

Supplementary Information

Amino acid derangements in adults with severe falciparum malaria

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Supplementary Materials

Supplementary Fig. S1. Total plasma free amino acid concentrations in adult patients and healthy controls from Bangladesh.

Supplementary Fig. S2a. Individual plasma free amino acids in adult patients and healthy controls from Bangladesh. (Part A).

Supplementary Fig. S2b. Individual plasma free amino acids in adult patients and healthy controls from Bangladesh. (Part B).

Supplementary Fig. S3. Directed acyclic graph for the causal effect identification of L-lactate on the total concentration of plasma free amino acids in adults with severe falciparum malaria.

Supplementary Fig. S4. Phenylalanine:Tyrosine ratio in adult patients with severe falciparum malaria from Bangladesh.

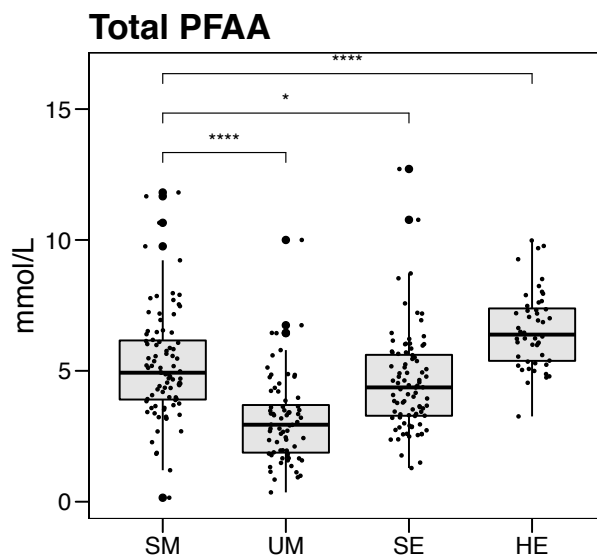


Figure 1. Total plasma free amino acid concentrations in adult patients and healthy controls from Bangladesh (mmol/L). Amino acids were measured by UHPLC-MRM-MS in adults with severe malaria (n=88), uncomplicated malaria (n=71), Sepsis (n=88), and healthy local controls (n=48). Boxplots with medians and inter quartile ranges are shown. Mann-Whitney U test: $p \leq 0.05 = *$, $p \leq 0.01 = **$, $p \leq 0.001 = ***$, $p \leq 0.0001 = ****$.

