**Supplementary tables S1, S2, S4, S5**

**Reduced serum sphingolipids constitute a molecular signature of malnutrition in hospitalized patients with decompensated cirrhosis**

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**Supplementary Table S1:** Hospital admission diagnoses and length of stay. Categorical variables are expressed as absolute values and frequencies. Continuous variables are expressed as medians with interquartile range (IQR).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Admission Diagnoses** | **Total (N=51)** | **Malnourished (N=22)** | **Nourished (N=29)** | ***P*** |
| **Variceal Bleeding, n (%)** | 5 (9.8%) | 1 (4.5%) | 4 (13.8%) | 0.375 |
| **Hepatic Encephalopathy, n (%)** | 24 (60.9%) | 12 (54.5%) | 12 (41.4%) | 0.405 |
| *Volume Derangements, n (%****)*** | \*\*\* | \*\*\* | \*\*\* | \*\*\* |
| **Ascites or Hydrothorax** | 39 (76.5%) | 17 (77.3%) | 22 (75.9%) | 1.000 |
| **Acute Kidney Injury** | 24 (60.9%) | 12 (54.5%) | 12 (41.4%) | 0.405 |
| *Infections, n (%)* | \*\*\* | \*\*\* | \*\*\* | \*\*\* |
| **Bacterial Peritonitis/Empyema** | 7 (13.7%) | 2 (9.1%) | 5 (17.2%) | 0.684 |
| **Urinary tract infection** | 3 (5.9%) | 2 (9.1%) | 1 (3.5%) | 0.571 |
| **Bacteremia/Endocarditis** | 4 (7.8%) | 2 (9.1%) | 2 (6.9%) | 1.000 |
| **Enteritis/Colitis** | 5 (9.8%) | 2 (9.1%) | 3 (10.3%) | 1.000 |
| **Hospital duration, days** | 7 (3 – 12) | 7.5 (3 – 12) | 7 (3 – 12) | 0.702 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristics** | **Total (N=51)** | **Malnourished (N=22)** | **Nourished (N=29)** | ***P*** |
| ***Inflammatory Cytokines*** |  |  |  |  |
| **Interleukin 1β, pg/ml** | 0.45 (0.45 – 10.43) | 0.45 (0.45 – 3.00) | 0.47 (0.45 – 12.12) | 0.3707 |
| **Interleukin 6, pg/ml** | 39.36 (19.03 – 98.39) | 37.72 (15.12 – 104.01) | 42.74 (20.05 – 82.38) | 0.8791 |
| **Tumor Necrosis Factor α, pg/ml** | 0.17 (0.17 – 1.93) | 0.17 (0.17 – 1.55) | 0.17 (0.17 – 1.93) | 0.6424 |
| ***Glucose Homeostatic Measurements*** |  |  |  |  |
| **Insulin, μU/L** | 25.3 (11.1 – 40.1) | 28.4 (11.7 – 41.0) | 21.2 (11.1 – 38.0) | 0.8047 |
| **Glucose, g/dl** | 119 (96 – 163) | 121 (92 – 163) | 119 (99 – 151) | 0.8047 |
| **HOMA-IR** | 6.9 (3.1 – 13.5) | 7.9 (3.1 – 14.1) | 6.9 (3.4 – 10.4) | 0.7900 |

**Supplementary Table S2:** Inflammatory cytokines and measures of insulin resistance

**Supplementary Table S4:** Pathway analysis reveals that only the sphingolipid metabolism pathway is enriched in metabolites differing between nourished and malnourished cohorts.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Pathway** | **Compounds in Pathway** | | | **All Study Compounds** | | | **Enrichment** | ***P*** |
|  | **Significant (k)** | **Detected (m)** | **Ratio (k/m)** | **Significant (n)** | **Detected (N)** | **Ratio (n/M)** | **[k/m]**  **[n/M]** |  |
| **Sphingolipid** | 12 | 35 | 0.34 | 71 | 747 | 00.1 | 3.61 | 3.11 × 10**-5** |
| **Glycine/Serine/Threonine** | 3 | 10 | 0.3 | 71 | 747 | 00.1 | 3.16 | 0.06 |
| **Plasmalogen** | 3 | 11 | 0.27 | 71 | 747 | 00.1 | 2.87 | 0.08 |
| **Secondary Bile Acid** | 4 | 18 | 0.22 | 71 | 747 | 00.1 | 2.34 | 0.08 |
| **Chemical** | 4 | 18 | 0.22 | 71 | 747 | 00.1 | 2.34 | 0.14 |
| **Long Chain Fatty Acid** | 3 | 14 | 0.21 | 71 | 747 | 00.1 | 2.25 | 0.39 |
| **Aminosugar** | 1 | 5 | 0.2 | 71 | 747 | 00.1 | 2.1 | 0.39 |
| **Glycolysis/Gluconeogenesis** | 1 | 5 | 0.2 | 71 | 747 | 00.1 | 2.1 | 0.39 |
| **Purine (Adenine)** | 1 | 5 | 0.2 | 71 | 747 | 00.1 | 2.1 | 0.39 |
| **Lysoplasmalogen** | 1 | 5 | 0.2 | 71 | 747 | 00.1 | 2.1 | 0.39 |
| **Tocopherol** | 1 | 5 | 0.2 | 71 | 747 | 00.1 | 2.1 | 0.39 |
| **Lysine** | 2 | 11 | 0.18 | 71 | 747 | 00.1 | 1.91 | 0.28 |
| **Phenylalanine/Tyrosine** | 6 | 33 | 0.18 | 71 | 747 | 00.1 | 1.91 | 0.08 |
| **Branch Chained Amino Acid** | 4 | 24 | 0.17 | 71 | 747 | 00.1 | 1.75 | 0.19 |
| **Monohydroxy Fatty Acid** | 2 | 13 | 0.15 | 71 | 747 | 00.1 | 1.62 | 0.35 |
| **Hemoglobin/Porphyrin** | 1 | 7 | 0.14 | 71 | 747 | 00.1 | 1.5 | 0.50 |
| **Purine (Xanthine/Inosine)** | 1 | 7 | 0.14 | 71 | 747 | 00.1 | 1.5 | 0.50 |
| **Food Components and Plants** | 5 | 36 | 0.14 | 71 | 747 | 00.1 | 1.46 | 0.25 |
| **Urea Cycle** | 2 | 16 | 0.12 | 71 | 747 | 00.1 | 1.32 | 0.46 |
| **Pyramidine (Uracil)** | 1 | 9 | 0.11 | 71 | 747 | 00.1 | 1.17 | 0.60 |
| **Glutamate** | 1 | 9 | 0.11 | 71 | 747 | 00.1 | 1.17 | 0.60 |
| **Lysolipid** | 3 | 28 | 0.11 | 71 | 747 | 00.1 | 1.13 | 0.51 |
| **Primary Bile Acid** | 1 | 10 | 0.1 | 71 | 747 | 00.1 | 1.05 | 0.63 |

