

jaundice to encephalopathy <7 days), 8 Subacute/Acute Liver Failure (S/ALF: jaundice to encephalopathy >7 days), and 18 healthy controls (HC). Flow cytometry was performed to investigate monocyte phenotype (CD14, CD16, HLA-DR, CD86, CD163, CD11b and CCR5).

**Results** Compared to HC, total monocyte count was elevated in S/ALF, but reduced in hyperALF ( $p<0.001$ ), while CD14hi/CD16+ monocytes were expanded in percentage of total monocytes and absolute numbers in S/ALF (17.4%; 0.14) compared to HC (4%; 0.014) ( $p<0.001$ ). Although the percentage of CD14hi/CD16+ monocytes in hyperALF was higher (5.6%,  $p<0.01$ ), the absolute number (0.013) was similar to HC. Though all CD14hi/CD16+ monocytes expressed HLA-DR, the Mean Fluorescence Intensity (MFI) was reduced compared to HC ( $<0.001$ ). HyperALF CD14hi/CD16+ monocytes had lower HLA-DR MFI compared to S/ALF ( $p<0.001$ ). A similar pattern was seen for CD86 expression ( $p<0.01$ ). CD14hi/CD16+ monocytes showed increased expression of CD163 in hyperALF but not in S/ALF compared to HC ( $<0.01$ ). Compared to HC, CD11b and CCR5 were up-regulated in all ALF groups ( $p<0.001$ ).

**Conclusion** We have demonstrated an expansion of CD14hi/CD16+ monocytes in ALI with an activated phenotype for adhesion and migration. CD14hi/CD16+ monocytes phenotypically resemble M1 macrophages in S/ALF, possibly reflecting a pathogenic role in the perpetuation of liver injury, while they resemble M2 in hyperALF and may be instrumental to the resolution of liver injury. This distinction requires further investigation should therapeutic strategies to target monocyte migration be attempted.

**Competing interests** None declared.

#### PTU-016 ALBUMIN RESTORES RENAL BLOOD FLOW (RBF) AUTOREGULATION IN PATIENTS WITH REFRACTORY ASCITES AND ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) THROUGH STABILISATION OF ENDOTHELIAL FUNCTION

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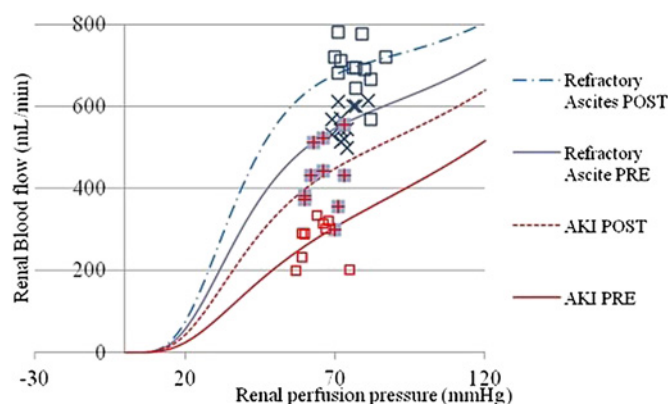
R Garcia Martinez,\* J O'Brien, L Noiret, N Davies, R Mookerjee, R Jalan. *Medicine, UCL Hepatology, London, UK*

**Introduction** Haemodynamic alterations in liver failure are associated with endothelial dysfunction, a pro-inflammatory state and sympathetic activation which lead to disturbed RBF autoregulation and renal failure. Albumin is a multifunctional protein that has been shown in several studies to prevent and treat renal dysfunction in patients with advanced cirrhosis and liver failure. We hypothesised that the beneficial effects of albumin in cirrhosis is likely to be through mechanisms in addition to volume expansion. The aims of the study were to investigate the effects of albumin on systemic and renal haemodynamics, inflammation and endothelial dysfunction in refractory ascites and patients with acute kidney injury (AKI) in the setting of ACLF.

**Methods** Twenty-two patients were recruited [Group 1, n=12, refractory ascites; Group 2, n=10 patients with AKI admitted with an acute deterioration of their liver function due to either alcoholic hepatitis or infection]. Both groups were treated with Albumin 60 g/d over 3–4 days. Cardiac output (CO) and renal blood flow (RBF) haemodynamics were measured. Endothelial dysfunction was assessed through measurement of von Willebrand factor (vWF) and serum nitrite (NO) levels. F2 $\alpha$  Isoprostanes (F2 $\alpha$ ), resting neutrophil burst and Interleukin (IL)-6 were quantified as markers of oxidative stress, endotoxemia and inflammation respectively.

