

P48

VALIDATION OF THE NEUTROPHIL TO LYMPHOCYTE RATIO AS A MARKER OF POOR OUTCOMES AND STEROID RESPONSIVENESS IN ALCOHOLIC HEPATITIS: THE GWENT EXPERIENCE

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Introduction The STOPAH study showed an improvement in short term mortality with prednisolone but failed to reach statistical significance. Forrest et al subsequently reported that a neutrophil – lymphocyte ratio (NLR) of 5–8 was a predictor of steroid response compared to those with an NLR <5 or >8. We reviewed the validity of the NLR as a marker of severity and steroid response in alcoholic hepatitis patients admitted to the Gwent liver unit.

Method We undertook a retrospective analysis of consecutive patients admitted with alcoholic hepatitis between January 2014 and March 2019. Patients were identified via coding and discharge notification diagnosis. Only patients diagnosed by a consultant gastroenterologist/hepatologist and with data available on electronic records were included. Baseline NLR and Glasgow alcoholic hepatitis score (GAHS) were recorded with a primary outcome of mortality. Additional observations included acute kidney injury (AKI), readmission within 90 days and day-7 Lille score for those treated with prednisolone.

Results Sixty-six patients were identified, of which 40 (61.6%) were male, with a median age of 47 (IQR 40–56). There were 12 patients (18.2%) with an NLR of 5–8. Patients with an NLR of 5–8 were more likely to be alive at 28 and 90 days than those with an NLR <5 or >8, however this trend did not continue at 1 year. Patients with an NLR 5–8 had lower rates of AKI (8%) and fewer readmissions within 90 days (33%) compared to those with NLR <5 (22% and 58% respectively) or >8 (52% and 45% respectively).

Twenty-seven patients received prednisolone. Patients with an NLR 5–8 were more likely to receive prednisolone than others (66.7%) and tended towards a better response. Patients with NLR 5–8 had more favourable Lille scores with a mean of 0.251 (SD ± 0.207) compared to patients with an NLR <5 and >8 (Mean 0.459 and 0.406 respectively). Prednisolone was continued past 7 days in 71% of patients with NLR 5–8 compared to those with NLR <5 (44%) or >8 (25%).

Conclusion Our data supports the previously reported finding that patients with NLR 5–8 are more likely to respond to prednisolone. They had lower mortality up to 90 days and were less likely to have AKI or readmission within 90 days. Furthermore, an NLR >8 was associated with particularly poor 1-year survival and high incidence of AKI. The NLR appears to be another useful method of risk stratification in alcoholic hepatitis.

P49

A GENOME-WIDE ASSOCIATION STUDY OF HEPATIC ENCEPHALOPATHY IN CHRONIC LIVER DISEASE

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Introduction Hepatic encephalopathy (HE) is a frequent complication of cirrhosis but its development is not inevitable. There is evidence, from candidate gene studies, that the propensity to develop HE may be genetically determined but the findings are inconsistent. The aim of this study was to undertake a GWAS of HE in chronic liver disease.

Methods Genomic DNA was available in 857 participants in the UK STOPAH alcoholic hepatitis trial and 120 participants in the Royal Free Hospital (RFH) HE surveillance study. All had chronic liver disease and the majority were of British/Irish ancestry. Information on HE status was available in 777 participants in STOPAH and 109 in the RFH cohort. Cases were defined in the STOPAH cohort as those presenting with/developing overt HE (OHE) within 28 days of admission based on West Haven criteria, and in the RFH cohort on a combination of West Haven criteria, the PHES test and EEG theta frequency. Controls were defined as STOPAH participants who did not present/develop OHE within 28 days and in the RFH cohort as participant classified as neuropsychiatrically unimpaired or as having minimal HE. Samples were genotyped using three different SNP arrays (Illumina core exome chip, Psych Chip and OmniExpress array). Separate GWAS analyses were undertaken of each array using Plink (v1.9) followed by meta-analysis in METAL (v1.5.0). The primary analysis was adjusted first for population stratification and second for age, sex, and model for end-stage liver disease (MELD) score. Linear regression association analysis was also conducted in the RFH cohort (n=111) using the additional HE defining variables.

Results A total of 206 (26.5%) of the STOPAH participants and 33 (30.3%) of the RFH cohort had OHE. Single variants in *TMEM135* (*Transmembrane Protein 135*), *CACNB2* (*Calcium Voltage-Gated Channel Auxiliary Subunit Beta 2*), and *WBP2* (*WW Domain Binding Protein 2*) showed suggestive association ($P < 1 \times 10^{-5}$) with OHE in the primary analysis; the association with *TMEM135*, was retained in the adjusted analyses. An association at genome-wide significance ($P=3.73 \times 10^{-8}$) was identified between the PHES score and a variant lying at a genetic locus containing genes *AMTN* (*Amelotin*) and *MUC7* (*Mucin 7, Secreted*), the gene of interest.

Conclusions *TMEM135* influences key metabolic pathways involved in the pathophysiology of HE, namely oxidative stress and glutamine and glutamate homeostasis. *MUC7* influences factors which result in a reduction in systemic inflammation and influences the gut microbiota. These interesting associations need further exploration in extended cohorts.

P50

AUTOIMMUNE HEPATITIS PATIENTS HAVE COMPARABLE OUTCOMES FROM SARS-COV-2 INFECTION TO PATIENTS WITH LIVER DISEASE OF OTHER AETIOLOGY DESPITE IMMUNOSUPPRESSION: INTERNATIONAL REGISTRY DATA

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Background Despite concerns that patients with autoimmune hepatitis (AIH) may be at increased risk of adverse outcomes from COVID-19 due to use of immunosuppression, the