Clinical hepatology

IDDF2020-ABS-0038 ANALYSIS AND IDENTIFICATION OF DISRUPTIVE GUT MICROBIOTA AND ITS PERTURBED METABOLIC FUNCTIONS AND RECOGNITION OF POTENTIAL NOVEL THERAPEUTIC TARGETS IN DECOMPENSATED CIRRHOSIS WITH SEPSIS

[1]Cyriac Abby Philips*, [2]Karthik Ganesan, [3]Shatakshi Ranade, [3]Varun Chopra, [3]Kunal Patil, [3]Sonie Shende, [3]Nikhil Phadke, [4]Rizwan Ahamed, [4]Philip Augustine. *[1]The Liver Unit and Monarch, Cochin Gastroenterology Group, Ernakulam Medical Center, India; [2]Center for Bioinformatics and Deep Data Mining, Helical-Bio, Ann Arbor, USA; [3]Cellular and Molecular Biology, Genepath-Dx, Pune, India; [4]Gastroenterology and Advanced G.I. Endoscopy, Cochin Gastroenterology Group, Ernakulam Medical Center, India*

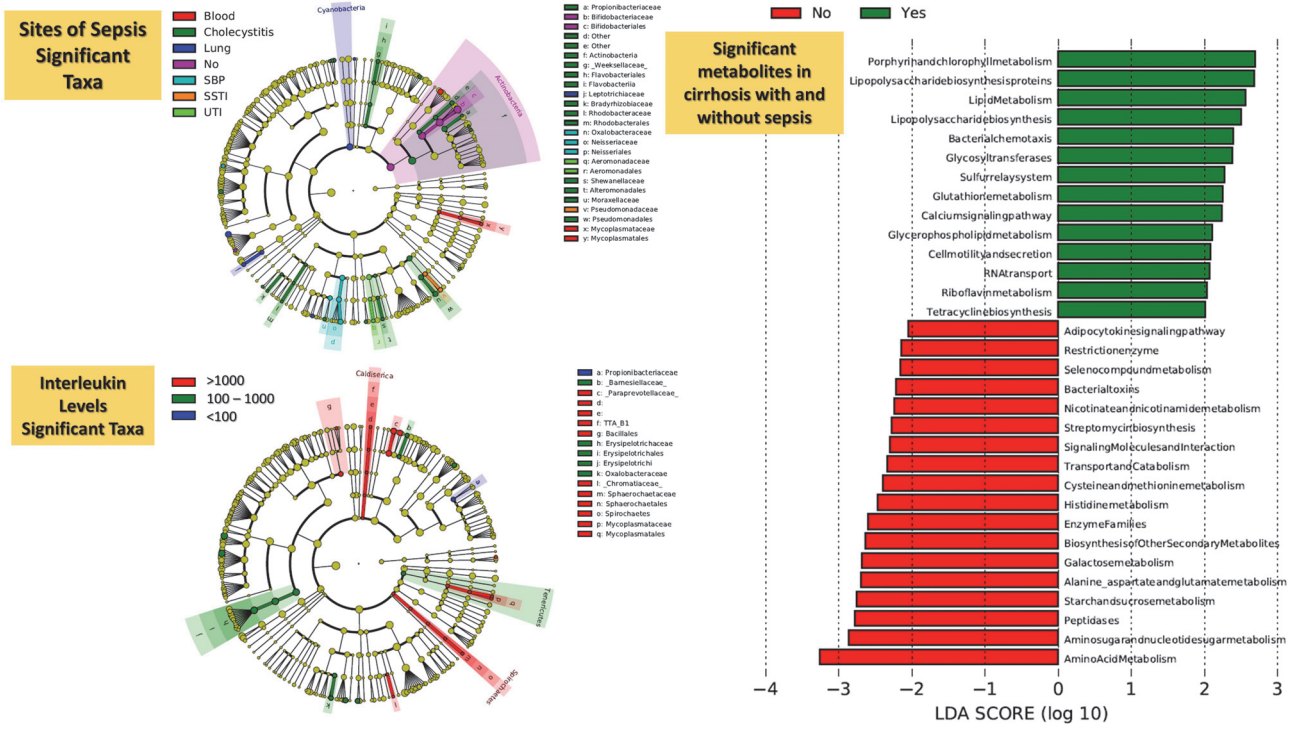
10.1136/gutjnl-2020-IDDF.12

Background The role of intestinal-dysbiosis leading to adverse outcomes is well known in sepsis and septic shock. Variations in bacterial diversity and microbiota-related functional-metabolic alterations within the gut microbiome in decompensated cirrhosis (DC) patients with sepsis remain unknown.

Methods 16-srRNA sequencing on stool samples (n=51,sepsis – 27/no-sepsis – 24) collected at admission were conducted in DC. Bacterial diversity, significant taxa and respective metabolic-profiling using QIIME®, PICRUSt™ and linear-discriminant-analysis-effect-size-method were performed based on sub-group comparisons [sepsis, no-sepsis/sites of sepsis/interleukin-6 cut-offs(<100, 100–1000, >1000)/episodes of infections/death or survival at same admission/overall survival].

Results Proteobacteria, Cyanobacteria and Actinobacteria related-genera associated with pathogenicity in conditions of immune-exhaustion(Corynebacterium, Lautropia) predominated in patients with sepsis. Metabolic-pathways associated with oxidative-stress(riboflavin, glutathione metabolism) and endotoxemia (lipopolysaccharide(LPS) synthesis, bacterial chemotaxis, sulfur-relay) were significantly upregulated in sepsis. Specific-taxa were found to be associated with sites of infection in DC patients. Eggerthella (associated with blood-stream infections with piperacillin-tazobactum use) was significant in bacteremic-DC patients in the presence of upregulated MAP-K signalling pathways(nutritional deprivation and cell-wall stress) while Acinetobacter, Priopionibacterium were significantly associated with biliary infections. Protective oxidant-pathways of cysteine/methionine metabolism that increase glutathione were upregulated in no-sepsis-group. Significant representation by Gammaproteobacteria-family of sulphur-metabolizing bacteria, exaggeration of orally predominant pathogens(Prevotella) and increase in pentose-phosphate-pathway(upregulated in severe LPS-related hyperinflammatory-stress) were notable in those with interleukin-6 >1000 (figure 1). Pathogenic-taxa of immune-deficient state was significant in DC with ≥2 sepsis-episodes and repeated antibiotic use. Megamonas was associated with survival during the same admission; while Kingella, Neisseria with death on follow up.

Conclusions Specific gut-microbiota and their metabolites are associated with sepsis and associated events in patients with DC. Identifying beneficial strains that reduce immune exhaustion and supplementation of favourable metabolites could improve therapeutics in DC and sepsis, for which large population-based studies remain an unmet need.



Abstract IDDF2020-ABS-0038 Figure 1 Significant bacterial taxa associated with sites of sepsis, interleukin-6 levels and metabolites associated with sepsis in patients with decompensated cirrhosis