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Gut Microbiota Dysbiosis in Patients with Hepatitis B Virus Infection

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Background

Gut Microbiota is composed of diverse populations of bacteria, protozoa, archaea, fungi and viruses (Tripathi et al., 2018)



- Firmicutes
- Bacteroidetes
- Actinobacteria
- Proteobacteria
- Verrucomicrobia

250 million are infected with HBV worldwide with risk of cirrhosis and HCC (Zeng et al., 2020)

The intestine communicates with the liver through the gut-liver axis which affects pathogenesis of Hepatitis B virus infection through release of cytokines causing hepatocyte damage (Tranah et al., 2020)

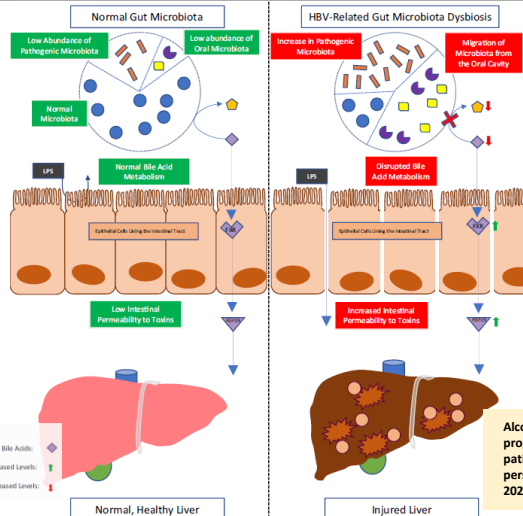
Legends:

Normal Gut Microbiota

Invasive Oral Microbiota

Secondary Bile Acids

Fibroblast growth factor 19 (FGF 19)

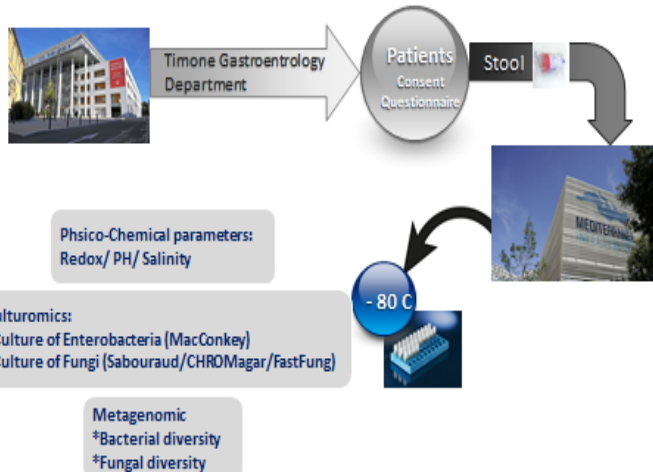


A growing body of literature suggests a connection between gut microbiota dysbiosis and disease progression in HBV patients (Zheng et al., 2020).

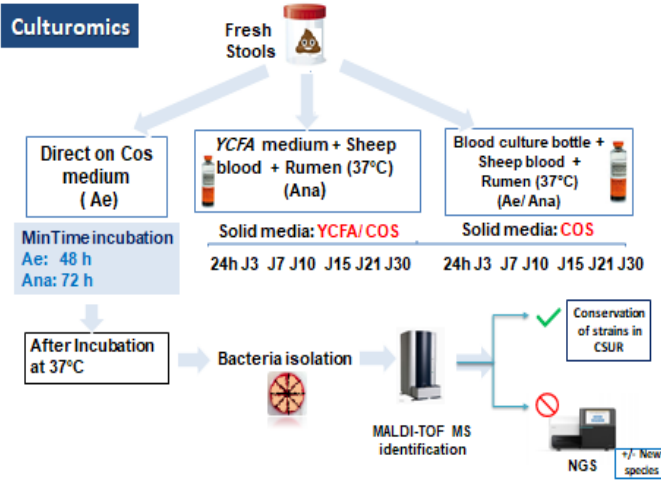
Alcohol abuse not only causes rapid progression of liver disease in HBV patients but also allows HBV to persist chronically (Ganesan et al., 2020)

Material & Methods

Study Design: Case-Control study

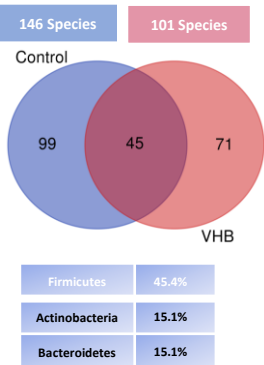


Culturomics

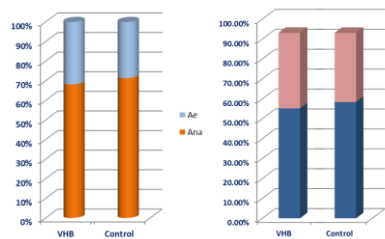


RESULTS

Venn diagram showing comparison between culturomics results of HBV and Control groups

