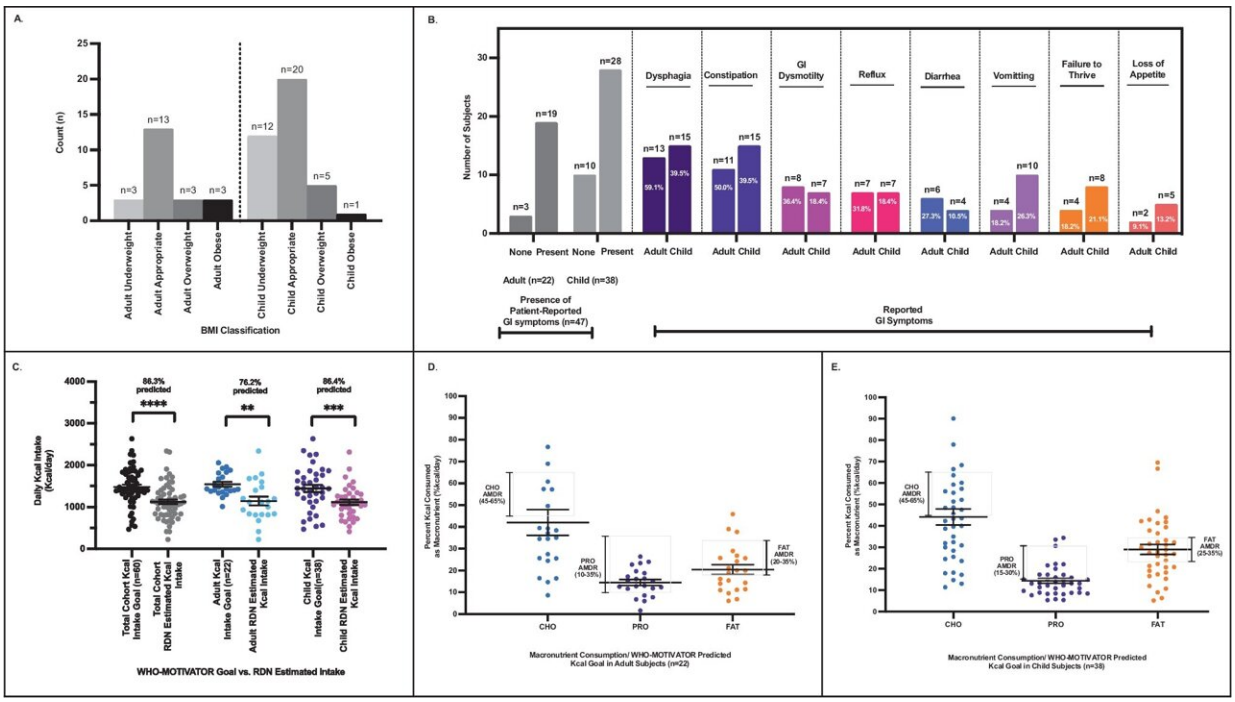
Researchers find about a quarter of mitochondrial disease patients suffer from malnutrition

December 20 2023



A BMI classification. Most subjects had appropriate BMI; 3/22 (13.6%) adults and 12/38 (31.6%) children were underweight. B Patient-reported gastrointestinal symptoms (GI). C Predicted and dietician (RDN)-estimated daily Kcal intake in adult and child subjects. D Macronutrient consumption/WHO-MOTIVATOR predicted Kcal goal in adult PMD subjects. Credit: *Neurotherapeutics* (2023). DOI: 10.1007/s13311-023-01418-9

A healthy diet is a key factor in making sure both children and adults have enough energy to get through the day. However, patients with primary mitochondrial disease have an additional challenge, since mitochondria function as the "batteries" of our cells, and the disease can impair the function of mitochondria and affect energy levels.

Now, a new study from researchers from Children's Hospital of Philadelphia (CHOP) found that most patients with primary mitochondrial disease consume significantly inadequate nutrition on top of their impaired mitochondrial function, emphasizing the urgent need for nutritional intervention in mitochondrial disease patients to improve their clinical outcomes.

The findings were recently published in the journal *Neurotherapeutics*.

Primary mitochondrial disease describes more than 300 distinct genetic disorders impacting multiple systems throughout the body because of impaired metabolism. The most common symptoms of primary mitochondrial disease include muscle weakness, muscle fatigue, exercise intolerance, gastrointestinal symptoms and imbalance. Gastrointestinal problems include difficulty swallowing, slow motility, abdominal pain and distension on eating, diarrhea and constipation. All these symptoms may affect the amount of food consumed.

Mitochondria are critical for converting nutrients from food into energy to power our organs for their everyday functions. While nutritional intervention is a promising therapeutic intervention in mitochondrial disease, knowledge of the ideal dietary strategies to implement is lacking. CHOP researchers conducted this study to define the nutritional status of patients with mitochondrial disease and how this relates to their symptoms. These findings could then be used to guide development of future nutritional strategies to be tested in a clinical trial.

In this study, researchers realized that Activity Factor guidelines set by the World Health Organization to predict total energy expenditure were less relevant to mitochondrial disease as the impact of muscle fatigue on physical activity—a common symptom in mitochondrial disease—was not taken into account. The researchers developed the Mitochondrial Disease Activity Factors (MOTIVATOR) system to better guide estimation of total energy expenditure in mitochondrial disease.

"Results of our prospective study of 22 adults and 38 children with confirmed primary mitochondrial disease revealed that the breadth of nutritional deficiencies that occur in our patients and are not being addressed," said the study's co-first author Donna DiVito, MS, RD, a dietitian in the Division of General Pediatrics at CHOP. "We observed significantly inadequate energy consumption across the patient cohort. Alarmingly, a quarter of the patients in the study met criteria for a diagnosis of malnutrition."

"Many patients with primary mitochondrial disease report symptoms that would impair nutritional intake, including swallowing difficulty, slow gut motility, constipation and poor appetite," said Maria Mascarenhas, MD, an attending physician of in the Division of Gastroenterology and medical director of the Clinical Nutrition Department at CHOP. "These symptoms may further impair food consumption and exacerbate their nutritional status."

The researchers found that the daily diet intake was estimated to be 1,143 calories (kcal) + 104.1 calories in adults and 1,114 calories + 62.3 calories in children, which is less than the standard 2,000 to 2,500 calorie diet recommended for adults. Half of the adults in the study and slightly less than half of children in the study consumed 75% or less of their predicted daily caloric needs, with malnutrition identified in about a quarter of all patients in the study.

Increased protein and fat intake were correlated with improved muscle strength and decreased muscle fatigue, and higher protein, fat and carbohydrate intake was associated with an improved quality of life.

"We hope that our results will inform the mitochondrial disease community of patients, families, physicians, researchers and industry of the critical need for nutritional management in mitochondrial disease patients. Systematic study is urgently needed to identify tolerable and effective nutritional interventions in mitochondrial disease," said senior study author Zarazuela Zolkipli-Cunningham, MBChB, MRCP, an attending physician and the Clinical Research Director of the Mitochondrial Medicine Program at CHOP.

"We also showed that our validated outcome measure of mitochondrial disease, the MM-COAST, provides a meaningful end-point to measure how a patient functions and feels in response to nutritional intervention."

More information: Donna DiVito et al, Optimized Nutrition in Mitochondrial Disease Correlates to Improved Muscle Fatigue, Strength, and Quality of Life, *Neurotherapeutics* (2023). DOI: 10.1007/s13311-023-01418-9

Provided by Children's Hospital of Philadelphia