**Results** Albumin therapy was associated with significant improvements in haemodynamic parameters (increased RBF, MAP, decreased

CO, HR;  $p<0.05$ ) which resulted in a shift in the RBF autoregulation curve towards normalisation (Abstract PTU-016 figure 1). In parallel, improvement of renal dysfunction (creatinine, creatinine clearance and Na<sup>+</sup> excretion;  $p<0.05$  each), sympathetic activation (noradrenaline levels;  $p<0.01$ ), inflammation/oxidative stress (F2 $\alpha$  and neutrophil burst;  $p<0.05$ ), endothelial dysfunction (vWF and NO metabolism  $p<0.05$ ) and the functional capacity of albumin (IMAR  $p<0.005$ ) was observed. Restoration of RBF correlated inversely with change in vWF ( $r^2=0.55$ ,  $p<0.001$ ).



Abstract PTU-016 Figure 1

**Conclusion** This study suggests that albumin infusion improves albumin function which has pleiotropic effects and results in a reduction in inflammation and improvement in endothelial function leading to improved systemic haemodynamics and renal blood flow autoregulation.

**Competing interests** None declared.

#### PTU-016a FUNCTIONAL DEFECTS IN CIRCULATING MONOCYTES MAY CONTRIBUTE TO SUSCEPTIBILITY TO INFECTION IN ALCOHOLIC HEPATITIS

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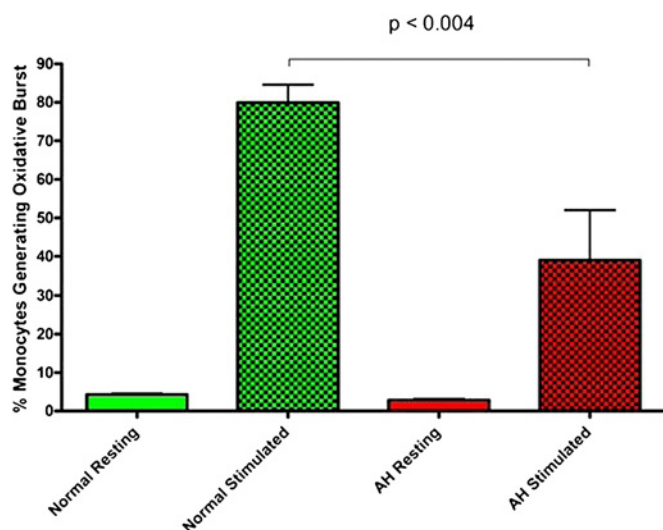
<sup>1</sup>N Vergis,\* <sup>1</sup>C G Antoniadou, <sup>2</sup>V Zingarelli, <sup>2</sup>R D Abeles, <sup>2</sup>Y Ma, <sup>2</sup>D Shawcross, <sup>2</sup>A Janmohamed, <sup>3</sup>D Patch, <sup>3</sup>W Rosenberg, <sup>4</sup>P Kennedy, <sup>4</sup>G Foster, <sup>1</sup>S Khan, <sup>2</sup>K Agarwal, <sup>2</sup>M Heneghan, <sup>2</sup>J O'Grady, <sup>2</sup>D Vergani, <sup>2</sup>J Wendon, <sup>1</sup>M Thursz. <sup>1</sup>Hepatology and Gastroenterology, Imperial College, London, UK; <sup>2</sup>Institute of Liver Studies, King's College Hospital, London, UK; <sup>3</sup>Hepatology, Royal Free Hospital, London, UK; <sup>4</sup>Hepatology, Royal London Hospital, London, UK

**Introduction** Infection is common in patients with severe alcoholic hepatitis (AH) and a significant contributor to mortality. Monocytes play an important role in bacterial elimination by phagocytosis, using intracellular oxidative killing and antigen presentation. Our study sought to evaluate monocyte phagocytosis and scavenger receptor expression in AH.

**Methods** Monocytes were collected from 14 patients with AH (DF >31, prior to treatment) and 22 healthy controls (HC). Using FACS, monoclonal antibodies to scavenger receptors (CD36, -64, -163, -206, DCIR) and HLA-DR were used for immunophenotyping. Subsequently, ex-vivo monocyte phagocytosis and oxidative burst activity was assessed using FITC-labelled opsonised and non-opsonised *Escherichia coli*.

**Results** The expression of scavenger receptors was deranged. In CD14+CD16- (classical) monocytes, CD163 MFI was reduced in AH compared to controls (587 vs 403;  $p=0.05$ ). CD36, -206 and DCIR expression was similar between HC and AH patients but CD64 MFI was raised (6002 vs 12599;  $p<0.001$ ). The proportion of monocytes phagocytosing *E coli* was lower in AH compared to HC

(77% vs 87%;  $p < 0.03$ ) but this was not a result of complement deficiency as phagocytosis did not depend on whether the bacteria were opsonised or not (73% vs 80%;  $p = 0.9$ ). The proportion of monocytes capable of generating an oxidative killing burst in response to phagocytosed *E coli* was markedly reduced (84% vs 47%;  $p < 0.004$ ) in AH patients compared to HC [Abstract PTU-016a figure 1]. Antigen presentation was also impaired: classical monocytes had significantly lower HLA-DR expression in AH compared to controls (73% vs 35%;  $p = 0.002$ ), with similar levels of HLA-DR expression detected in the CD14+CD16+ monocyte subset (94% vs 74%;  $p = 0.4$ ).