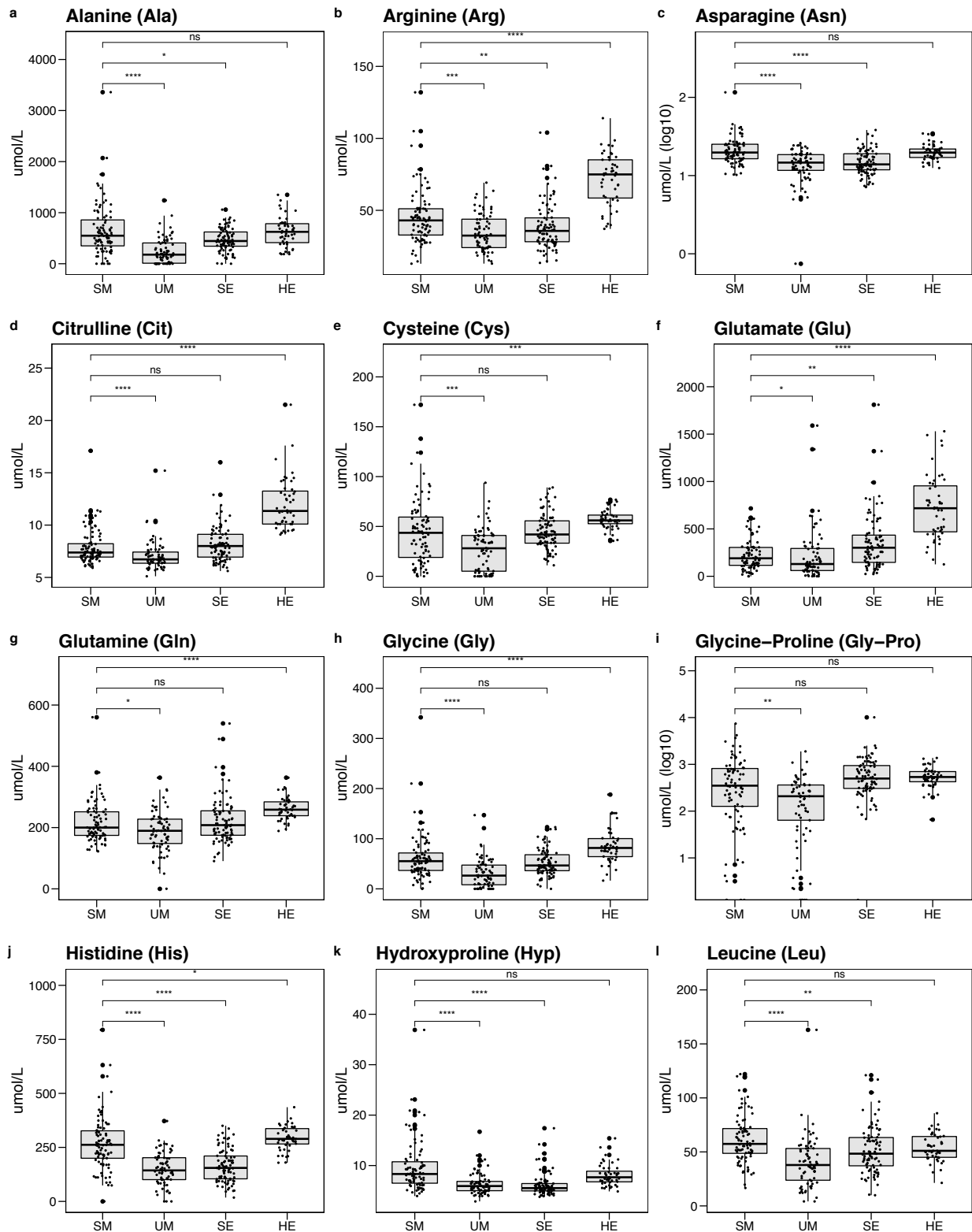


Figure 2. Individual plasma free amino acids in adult patients and healthy controls from Bangladesh; (μmol/L) (Part A). Amino acids were measured by UHPLC-MRM-MS in plasma of study participants (n=295) from Bangladesh. Boxplots with medians and inter quartile ranges are shown. Mann-Whitney U test: $p \leq 0.05 = *$, $p \leq 0.01 = **$, $p \leq 0.001 = ***$, $p \leq 0.0001 = ****$.

