

Abstract OP06 Table 1 Gene expression analysis of hepatic injury and fibrogenic markers

Gene	3 Months Postpartum			12 Months Postpartum		
	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
IL-6	1.00±0.21	1.44±0.41	2.01±0.45	0.38±0.48	1.53±0.37	9.65±2.31
TNF-α	1.00±0.30	1.32±0.79	2.13±0.33	1.14±0.36	4.59±0.98	8.65±1.12
α-SMA	1.00±0.24	3.06±0.98	2.86±0.28	0.87±0.22	1.96±0.87	23.86±8.5
Collagen	1.00±0.36	3.45±0.69	3.05±0.53	0.37±0.15	4.96±2.42	6.62±3.23

Conclusion Maternal obesity programs development of offspring NAFLD with progression to fibrosis in the context of a post-weaning hyper-caloric diet. Innate immune dysfunction may be responsible for the observed programmed phenotype.

BASL: Oral presentations Friday 9th September 2011

Clinical hepatology

OP07 PHENOTYPIC DESCRIPTION OF A LARGE COHORT OF PSC PATIENTS IN THE UK

doi:10.1136/gutjnl-2011-300857b.7

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Introduction Primary Sclerosing cholangitis (PSC), a chronic cholestatic liver disease of unknown aetiology or pathogenesis, remains an area for active research.

Aim The demographic and phenotypic characteristics of a UK cohort of 1194 patients with PSC are described.

Method All patients were recruited as part of an ongoing national collaborative effort (PSC-UK) between October 2008 and May 2011. The diagnosis of PSC was confirmed on the basis of characteristic ERCP, MRCP or histology. Patients with small-duct PSC were also included. All patients completed a descriptive phenotypic questionnaire sent at recruitment. Demographic, phenotypic data and family history were extracted from the participant questionnaires.

Results 1194 patients have returned completed questionnaires. Median age at recruitment was 59 years and 63% were male (male to female ratio =1.7:1). 64% of patients were lifelong non-smokers and only 4.3% were smoking at recruitment. 63.5% reported inflammatory bowel disease, split into 87% with Ulcerative colitis and 13% with Crohn's disease. 1.5% had a sibling with PSC and 14% had a sibling with inflammatory bowel disease. Further, 0.5% had one or more children with PSC and 4.6% had children with inflammatory bowel disease. 24% were asymptomatic, but over 50% reported itching and fatigue as the presenting symptom. Jaundice was present in 35%. The most common associated autoimmune disease was thyroid disease, present in 9% followed by Coeliac disease in 2.1% and type 1 diabetes mellitus in 1.8%. 16% of patients reported pan-procto or sub-total colectomy and 12.2% had undergone cholecystectomy. 2.7% of patients reported a history of colon cancer and 1.25% patients had a history of skin cancer.

Conclusion This is the largest reported demographic and phenotypic description of a single cohort of PSC patients. PSC is more common in young, non-smoking male patients. The frequency of associated inflammatory bowel disease is similar to that reported in other studies. It is plausible that siblings of patients with PSC have an increased risk of not only PSC but also inflammatory bowel disease. These data are consistent with increasing evidence pointing to a role of genetic factors in the pathogenesis of PSC.

OP08 NAFLD RELATED HCC IS RISING DRAMATICALLY IN THE NORTH OF ENGLAND

doi:10.1136/gutjnl-2011-300857b.8

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Introduction A reported increase in hepatocellular cancer (HCC) in western nations has been attributed to the rising prevalence of predisposing hepatitis C (HCV) related chronic liver disease. In parallel, however, the prevalence of the metabolic syndrome has risen markedly, and both a raised BMI and type 2 diabetes, characteristic features of the syndrome, are independently associated with an increased risk of HCC development.

Aim We have assessed the prevalence of the metabolic syndrome in our patients with HCC.

Method 686 consecutive patients with HCC, diagnosed as per EASL guidelines, referred to our unit over a 10-year period (2000 and 2010), have been studied and demographic, laboratory, radiological variables, treatments and survival recorded.