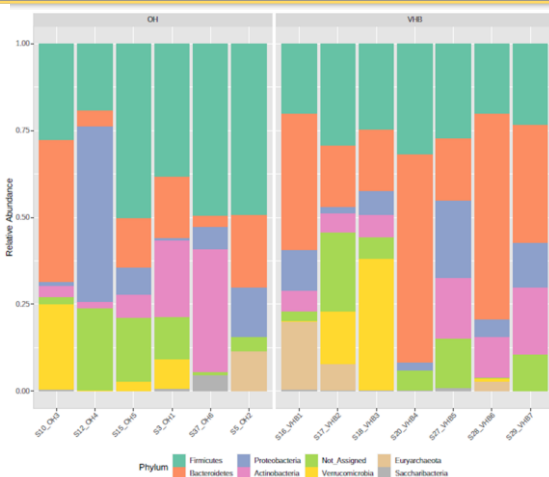


*Seven stool samples of HBV patients have been tested so far
*Results have been compared to both Control group and Alcoholic (OH) group



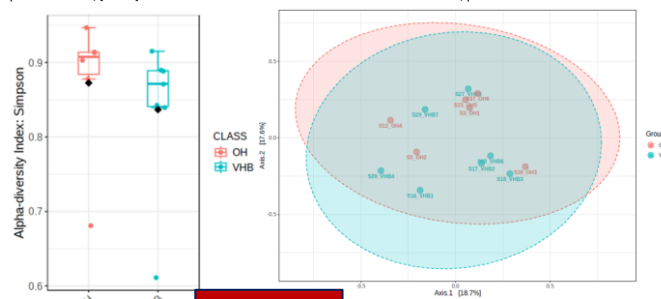
Top 30 Enriched species

- | Metagenomics | Culturomics |
|--|---|
| <i>Coprococcus_eutactus</i> | <i>Bacteroides_fragilis*</i> |
| <i>Senegalimassilia_anaerobia / Senegalimassilia_anaerobia / D</i> | <i>Bacteroides_stercoris*</i> |
| <i>Enterobacter_timonensis / Citrobacter_koseri / Enterobacter</i> | <i>Bifidobacterium_langum*</i> |
| <i>Bifidobacterium_adolescentis / Bifidobacterium_faecale / Bifi</i> | <i>Blaustia_hydrogenotrophica*</i> |
| <i>Prevotella_copri</i> | <i>Eggerthella_timonensis*</i> |
| <i>Bacteroides_fragilis</i> | <i>Negativicoccus_succinivorans*</i> |
| <i>Eubacterium_hallii</i> | <i>Parabacteroides_johnsonii*</i> |
| <i>Kandleria_vitulina</i> | <i>Pediococcus_acidilactici</i> |
| <i>Raoultella_omithinolytica</i> | <i>Polynesia_massiliensis</i> |
| <i>Bacteroides_finegoldii</i> | <i>Alistipes_illumii*</i> |
| <i>Intestinibacter_bartlettii</i> | <i>Alistipes_obesi*</i> |
| <i>Hafnia_alvei / Obesumbacterium_proteus</i> | <i>Alistipes_anderdonkii*</i> |
| <i>Collinsella_aerofaciens</i> | <i>Anaerococcus_vaginalis*</i> |
| <i>Paraoecilibacter_massiliensis</i> | <i>Anaerostignum_lactatifermentans*</i> |
| <i>Eubacterium_eligens</i> | <i>Bacillus_thermoamylovorans</i> |
| <i>Romboutsia_timonensis</i> | <i>Bacteroides_caccae*</i> |
| <i>Ruminococcus_torques</i> | <i>Bacteroides_cellulosilyticus*</i> |
| <i>Clostridium_intestinalis</i> | <i>Bacteroides_eggerthii*</i> |
| <i>Desulfovibrio_piger</i> | <i>Bacteroides_faecis*</i> |
| <i>Faecalimicrobium_massiliense</i> | <i>Bacteroides_finegoldii*</i> |
| <i>Haemophilus_parinfluenzae</i> | <i>Bacteroides_nordii*</i> |
| <i>Howardella_urelytica</i> | <i>Bifidobacterium_animalis*</i> |
| <i>Libanibacterium_massiliensis</i> | <i>Bifidobacterium_scaradovi*</i> |
| <i>Enterobacter_aerogenes / Raoultella_terrigena</i> | <i>Blaustia_caecimuris*</i> |
| <i>Olsenella_cagae</i> | <i>Blaustia_coccoides*</i> |
| <i>Roseburia_intestinalis</i> | <i>Blaustia_marasmi*</i> |
| <i>Succinivibrio_dextrinosolvens</i> | <i>Butyrivimonas_mediterraneensis*</i> |
| <i>Bacteroides_xylanisolvens</i> | <i>Butyrivimonas_phocensis*</i> |
| <i>Roseburia_faecis</i> | <i>Clostridium_hylemonae*</i> |
| <i>Slackia_isoflavonicvertens</i> | <i>Clostridium_jeddahense*</i> |
| <i>Faecalibacterium_massiliensis</i> | <i>Clostridium_perfringens*</i> |
| <i>Gemmiger_formicilis</i> | <i>Caprobacillus_cateniformis*</i> |



Alpha diversity (Simpson index)
p-value: 0.5309; [T-test] statistic: 0.64722

Beta diversity (PCoA, Bray Curtis index)
F-value: 1.3518; p-value < 0.135



Conclusions

- HBV is associated with gut dysbiosis including a gain and a loss in different bacterial species
- More patients have to be studied to determine specific microbiota pattern in different stages of HBV
- Role of alcohol producing bacteria has to be assessed in patient with HBV in comparison to alcoholic patients