Method 44 children with AIH (33 AIH-1 and 11 AIH-2, median age 13.5 yrs, 23 females), 65 FDR from 34 families [23 fathers, 47 yrs (38–58); 28 mothers, 44 yrs (24–53) and 14 siblings, 7 females, 13 yrs (5–24)] and 42 healthy subjects [HS, 36 yrs (22–54), 37 females] were studied. Tregs were purified from PBMCs using immunomagnetic beads and their phenotype and frequency was assessed by flowcytometry. CD25^{neg} cells were used as responders in co-culture with Tregs and their proliferation was measured by ³H-thymidine incorporation. HLA genotyping was performed by PCR using gene specific primers.

Results The frequency of the disease predisposing gene HLA DR3 was significantly higher in patients (71%) and their FDR (56%) than in HS (23%, $p<0.0001$ and $p<0.005$). The frequency of homozygous DR3 was higher in patients (29%) than in FDR (9%, $p=0.015$) and HS (0%, $p=0.001$). In patients the frequency of HLA A1-B8-DR3 haplotype (42%) was higher than in FDR (27%, $p=0.15$) and HS (16%, $p=0.02$). The frequency of conventional CD4^{pos}CD25^{pos} Tregs was lower in patients (6.2 ± 0.5) than in FDR (9.3 ± 0.7 , $p=0.0016$) and HS (9.7 ± 0.8 , $p=0.001$). Though the frequency of CD4^{pos}CD25^{high}CD127^{neg} 'True' Tregs was similar among patients, FDR and HS (6.0 ± 0.6 , 6.3 ± 0.4 and 6.2 ± 0.5), their suppressive function was lower in patients (13.6% reduction of CD25^{neg} cell proliferation) than in FDR (28.8%, $p=0.007$) and HS (36.9%, $p<0.0001$). Among subjects positive for HLA DR3, the frequency of conventional Tregs was lower in patients (5.6 ± 0.5) than in FDR (8.4 ± 0.97 , $p=0.01$) and in HS (9.1 ± 1.4 , $p=0.006$). Among subjects positive for HLA A1-B8-DR3 haplotype, the frequency of Tregs was lower in patients (6.0 ± 0.7) than in FDR (9.1 ± 1.5 , $p=0.045$) and HS (9.8 ± 1.8 , $p=0.02$).

Conclusion A numerical and functional impairment of Tregs in AIH patients is associated with possession of HLA disease predisposing genes, and in particular HLA DR3 homozygosity. Possession of DR3 was not associated to a similar immune regulatory impairment in FDR and HS, suggesting that a gene dose effect contributes to the impairment of immunoregulation and to the development of AIH.

P05 COMBINATION OF SERUM BIOMARKERS FOR THE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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¹P Johnson, ¹M Teng, ¹S Pirrie, ²D Palmer, ¹S Berhane, ¹D Stocken. ¹University of Birmingham, UK; ²University of Liverpool, UK

Introduction The most commonly used serum biomarker for the diagnosis of hepatocellular carcinoma (HCC) is α fetoprotein (AFP). However, AFP is also modestly raised in patients with chronic liver disease, particularly in those who are at a higher risk of developing HCC. A number of other circulating markers such as des- γ carboxy prothrombin (DCP) and the Lens culinaris agglutinin-reactive fraction of α -fetoprotein (L3) have been shown to have diagnostic discrimination which may, in certain situations, be superior to AFP.

Aim We therefore aimed to build a model that combined these biomarkers with baseline liver function tests, in order to identify those factors which predict HCC and might improve diagnostic efficacy of AFP alone.

Method A prospective study was specifically designed to assess the diagnostic efficacy of biomarkers. 461 serum samples were collected between 2007 and 2011: 252 were controls samples from patients with chronic liver disease with no evidence of HCC within 6 months of the sample; 59 were from patients with early HCC which was potentially curable and 150 were from patients with late HCC. AFP, AFP-L3 and DCP were measured in serum samples using a new micro total analysis system (Wako Chemicals GmbH, Neuss, Germany). Patients were classified into two groups (HCC, control) for the primary analysis. Independent predictors of HCC were identified from multivariable logistic regression analyses. The

impact of AFP, DCP and L3 are reported based on the area under the receiver operator curve (AUC).

Results Univariate analysis showed AFP alone to have OR=2.96 (2.34 to 3.73 95% CI), AUC =0.8723, $p<0.001$. A multivariable model selected age, sex, AST, ALP and INR as independent predictors of HCC with an overall model AUC =0.8857. Including AFP, DCP and L3 to this model increased the AUC to 0.9489, 0.9290, 0.9254 respectively. The final model included age, sex, AFP, DCP and INR gave an AUC of 0.9661 (95% CI 0.95 to 0.98) for all patients and 0.944 (95% CI 0.914 to 0.974) for early HCC patients.