Results The numbers of patients referred from our catchment population of 3.5 million has increased more than 10-fold in 10 years, reaching 133 in 2010. While numbers with underlying hepatitis B, haemochromatosis, autoimmune or cryptogenic cirrhosis have remained constant, those with underlying HCV or ALD have increased fivefold up to 10 and 35 per year respectively. The most dramatic increase, however, has been in those patients with NAFLD, increasing from 1 or 2 to over 30 per year in 2009 and 2010. There has also been an increase in HCC arising in individuals without chronic liver disease, 40 and 65% of which had diabetes and the metabolic syndrome respectively. Patients with NAFLD related HCC were significantly older (median age of 72 yrs vs 65 and 61 for ALD and HCV respectively). While NAFLD HCC cases were less likely to be detected by surveillance, they were more likely to be detected incidentally. Survival was determined by stage at presentation for all etiologies, and was not adversely affected by advanced age in the NAFLD population.

Conclusion NAFLD related HCC now equals that related to ALD in Northern England. The median age at presentation was higher for NAFLD HCC patients, but this did not adversely affect their survival. While relatively few NAFLD HCC cases were detected by surveillance, and the prognosis was particularly poor for those presenting with symptomatic disease (median 8.14 months), this was offset by an increase in incidental HCC detection, largely in diabetic follow-up clinics. The median survival of incidental patients (median 21.2 months) was similar to that of detected by surveillance (18.68 months). A raised awareness of the risk of HCC in older diabetic patients may reduce the numbers of those presenting with advanced symptomatic disease.

OP09 TIPS OUTCOMES FOR REFRACTORY ASCITES: A SINGLE CENTRE EXPERIENCE

doi:10.1136/gutjnl-2011-300857b.9

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Introduction Transjugular intrahepatic portosystemic shunt (TIPS) insertion is established as an important intervention in the

management of refractory ascites. We conducted a retrospective analysis of a large series of patients undergoing TIPS insertion for this indication.

Aim The aims of this study were to describe the series of patients undergoing TIPS insertion for refractory ascites at the Royal Free Hospital particularly with regards to survival and procedural success.

Method A retrospective analysis of the Royal Free Hospital radiology database was conducted to identify all patients who underwent all TIPS procedures between January 1991 and January 2011. Patient records were used to subsequently identify those patients in whom refractory ascites was the principal indication for TIPS insertion and to characterise this patient cohort. Patients were excluded if hydrothorax was the primary indication for TIPS insertion. All patients underwent baseline EEG/echocardiography and cross sectional imaging as part of their pre-procedural work up. Patients were requiring regular paracentesis and were either diuretic insensitive or intolerant.

Results 1073 TIPS-related procedures were conducted at the Royal Free Hospital between January 1991 and January 2011. Of these, 159 patients underwent TIPS insertion for refractory ascites. Within this patients cohort, the underlying aetiology of cirrhosis was: alcohol 56.0% (89/159), hepatitis C 12.6% (20/159), cryptogenic 8.8%(14/159) and other causes 22.6% (36/159). 29% (46/159) of the patients were female, 71% (113/159) were male. The mean age at the time of TIPS insertion was 54.3 (± 0.94) yrs. The mean pre-TIPS MELD score was 15.26 (± 0.57) with a mean pre-TIPS EEG frequency of 7.51 Hz (± 0.20). The mean post-procedural portal pressure gradient was 11.0 mm Hg (± 0.57). Six month, 12 month and 2-year survival post-TIPS insertion was 78%, 50% and 50% respectively. At 6 months, 63% of patients had no or minimal ascites, 29% had moderate volume ascites and only 8% had persistent large volume ascites. At 12 months, 69% of patients had no or minimal ascites, 21% had moderate volume ascites and 10% had persistent ascites requiring paracentesis.

Conclusion In a carefully selected group of patients, TIPS is an effective intervention in the management of refractory ascites.

OP10 END-STAGE METHOTREXATE-ASSOCIATED CHRONIC LIVER DISEASE IN THE USA: INTERACTION OF DRUG, HOST AND ENVIRONMENTAL FACTORS

doi:10.1136/gutjnl-2011-300857b.10

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Introduction Methotrexate (MTX) is an effective and widely used immunosuppressant; however, long-term therapy has been associated with steatosis, progressive hepatic fibrosis and cirrhosis. Given the similarity of the histopathological features of methotrexate-associated chronic liver disease (MTX-CLD), non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD), we hypothesised that these diseases may share a common pathogenesis.

