considered, we found that the PBC group had significant impairment in arising, eating, walking, reach and grip activity but not in dressing or hygiene. Functional impairment correlated positively with greater PBC-40 Fatigue, Cognitive and Social & Emotional domain scores and higher autonomic symptom burden determined by OGS score. Change in the PBC-40 Cognitive and Social & Emotional domain scores between 2005 and 2009 strongly predicted functional ability in 2009 Multivariate analysis confirmed that total PROMIS HAQ scores were predicted independently by PBC-40 Social & Emotional domain scores ($p=0.02$; $\beta=0.3$) and orthostatic symptoms ($p=0.04$; $\beta=0.3$).

Conclusion PBC is associated with a substantial impairment of functional capacity to a greater degree than has previously been appreciated. The distribution of symptoms of PBC evolves over time, with cognitive symptoms making an ever-greater contribution to the overall burden. The major determinant responsible for both functional impairment and the specific symptoms contributing to it appears to be autonomic dysfunction which is potentially modifiable by treatment.

P21 THE EVALUATION OF SERUM FERRITIN AND TRASFERRIN SATURATION IN THE DIAGNOSIS OF HAEMOCHROMATOSIS IN AN ETHNICALLY DIVERSE POPULATION

doi:10.1136/gut.2010.223362.47

S Al-shamma, S Khaled, P Kennedy, A Provan. *The Royal London Hospital, UK*

Introduction Hereditary haemochromatosis (HH) is the most common genetic abnormality in populations of Northern European ancestry. There are limited data on the frequency of HFE in populations from the Indian subcontinent. Elevated serum ferritin (Fe) and transferrin saturation (TSAT) are often used as the basis for referral for HFE gene analysis.

Aim We undertook this study to evaluate the performance of elevated Fe and TSAT in the diagnostic algorithm of HH in a Caucasian population and how it compared when applied to an Indian population.

Method Data on all patients referred from the gastroenterology service for HFE gene analysis between 2001 and 2009 were evaluated. Serum Fe and TSAT were recorded where available to assess their utility in predicting HFE gene mutations and subsequent requirement for venesection. An estimation of the prevalence of iron overload due to HFE gene mutations in our large Indian population was sought.

Results 307 patients with elevated Fe levels underwent HFE genetic analysis. 146/307 (48%) patients had a TSAT performed at the time of referral. 34/307 (11%) were homozygotes for C282Y mutation, while 18 (6%) were compound heterozygotes. Almost half of those tested 147/307 (48%) had no genetic mutation.

Abstract P21 Table 1 Results Median serum Fe and TSAT values for different HFE genotypes

	Ferritin (μmol/l)	TSAT (%)
WT/WT*	472	33.5
WT/H63D or C282Y	424	37
H63D/H63D	484	41
Hd3D/C282Y	684.5	52.5
C282Y/C282Y	871	82

WT*; wild type.

A TSAT >45% was found in 42/146 tested patients. All C282Y/C282Y patients tested had a TSAT >45%, almost a quarter of whom (23.5%) had a TSAT <55%. All WT/WT patients with a TSAT >45% had alcoholic liver disease. The positive predictive value of a TSAT >45% in detecting a C282Y/C282Y or C282Y/H63D mutation was 54.7% compared to 14.5% for ferritin. The negative predictive value of a TSAT >45% in excluding a C282Y/C282Y or C282Y/H63D mutation was 96.2%. 32/307 (10.4%) patients from the Indian sub-continent underwent HFE genetic testing. The mean Fe was 421 with a mean TSAT of 40.3% compared to 564 and 47.7%, respectively, for the Caucasian population ($p<0.05$.) In this subgroup, there was one H63D/H63D mutation and 6 (19%) H63D/WT heterozygotes. None had a C282Y mutation. TSAT had a NPV of 100% in excluding clinically significant HH.

Conclusion TSAT has an excellent NPV and should be an integral part of the diagnostic algorithm for HH, where a cut-off value of 45% detects all C282Y homozygotes, while a higher cut-off value may miss some patients. This translates well into Indian populations. HFE gene mutations are extremely rare in patients of Indian descent and other aetiologies for elevated Fe/TSAT should be sought.

P22 DERANGEMENTS IN ENERGY, AMINO-ACID AND GUT MICROBIAL METABOLISM IN HEPATIC ENCEPHALOPATHY: A METABOLOMIC APPROACH

doi:10.1136/gut.2010.223362.48

J Bajaj, N Patel, D Heuman, A Sanyal, D Bell. *Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University, USA*

Introduction Hepatic encephalopathy (HE) pathogenesis is related to gut microbial products, which lead to deranged cerebral bioenergetics. Biofluid MR spectroscopy (MRS) can be used to determine changes in bioenergetics, gut microbial products, amino acid and lipid metabolites. Lactulose is used as a first-line HE Rx despite a poor evidence basis.