Conclusion A combination of serum markers may produce a clinically useful diagnostic test for HCC compared to AFP alone. Further validation of our model is underway on an independent dataset. These findings suggest that our model may enhance or replace the current screening approach for patients with liver cirrhosis, particularly since it appears to have efficacy even in patients with early, potentially curable, disease.

P06 ROLE OF SERUM HYALURONIC ACID IN PREDICTING MORTALITY IN PATIENTS WITH CHRONIC LIVER DISEASE

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¹N Plevis, ²N C Mcavoy, ²P C Hayes. ¹University of Edinburgh, UK; ²Department of Hepatology, Royal Infirmary of Edinburgh, UK

Introduction Currently liver biopsies are used to assess extent of liver fibrosis and provide prognostic information in liver disease. Hyaluronic acid (HA) is a non-invasive serum marker that has been shown to correlate well with different degrees of hepatic fibrosis. Despite this the prognostic abilities of HA still remain to be established.

Aim In this study we aim to establish the relationship between levels of serum HA and survival, as well as determine the sensitivity and specificity of HA for predicting death in patients with chronic liver disease of varying aetiology.

Method Patients seen at the department of hepatology, Royal Infirmary of Edinburgh between 1995 and 2010 who had serum HA levels measured were followed up for death from the date of HA measurement until the 1 November 2010 by examination of clinical records on TRAK (NHS Lothian). The cumulative probability for survival from liver related death and overall deaths at 1-, 5- and 8-year follow-up was determined. Receiver operating characteristic (ROC) curves were generated to assess the sensitivity and specificity of HA levels at predicting liver-related death at 1, 3 and 5 years.

Results HA levels were available for 632 patients. The median follow-up time (from HA measurement to death or 'last known alive') was 2.7 years (range 0.0–8.0; IQR 0.9–4.4). Survival analysis showed that HA levels >400 μ g/l are associated with a significantly lower probability of survival from liver related death compared to patients with values of <100 μ g/l and 100–400 μ g/l at 1 year (88%, $p<0.01$), 5 years (68%, $p<0.001$) and 8 years (49%, $p<0.05$). In addition, the probability of survival from liver related death at 8 years was also significantly less in patients with HA value of 100–400 μ g/l compared to patients with HA <100 μ g/l (83%, $p<0.05$). Similar results were observed when assessing probability of survival from overall deaths. The unadjusted area under the ROC curve for predicting liver related mortality for HA at 1-, 3- and 5 years was 0.89 (CI 95% 0.84 to 0.94), 0.85 (CI 95% 0.79 to 0.91) and 0.79 (CI 95% 0.71 to 0.87) respectively. Optimum cut-off value for 1-, 3- and 5 year for predicting liver death was 326 μ g/l (88% sensitivity/79% specificity), 267 μ g/l (74% sensitivity/79% specificity) and 203 μ g/l (71% sensitivity/72% specificity) respectively.

Conclusion In this study we have shown that patients with high levels of serum HA have an increased liver and all cause mortality. In addition, HA levels are both sensitive as well as specific at determining liver related mortality. This highlights the potential use of

HA as a non-invasive marker for prognosis in patients with chronic liver disease of varying aetiology.

P07 SOCIO-DEMOGRAPHIC AND BEHAVIOURAL DETERMINANTS OF ABNORMAL LIVER FUNCTION IN A MULTI ETHNIC POPULATION IN THE UK: THE LOLIPOP STUDY

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¹S D S Fraser, ¹J Parkes, ¹P J Roderick, ²J S Kooner, ²J Chambers. ¹University of Southampton, UK; ²Imperial College, London, UK

Introduction Fatty liver disease (FLD) is common, with an estimated prevalence between 10 and 24% of the general population. Most patients are asymptomatic, and identified via incidental abnormal liver function tests, particularly alanine transaminase (ALT) and γ -glutamyltransferase (GGT). There are few population data on the prevalence or determinants of abnormal liver function.

Aim To determine the characteristics and associations of people with elevated values 1.5 times normal of both ALT and GGT in a population sample (upper limit of normal (ULN)=ALT $\geq$ 37 $\pm$ 31 IU/l; GGT $\geq$ 55 $\pm$ 38 IU/l) as an indicator of FLD.

Method The London Life Sciences Prospective Population Study (LOLIPOP study) is a population based cohort study of cardiovascular risk and outcomes in west London, an area with a high ethnic minority population. Adults aged 35–74 from 58 general practices were invited to cardiovascular screening which included questionnaire, clinical measurement and blood sampling. Response rate was 62%. Cross sectional data were obtained on 31 507, European white (n=2222), Indian Asian (n=19 769) and Black (n=2516). ALT and GGT were measured from a single serum sample. To identify key socio-demographic variables and potentially modifiable lifestyle factors, including BMI and alcohol intake, we used logistic regression models examining associations with elevated ALT and GGT.