Method We analysed the diagnostic records of all individuals who have been listed for liver transplantation in the USA and reported to the Organ Procurement and Transplantation Network (OPTN) during the period 1 October 1987 and 22 May 2009 to identify those whose liver disease was deemed to have been, wholly or partly, caused by methotrexate (MTX-CLD). We compared the demographic, clinical and laboratory characteristics of adult individuals with MTX-CLD with those listed for ALD and NAFLD.

Results Among 148 639 unique listings for liver transplantation, we identified 105 individuals with MTX-CLD, and these were compared

with individuals listed for ALD (n=17 592) and NAFLD (n=3259). Concurrent liver disease among individuals with MTX-CLD included ALD in 4.8%, NAFLD in 7.7%, hepatocellular carcinoma in 2.9%, hepatitis C infection in 1% and other drug-induced liver disease in 1%. Compared to the ALD group, those with MTX-CLD were older (median age 57 vs 51 years, $p < 0.0001$), more likely to be Caucasian (91.4% vs 80.9%, $p < 0.007$), female (46.2% vs 19.2%, $p < 0.001$) and diabetic (36.8% vs 18.3%, $p < 0.001$), and had a higher body mass index (median 28.2 vs 27.2 kg/m², $p < 0.03$), but a lower median MELD score (14.5 vs 16, $p < 0.007$). In contrast, compared to individuals with NAFLD, those with MTX-CLD were less likely to be diabetic (36.8% vs 47.7%, $p < 0.05$) and had a lower median body mass index (28.2 vs 32.1 kg/m², $p < 0.0001$), but a similar age, gender, ethnicity and MELD distribution. The prevalence of hypertension and vascular disease did not differ among the three groups, nor did their complications (ascites, encephalopathy, spontaneous bacterial peritonitis) profile.

Conclusion This is the largest analysis of end-stage MTX-CLD reported to date, demonstrating that it is a rare form of cirrhosis that has a distinct risk factor profile from those of ALD and, to a lesser extent, NAFLD. The severity of MTX hepatotoxicity may be potentiated by host (ethnicity) and environmental (diabetes, obesity) factors, ultimately leading to decompensated disease. A common pathogenic process may underlie MTX-CLD, ALD and NAFLD.

OP11 ARE SIMPLE NON-INVASIVE SCORING SYSTEMS FOR FIBROSIS RELIABLE IN PATIENTS WITH NAFLD AND NORMAL ALT LEVELS?

doi:10.1136/gutjnl-2011-300857b.11

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Introduction With a quarter of the UK population estimated to have some degree of NAFLD, there is a need for a robust and economical population based screen to identify individuals with advanced fibrosis. It is recognised that many patients with NAFLD have normal-range ALT levels. Non-invasive scoring systems may exclude advanced disease without the need for liver biopsy, however reliability of these tests in this population has not been determined.

Aim To assess performance of several simple non-invasive tests for fibrosis in patients with biopsy-proven NAFLD and normal ALT levels.

Method Patients who were reviewed in the Freeman Hospital fatty liver clinic between 1999 and 2009 were included. Liver biopsies were assessed using the Kleiner score. The AST/ALT ratio, BARD, FIB-4 and NAFLD fibrosis scores were calculated from blood tests taken within 6 months of liver biopsy.

Results 305 patients were included (70 with normal ALT [ALT <30 IU/l for females and ALT <45 IU/l for males] and 235 with raised ALT). 24% of subjects with normal ALT and 17% with raised ALT had advanced fibrosis (Kleiner stage 3–4). Patients with normal ALT were significantly younger ($p = 0.004$) and had lower BMI ($p = 0.03$) than those with raised ALT. The area under ROC curve (AUROC), sensitivity, specificity, positive and negative predictive values for a diagnosis of advanced fibrosis using each score is shown in Abstract OP11 table 1. In addition, the proportion of patients with a score below the cut-off who would avoid liver biopsy is displayed. The specificity of the AST/ALT ratio, BARD and NAFLD fibrosis scores for advanced fibrosis was low in patients with normal ALT, which would result in a high proportion of patients with mild disease having a liver biopsy. FIB-4 score performed best overall.