Aim To evaluate the clinical and metabolic consequences of lactulose withdrawal in HE.

Method Patients with cirrhosis on lactulose for precipitated HE underwent cognitive testing with inhibitory control (ICT), urine and serum collection for MRS and inflammatory markers while on lactulose. Lactulose was then withdrawn and patients followed for 30 days with visits at day 2, 14 and 30; ICT, serum and urine testing were repeated at every visit. Relapse of HE was defined clinically. Multivariate analysis of urine and serum metabolites involved principal components analysis (PCA) and partial least squares discriminant analysis (PLS-DA). Univariate analysis was applied to hypothesis-driven metabolites, multivariate-driven metabolites and inflammatory marker concentrations.

Results 7 cirrhotic men (age 53±7 years, 5 HCV, 2 alcohol) on lactulose for 6±5 months for precipitated HE (5 GI bleed, 2 infections) were included. Three patients clinically relapsed 38±6 days post-withdrawal; all 3 had >15 ICT lures while on lactulose. None of those who scored <15 ICT lures on lactulose relapsed. Lure increase OR, 2.5 (CI: 1.7 to 3.6) predicted relapse. Using ICT lures >15 as a cut-off for HE relapse, MRS distinguished with a sensitivity and specificity of 70.0%/63.6% using urine and 100%/100% using serum on PLS-DA. Urine PLS-DA: In relapsers, urine TMAO was reduced indicating altered gut bacterial metabolism while malonic acid and citrate were higher demonstrating impaired energetics. Glycine and phenylalanine, associated with false neuro-transmitters, were also increased in relapsers along with creatinine. Serum PLS-DA: Relapsers had higher choline and its metabolite, dimethylglycine levels which is associated with extrusion of choline after astrocyte swelling in HE as well as higher levels of lipids. Univariate analysis confirmed that relapsers had lower TMAO ($p=0.00280$) and higher choline ($p=0.0414$), LDL (0.0265) and creatinine ($p=0.00970$). Inflammation was depressed in relapsers compared to others evidenced by decreased endotoxin ($p=0.03$), IFN-γ ($p=0.045$), IL-4 (0.0002) and TNF-α

(p=0.0013) suggesting a compensatory anti-inflammatory response syndrome.
Conclusion HE relapse post-lactulose withdrawal is associated with derangements in bioenergetics, amino-acid, lipid and gut microbial metabolism as well as depression of the inflammatory response.

P23 ABSTRACT WITHDRAWN

P24 CYTOKINE BIOMARKER PROFILING IN ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE: IMPORTANCE OF MONOCYTE CHEMOTACTIC PROTEIN-1 IN PROGNOSIS AND HEPATIC ENCEPHALOPATHY

doi:10.1136/gut.2010.223362.50

H Antoniades, B Mathew, M McPhail, R Srirajaskanthan, P Berry, W Bernal, M Hussain, G Auzinger, J Wendon. *Hepatology and Transplantation, King's College London, UK*

Introduction Inflammatory cytokines have recently been described as reflecting severity of liver injury, grade of encephalopathy and prognosis in acute liver failure (ALF). The role of monocyte chemotactic protein-1 and peripheral monocyte count has not been well studied.
Method 35 consecutive patients admitted to our institution with a diagnosis of acetaminophen induced ALF were studied for the effect of a biomarker profile of inflammatory cytokines (IL-4, IL-6, IL-10, MCP-1, TNF-a, IFN-g) levels at admission on grade of hepatic encephalopathy (HE) and prognosis. Modified King's College Criteria (KCC) was used in deciding whether to perform ELT. Assessment of HE and prognostic markers was investigated using logistic regression and receiver operating characteristic (ROC) curve analysis.
Results MCP-1 levels were significantly correlated with standard markers of severity of liver injury (INR: R=0.737, p<0.001; lactate: R=0.772, p<0.001; AST:R=0.545, p<0.001) and with IL-6 (R=0.576, p=0.003) and IL-10 (R=0.679, p<0.001). MCP-1 levels were significantly reduced in spontaneous survivors (1149 (range 168–12 998) compared to patients who died/underwent orthotopic liver transplantation (OLT) (7925 (1694–30 625), p<0.001, Mann–Whitney U test. The area under the ROC curve (AUROC) for MCP-1 and prediction of poor outcome was 0.88 (95% CI 0.68 to 0.97, p<0.001). There was no significant difference in performance of MCP-1 compared with IL-4 (AUROC 0.80 (0.59–0.93)) IL-6 (AUROC 0.83 (0.63–0.95)) or IL-10 (AUROC 0.84 (0.64–0.95) p>0.05 for all; De Long method). MCP-1 performed better than peripheral monocyte count (AUROC 0.75 (0.57–0.85). TNF-α, TGF-β1 and IFN-γ levels did not predict outcome. IL-6 better predicted the development of severe (grade 3–4) HE (AUROC 0.91 (0.72–0.98) compared with MCP-1 (AUROC 0.71 (0.49–0.87), p=0.087 (De Long method)).
Conclusion MCP-1 has similar behaviour to IL-4, IL-6 and IL-10 in outcome prediction in acetaminophen induced acute liver failure and better reflects poor prognosis than peripheral monocyte count. IL-6 may better reflect the severity of HE suggesting different roles for interleukins and MCP-1 in the pathogenesis of the inflammatory milieu in ALF.