Results The number with GGT and ALT measures was 31 465 (99.9% of total). The prevalence of elevated GGT above 1.5 times the ULN (GGT 1.5) was 10.4% (3265/31 465), for ALT 8% (2517/31 465) and for both 3.2% (996/31 465). 40% of those with ALT 1.5 had GGT 1.5, and 32% of those with GGT 1.5 had ALT 1.5. The independent odds of having both raised were increased in: younger people (OR 3.00 (95% CI 2.28 to 3.94) for 35–44 compared to 65–74 age group), south Asians (OR 1.29 (95% CI 1.10 to 1.51) compared to White), greater alcohol intake (OR 6.52 (95% CI 5.36 to 7.95) for >28 units per week compared to no alcohol), raised BMI (OR 2.34 (95% CI 1.94 to 2.83) obese compared to normal), and diabetes (OR 1.32 (95% CI 1.07 to 1.63), with a dose related gradient for alcohol consumption. Gender, deprivation, and taking statin were not significantly associated, and no interaction observed between alcohol and gender or BMI.

Conclusion The prevalence of abnormal liver function tests, suggesting FLD, was common (directly standardised prevalence of 3.3% in this age group in the England and Wales population). BMI, and alcohol independently increased risk across the range of their values, highlighting the importance of considering both in preventing severe liver disease and counselling patients.

P08 SPONTANEOUS BACTERIAL PERITONITIS PROPHYLAXIS: REDUCING THE INCIDENCE OF C DIFFICILE INFECTION

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¹H Jafferbhoy, ¹M H Miller, ¹C Shekar, ²M Lockhart, ¹J F Dillon. ¹GUT Group Biomedical Research Institute, Dundee University; ²Department of Microbiology, Ninewells Hospital

Introduction Spontaneous bacterial peritonitis is a serious and life-threatening complication of cirrhosis, especially common in

hospitalised patients. Antibiotic prophylaxis is effective but can lead to an increased incidence of hospital-acquired infections such as *Clostridium difficile*.

Aim We evaluated whether two alternative prophylaxis agents were equally efficacious in preventing SBP, and the impact on risk of *C difficile* infection.

Method A consecutive, cohort study of hospitalised patients with cirrhosis and ascites, over a 3-year period in a tertiary hospital. In the first cohort (2007–2009), ascitic patients requiring prophylaxis received Norfloxacin 400 mg/d during their hospital admission. In the second cohort (2009–2010) patients received prophylactic Co-trimoxazole 960 mg/d during their hospital admission. Data were extracted by case note review and the two cohorts compared.

Results 174 patients admitted during 2007–2010 accounted for 231 hospital episodes with ascites. The Norfloxacin group had 154 episodes and the Co-trimoxazole group had 77. The mean age of the cohort was 57.4 years (SD 12.4) and 62% were male. Alcoholic cirrhosis was the major aetiology accounting for 79% of cases. The mean Child-Pugh and UKELD scores were 10.7 and 54 respectively. The overall incidence of SBP in our cohort was 19%. Abstract P08 table 1 demonstrates that the incidence of hospital acquired SBP, prophylaxis failure and mortality was not statistically different between the two therapies. However, selective bowel sterilisation with Co-trimoxazole did not lead to an increase *C difficile* infection rate.

Abstract P08 Table 1 Outcome of patients hospitalised with cirrhosis and ascites

	Norfloxacin	Co-trimoxazole	p Value
Episodes*	134	67	
Hospital acquired SBP	9 (6.71%)	7 (10.44%)	NS
Prophylaxis failure %	5/130 (3.84%)	4/64 (6.24%)	NS
<i>C difficile</i> rate %	13 (9.7%)	0	0.009
30-day mortality %	25 (18.65%)	15 (22.38%)	NS
90-day mortality %	41 (30.59%)	16 (23.88%)	NS

*Excluding patients with community acquired SBP.

Conclusion Survival of cirrhotic patients with ascites is inversely related to severity of Liver disease, worsened with development of infections such as spontaneous bacterial peritonitis and *C difficile*. This study shows that Co-trimoxazole inpatient prophylaxis against SBP is as effective as quinolone based regimes, but has the advantage of a dramatic reduction in *C difficile* infection. At the same time the importance of measures like hand hygiene compliance, environmental cleanliness and strict policy of in hospital antibiotic prescribing cannot be underestimated.

P09 VALIDATION OF A NOVEL BIOMARKER MODEL FOR THE PREDICTION OF NON-ALCOHOLIC STEATOHEPATITIS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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¹S Tanwar, ²P Trembling, ³I N Guha, ⁴J Parkes, ⁵P Kaye, ⁶A D Burt, ⁷S D Ryder, ⁴G P Aithal, ⁸C P Day, ⁹W M Rosenberg. ¹Centre for Hepatology, University College, London, UK; ²Centre for Hepatology; ³University College London; ⁴UK; ⁵University Hospital; ⁶Queen's Medical Centre; ⁷Nottingham; ⁸Public Health Sciences and Medical Statistics; ⁹University of Southampton

Introduction The detection of non-alcoholic steatohepatitis (NASH) within non-alcoholic fatty liver disease (NAFLD) is important both