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Title: Urine metabolomic signature of lysine deficiency in stunted children.

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Abstract (300words)- 278 *without the bold headers below*

A briefing on the main problem studied – The risk of essential amino acid deficiency (EAAD), like lysine in cereal-based diets, can impact growth in young children. Specific urine metabolic signatures can be used for rapid non-invasive screening for EAAD in stunted children, and to design targeted nutritional therapy.

A clear statement of the hypothesis or expected results – A specific urinary metabolic footprint of lysine (EAAD) deficiency and of lysine supplementation can be observed in stunted children.

The methods used to test the hypothesis – A parallel group intervention trial of a daily 3-months lysine supplementation (80 mg/kg/day in an orange flavored drink) was conducted in stunted (height-for-age Z-score <-2SD, n=24) 6-11 years old South Indian children to evaluate urinary biomarkers for EAAD, in comparison with control non-stunted children (n=27) who received an orange flavored placebo drink during study period.

A description of the experimental design and statistical analysis – At baseline and monthly intervals, clinical examinations, height, weight, circumferences (cranial, forearm, upper-arm, waist), skin folds, muscle strength, food intake-recalls were measured, along with urine and blood sampling at baseline and end-line. The urine metabolome was analyzed by Q Exactive orbitrap-based mass spectrometer (Thermo Scientific) using Compound Discoverer (Thermo Scientific). Differences in anthropometry were analyzed by t-test and repeated measures models.

A brief description of the main results – Anthropometric measurements were significantly different (p<0.01) at baseline and end of 3-months. Preliminary urine metabolomic profiles showed a difference between groups in lysine-related metabolites at baseline and an alteration with supplementation. Metabolites of tryptophan degradation and utilization, and related to threonine, methionine, cysteine and branched chain amino acids biosynthesis pathways were also different at baseline between groups and with lysine supplementation.

A synthetic conclusion derived from the data presented – The urine metabolomic profiles with EAAD is different between stunted and non-stunted children at baseline and in response to lysine supplementation. A validation of urine metabolomic profiles using the blood metabolomic profiles could provide more insights towards designing targeted nutritional therapies.