P25 QUANTITATIVE COMPARISON OF MICROBUBBLE ULTRASOUND TECHNIQUES FOR THE ASSESSMENT OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS C

doi:10.1136/gut.2010.223362.51

J Cobbold, D Patel, J F L Cobbold, J Fitzpatrick, M M E Crossey, N Patel, H C Thomas, S D Taylor-Robinson. *Robert Steiner MR Unit, Hammersmith Hospital, London, UK*

Introduction There is increasing interest in the development of imaging-based non-invasive markers for the assessment of chronic liver disease severity. Contrast enhanced ultrasound uses microbubbles as kinetic tracers to assess liver disease severity by exploiting the intra- and extra-hepatic haemodynamic changes accompanying fibrosis and cirrhosis. Transit times of a peripherally administered microbubble bolus are reduced with increasing disease severity. Transit times have previously been calculated to include intra- and extra- hepatic components (the hepatic vein transit time, HVTT) or just the intra-hepatic component (hepatic transit time, HTT), but diagnostic accuracy has not been compared directly.
Aim The aims of this study were: 1. to compare the diagnostic accuracy of HVTT and HTT in gauging the severity of chronic hepatitis C (CHC) and 2. to assess the inter- and intra-observer reliability of the microbubble technique.
Method 75 patients with biopsy-proven CHC were studied, staged using the Ishak system. Recordings of Doppler US scans performed using the microbubble contrast agent SonoVueTM, were retrospectively analysed by two independent observers, blinded to clinical data, to determine the HVTT, defined as the time taken for the microbubble to travel from the antecubital vein to the hepatic vein, and the HTT, defined as the difference between the hepatic vein arrival time and the hepatic artery arrival time. Each patient had two recordings (with separate microbubble injections) at a 10 min interval. Diagnostic accuracy was assessed using the area under the receiver operator characteristic (AUROC) curve. Inter- and intra-observer reliability and inter-injection reliability were assessed using the intraclass correlation coefficient (ICC).
Results 35 patients had mild fibrosis (stage 0–2), 23 had moderate-to-severe fibrosis (stage 3–4) and 17 had cirrhosis (stage 5–6). The diagnostic accuracy (95% CI) of HTT and HVTT for the diagnosis of cirrhosis (stage>4) were 0.78 (0.64–0.92) and 0.71 (0.55–0.86). Diagnostic accuracy (95% CI) of HTT and HVTT for the diagnosis of fibrosis stage >2 were 0.75 (0.65–0.86) and 0.71 (0.59–0.83). Inter-observer reliability (95% CI) for HTT and HVTT were 0.92 (0.87–0.95) and 0.94 (0.91–0.97). Intra-observer reliability for HTT and HVTT were 0.98 (0.97–0.99) and 0.99 (0.98–0.99); inter-recording reliability were0.97 (0.96–0.98) and 0.97 (0.95–0.98) respectively.
Conclusion HTT is more accurate than HVTT for the diagnosis of cirrhosis and moderate-to-severe fibrosis, while the reliability both of repeated recordings and of operators' assessment of recordings was very high. HTT reflects the intra-hepatic haemodynamic changes seen in more advanced chronic liver disease accounting for shorter transit times.

P26 HEPATOCELLULAR CARCINOMA SURVEILLANCE IN PATIENTS WITH ESTABLISHED CIRRHOSIS: THE BIRMINGHAM EXPERIENCE

doi:10.1136/gut.2010.223362.52

[1]H Bridgestock, [1]R Desai, [2]J Neuberger. *[1]Birmingham Heartlands Hospital, UK; [2]Liver Unit, Queen Elizabeth Hospital, UK*

Introduction HCC causes approximately 1500 deaths per year in the UK and 95% of patients these have known established cirrhosis. Surveillance programme for patients with cirrhosis using six monthly α-fetoprotein (AFP) monitoring and ultrasound scanning (USS) is therefore recommended to ensure early identification of HCC at a stage when curative treatment is still possible. HCC identified by surveillance rather than incidental or symptomatic diagnosis results in better outcome and increased survival.
Aim Here we show the results of an audit of HCC surveillance at the Liver Transplantation Unit in Queen Elizabeth Hospital Birmingham against the British Society of Gastroenterology guidelines.