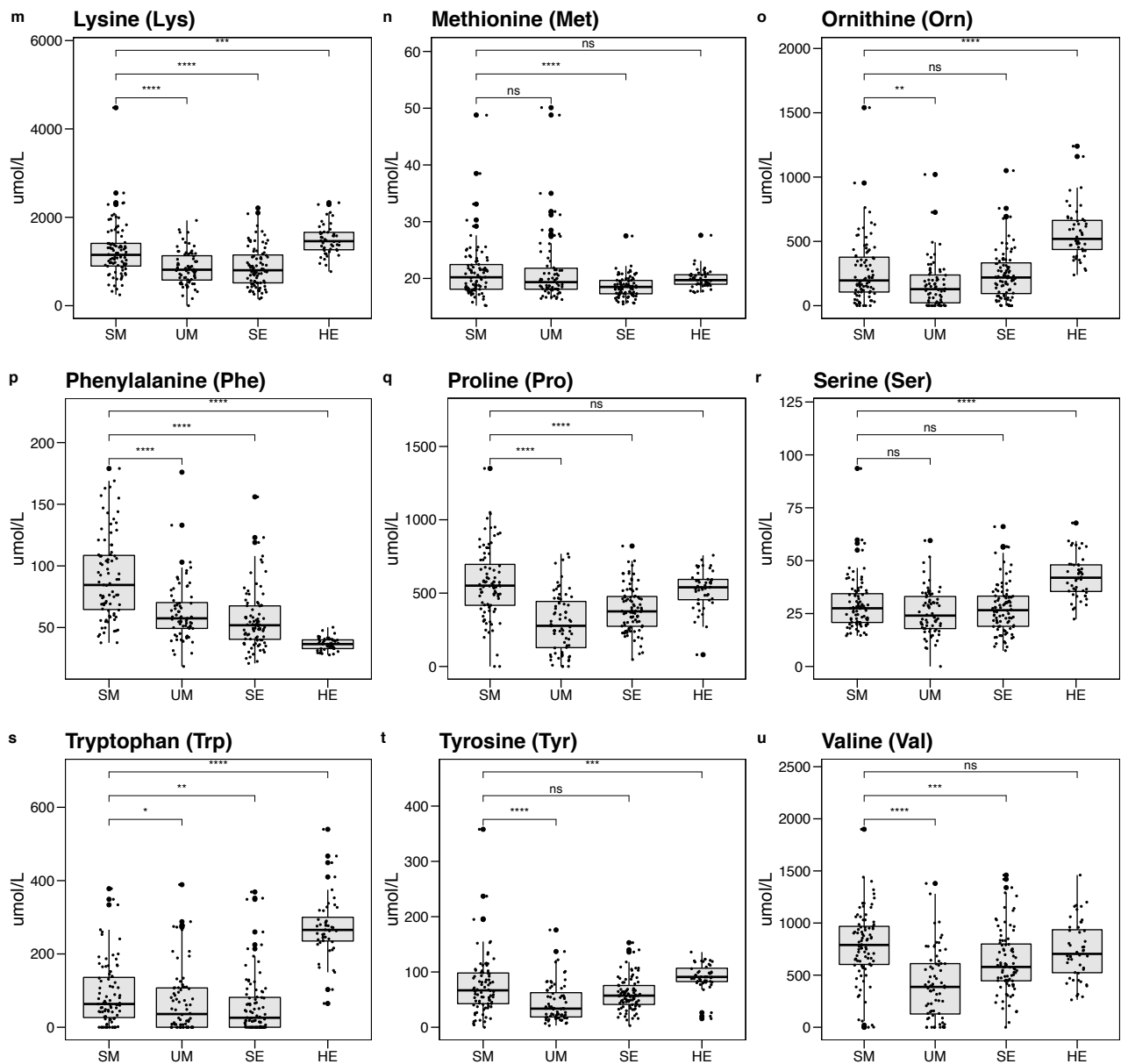


Figure 3. Individual plasma free amino acids in adult patients and healthy controls from Bangladesh; ($\mu\text{mol/L}$) (Part B). Amino acids were measured by UHPLC-MRM-MS in plasma of study participants ($n=295$) from Bangladesh. Boxplots with medians and inter quartile ranges are shown. Mann-Whitney U test: $p \leq 0.05 = *$, $p \leq 0.01 = **$, $p \leq 0.001 = ***$, $p \leq 0.0001 = ****$.

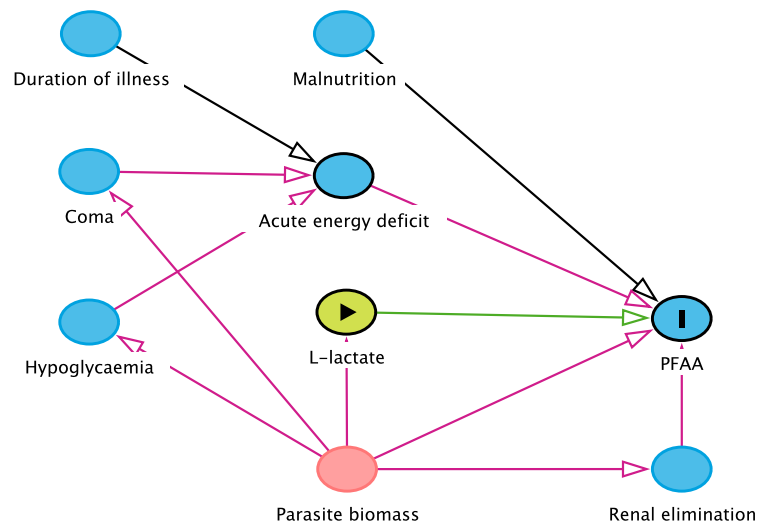


Figure 4. Directed acyclic graph for the causal effect identification of L-lactate on the total concentration of plasma free amino acids in adults with severe falciparum malaria. L-lactate (depicted using the green vertex) was set as the ‘exposure’ variable of interest, and ‘PFAA’ the outcome variable. Each factor is denoted by a vertex in the graph. The direct effect of L-lactate (tissue hypoxia) on PFAA (green pathway) can be derived with minimal sufficient adjustment sets by adjustment for parasite biomass. (reproducible DAG can be found at dagitty.net/mlGs7Fc).

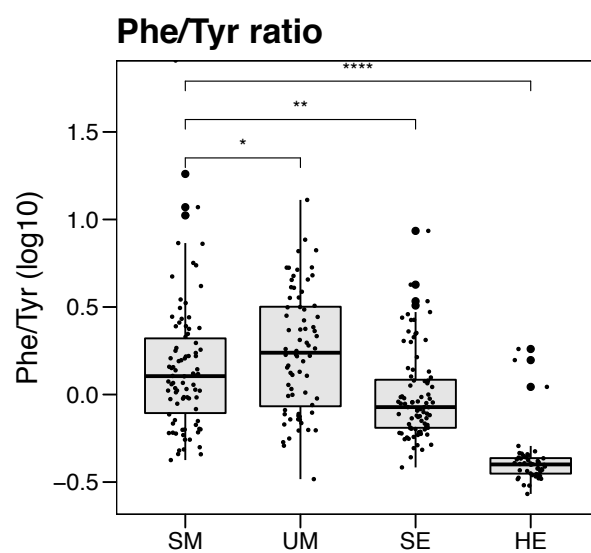


Figure 5. Phenylalanine:Tyrosine ratio in adult patients with severe falciparum malaria from Bangladesh. Boxplots with medians and inter quartile ranges are shown. Mann-Whitney U test: $p \leq 0.05 = *$, $p \leq 0.01 = **$, $p \leq 0.001 = ***$, $p \leq 0.0001 = ****$.