**Supplementary Table S5:** Spearman correlations between sphingolipid metabolites and MELD

|  |  |  |
| --- | --- | --- |
| **Molecule** | **Rho** | ***P*** |
| **Sphinganine** | 0.1557 | 0.2752 |
| **Sphinganine-1-phosphate** | 0.0450 | 0.7591 |
| **N-palmitoyl-sphinganine (d18:0/16:0)** | 0.0665 | 0.6428 |
| **Myristoyl dihydrosphingomyelin (d18:0/14:0)\*** | 0.1490 | 0.2966 |
| **Palmitoyl dihydrosphingomyelin (d18:0/16:0)\*** | 0.0931 | 0.5156 |
| **Behenoyl dihydrosphingomyelin (d18:0/22:0)\*** | -0.1155 | 0.4196 |
| **Palmitoyl sphingomyelin (d18:1/16:0)** | -0.0510 | 0.7724 |
| **Stearoyl sphingomyelin (d18:1/18:0)** | -0.5556 | 0.0000 |
| **Behenoyl sphingomyelin (d18:1/22:0)\*** | -0.2842 | 0.0433 |
| **Tricosanoyl sphingomyelin (d18:1/23:0)\*** | -0.4032 | 0.0034 |
| **Lignoceroyl sphingomyelin (d18:1/24:0)** | -0.2889 | 0.0398 |
| **sphingomyelin (d18:1/14:0, d16:1/16:0)\*** | 0.0492 | 0.3756 |
| **sphingomyelin (d18:2/14:0, d18:1/14:1)\*** | 0.0800 | 0.5769 |
| **sphingomyelin (d17:1/16:0, d18:1/15:0, d16:1/17:0)\*** | -0.1835 | 0.1974 |
| **sphingomyelin (d18:2/16:0, d18:1/16:1)\*** | 0.1044 | 0.4660 |
| **sphingomyelin (d18:1/17:0, d17:1/18:0, d19:1/16:0)** | -0.5050 | 0.0002 |
| **sphingomyelin (d18:1/18:1, d18:2/18:0)** | -0.4166 | 0.0024 |
| **sphingomyelin (d18:1/20:0, d16:1/22:0)\*** | -0.5280 | 0.0000 |
| **sphingomyelin (d18:1/20:1, d18:2/20:0)\*** | -0.4219 | 0.002 |
| **sphingomyelin (d18:1/21:0, d17:1/22:0, d16:1/23:0)\*** | -0.4253 | 0.0019 |
| **sphingomyelin (d18:1/22:1, d18:2/22:0, d16:1/24:1)\*** | -0.3817 | 0.0057 |
| **sphingomyelin (d18:2/23:0, d18:1/23:1, d17:1/24:1)\*** | -0.3459 | 0.0129 |
| **sphingomyelin (d18:1/24:1, d18:2/24:0)\*** | 0.0281 | 0.8447 |
| **sphingomyelin (d18:2/24:1, d18:1/24:2)\*** | -0.1153 | 0.4203 |
| **sphingosine** | 0.0019 | 0.9897 |
| **sphingosine 1-phosphate** | -0.2054 | 0.1481 |
| **sphingomyelin (d18:0/20:0, d16:0/22:0)\*** | -0.1267 | 0.3756 |
| **sphingomyelin (d18:2/18:1)\*** | -0.5101 | 0.0001 |
| s**phingomyelin (d18:1/19:0, d19:1/18:0)\*** | -0.5820 | 0.0000 |
| **N-palmitoyl-sphingosine (d18:1/16:0)** | -0.0801 | 0.5762 |
| **glycosyl-N-palmitoyl-sphingosine (d18:1/16:0)** | 0.1396 | 0.3285 |
| **glycosyl-N-stearoyl-sphingosine (d18:1/18:0)** | -0.1027 | 0.4734 |
| **lactosyl-N-palmitoyl-sphingosine (d18:1/16:0)** | 0.0593 | 0.6791 |
| **N-stearoyl-sphingosine (d18:1/18:0)\*** | -0.4957 | 0.0002 |
| **lactosyl-N-nervonoyl-sphingosine (d18:1/24:1)\*** | 0.4268 | 0.0018 |