in patients with AH by probing the mitochondrial function of circulating monocytes and neutrophils in AH.

**Methods** Experiments were performed on whole blood after red cell lysis from 5 AH patients and 4 healthy controls (HC) with and without 10 ng/ml or 100 ng/ml lipopolysaccharide (LPS) stimulation for 4 hours. Flow cytometry was used to quantify mitochondrial mass, polarization and superoxide leak using MitoTracker Green (MT), MitoStatus Red (MS), MitoSOX Red probes. To control for variations in mass Mitochondrial Polarization Ratio (MPR) was calculated from MS:MT fluorescence ratio. IL-1β, IL-6, IL-8 & TNFα production were quantified using intracellular cytokine signalling. Carbonyl cyanide m-chlorophenyl hydrazone (CCCP), a mitochondrial membrane depolarising agent, was used to recapitulate membrane depolarisation in healthy monocyte mitochondria at doses ranging from 0–100μM.

**Results** Stimulated TNFα production was impaired in AH monocytes (12070 vs 37200 MFI; p=0.02). Mitochondrial mass was greater in AH monocytes vs HC (23802 vs 12926 MFI; p=0.02) and had greater mitochondrial superoxide leak (1791 vs 894 MFI; p=0.03). Unstimulated AH monocyte MPR was lower than HC (0.522 vs 0.815; p=0.032). Unlike HC, AH monocytes failed to hyperpolarize with stimulation (HC 10 ng/mL vs 100 ng/mL LPS 1.28 vs 1.57 MPR, p=0.046 compared to AH 10 ng/mL vs 100 ng/mL LPS 0.58 vs 0.6 MPR, p=ns: figure 1). Similar trends were demonstrated in AH neutrophils. Monocyte MPR correlated strongly with TNFα production (r=0.733; p=0.031) whereas mitochondrial superoxide leak had strong negative correlation (r=-0.8776; p=0.004). Exposure of HC to mitochondrial depolarising agent CCCP reduced production of TNFα in a dose dependent manner (0 vs 10 vs 50 vs 100μM CCCP; TNFα 45850 vs 39404 vs 29130 vs 14698 MFI).

**Conclusion** AH monocytes and neutrophils harbour dysfunctional mitochondria. Specific defects in mitochondrial membrane polarization and superoxide leak correlate strongly with impaired TNFα production from AH monocytes, a phenomenon that has been repeatedly associated with increased susceptibility to infection. Further investigation into the precise nature of these mitochondrial defects may identify reversible targets to reduce susceptibility to infection for alcoholic hepatitis patients.

**Abstract 204**

**Figure 1** MPR in response to LPS stimulation

**Conclusion** AH monocytes and neutrophils harbour dysfunctional mitochondria. Specific defects in mitochondrial membrane polarization and superoxide leak correlate strongly with impaired TNFα production from AH monocytes, a phenomenon that has been repeatedly associated with increased susceptibility to infection. Further investigation into the precise nature of these mitochondrial defects may identify reversible targets to reduce susceptibility to infection for alcoholic hepatitis patients.

**References**

P206 GEOGRAPHICAL VARIATION OF CHRONIC LIVER DISEASE RISK FACTORS ACROSS THE UK

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Introduction Chronic liver disease (CLD) is a largely preventable condition with increasing burden on NHS resources. The aim of this study was to determine geographical variation in liver risk factors for CLD and association with regional Gross Disposable Household Income (GDHI).

Methods Between 2018–2019, a cross-sectional survey was conducted across the UK to screen for obesity, alcohol intake, diet, and viral hepatitis. In 2019, liver transient elastography (FibroScan) measurement was introduced. Spearman’s correlation coefficient (rs) was used to assess linear relationships between ordinal and discrete variables.

Results We analysed the data from 2152 individuals aged 18+ (males, n=1092, 51%; females, n=1058, 49%) across 25 UK towns. 24% (n=519) exhibited high-risk levels of alcohol consumption, 30% (n=637) had high-risk diets, 25% (n=531) were obese, and 33% (n=704) had risk factors for viral-induced liver disease. FibroScan readings were available for 1044 individuals. Male gender, >40 years of age, obesity, and a high-risk diet were associated with a FibroScan score >7 kPa in univariate analysis. In multivariate analysis, male gender (odds ratio [OR], 1.651; 95% confidence interval [CI], 1.164–2.341; p=0.005), >40 years of age (OR, 1.846; 95% CI, 1.192–2.860; p=0.006), and obesity (OR, 3.245; 95% CI, 1.927–5.465; p<0.001) were independent predictors of a FibroScan reading >7 kPa. Across UK towns, there was a weak negative association between FibroScan readings >7 kPa (range 9–26%) and GDHI (r=-0.309, P=0.355). Disparity of CLD risk factors in UK towns (alcohol, 4–34%; diet, 17–53%; obesity, 11–34%; viral, 22–70%) was not significantly associated with GDHI (r=0.026, -0.264, -0.277, and .117, respectively).

Conclusions UK towns displayed noteworthy disparity in the prevalence of CLD risk factors, which was not adequately explained by regional economic performance. Further studies are required to explain this disparity, accounting for societal factors and comorbidities, to inform resource allocation and policy-making.

P207 TRANSIENT ELASTOGRAPHY MAY OVERESTIMATE RISK OF SEVERE FIBROSIS IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

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Introduction Primary sclerosing cholangitis (PSC) is a chronic, immune mediated cholestatic disease that leads to progressive liver fibrosis and cirrhosis. There is a need for reliable markers of disease activity and prognosis in patients with PSC. In recent years Transient Elastography has been validated as a non-invasive screening tool for severe fibrosis and cirrhosis in this patient cohort with cut-off values of 9.6 KPA for severe fibrosis and 14.4 KPA for cirrhosis.

Methods We retrospectively reviewed data from our PSC patient cohort to identify patients who had undergone a liver biopsy and transient elastography. We then used this data to work out sensitivity, specificity, positive predictive value and negative predictive value of transient elastography in PSC using a cut off of 9.6 KPA for severe fibrosis.

Results Data from 52 patients with PSC was available for this review. 16 patients had both liver biopsy and transient elastography. 5 patients had liver stiffness > 9.6 kpa and 3 had a liver stiffness of >14.4 KPA. 1 of the 5 patients had cirrhosis and had a liver stiffness of 22.6 KPA. None of the remaining 4 had severe fibrosis or cirrhosis. Of the 11 patients with liver stiffness < 9.6 KPA, 1 had bridging fibrosis on biopsy. Using a cut off of 9.6KPA, the sensitivity, specificity, positive predictive value and negative predictive value for severe fibrosis was 50%, 71%, 20% and 91% respectively. All 5 patients with liver stiffness of >9.6 kpa had an ALP > 247 IU/L (range 247–832 IU/L) which is 1.9 x upper limit of normal (ULN) as per our reference ULN of 130 IU/L.

Conclusions In patients with PSC, using transient elastography cut offs suggested previously may overestimate the presence of advanced fibrosis. This is more likely in patients with a raised ALP of > 1.9 x ULN. The single false negative result seen in our cohort is likely due to patchy nature of fibrotic disease in this cohort and again warrants caution when interpreting liver stiffness results.

REFERENCE