Abstract PTU-016a Figure 1

**Conclusion** It appears that there are a number of functional defects in circulating monocytes in patients with AH. The marked impairment of phagocytosis and intracellular killing may contribute to the increased susceptibility to infection in this group of patients.

**Competing interests** None declared.

## General Liver I

### PTU-017 IGG4 +VE AUTOIMMUNE HEPATITIS IS NOT OBSERVED AMONG PATIENTS OF NON-ASIAN ORIGIN

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A D Yeoman,\* Y Zen, M A Heneghan. *Institute of Liver Studies, Kings College Hospital NHS Foundation Trust, London, UK*

**Introduction** IgG4 mediated autoimmune disease has recently been described in relation to pancreatitis and sclerosing cholangitis. Furthermore recent reports, mainly from Japan, have also identified cases of autoimmune hepatitis (AIH) in which an IgG4 positive hepatic inflammatory infiltrate predominates.

**Methods** We set out to establish the frequency with which IgG4 +ve plasma cells are observed in a cohort of patients with AIH without pancreatitis or sclerosing cholangitis. Immuno-histochemical analysis via application of a monoclonal antibody to IgG4 was undertaken on archived liver tissue specimens. Three fields per biopsy specimen were analysed and the number of IgG4+ve plasma cells per high powered field (HPF) and the proportion of these as a total of the plasma cell infiltrate were recorded. As per recent publications<sup>1 2</sup> a biopsy specimen was determined to be IgG4 +ve if more than 10 IgG4 +ve plasma cells were seen per high powered field (HPF) AND where this number equated to >40% of

the total plasma cell infiltrate. Immunohistochemical and histo-pathological analysis was undertaken by a single, experienced, hepato-pathologist (YZ).

**Results** Sixty-three liver tissue specimens underwent immuno-histochemical analysis. These specimens derived from 53 Caucasian and 10 Afro-Caribbean patients. All patients met the revised International Autoimmune Hepatitis Group diagnostic criteria for probable or definite AIH. The median age of patients at diagnosis was 31 years and 78% were female. Among this cohort 44 patients presented with chronic disease and histological evidence of chronic active hepatitis while 19 presented with acute disease in whom histology demonstrated hepatic collapse in 16 and severe lobular hepatitis in three patients. Only 7 of 63 samples (11%) demonstrated >10 IgG4 +ve cells/HPF. While there was a greater number of biopsy specimens with >10 IgG4 +ve plasma cells per HPF in acute vs chronic presentations this did not reach statistical significance (16% vs 9%,  $p = 0.44$ ). Additionally, there was no difference in the frequency of this finding between males and females (males 21% females 8%  $p = 0.4$ ) or between different ethnic groups (11% in Caucasians vs 10% in Afro-Caribbeans,  $p = 0.99$ ). Importantly, in none of the seven cases in which >10 IgG4 +ve plasma cells/HPF were noted did the proportion of IgG4 +ve plasma cells equate to >40% of the total plasma cell infiltrate.

**Conclusion** While a small proportion of non-Asian AIH patients demonstrate >10 IgG4 +ve plasma cells/HPF, in no individual did this represent >40% of the total hepatic plasma cell infiltrate. Consequently, significant IgG4 +ve plasma cell infiltrates are not observed among non-Asian patients with AIH presenting to our institution.

**Competing interests** None declared.

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### PTU-018 CYSTATIN C AND PROTEIN: CREATININE RATIO; POTENTIAL PREDICTORS OF EARLY ACUTE KIDNEY INJURY, RENAL REPLACEMENT THERAPY AND IN-HOSPITAL DEATH IN PATIENTS WITH CIRRHOSIS

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<sup>1</sup>A Slack,\* <sup>1</sup>J Wendon, <sup>1</sup>M J McPhail, <sup>2</sup>R Sherwood, <sup>2</sup>R Musto, <sup>1</sup>M Heneghan. <sup>1</sup>Institute of Liver Studies, King's College Hospital, London, UK; <sup>2</sup>Clinical Biochemistry, King's College Hospital, London, UK

**Introduction** Acute kidney injury (AKI) is common, but difficult to predict in patients with cirrhosis as lower baseline serum creatinine can mask significant chronic kidney dysfunction. Cystatin C is a biomarker of glomerular filtration rate (GFR), which may overcome this weakness. Quantifying proteinuria using the widely available protein:creatinine ratio (PCR) may better the degree of structural glomerular damage.

**Methods** 34 patients with cirrhosis and mean (SD) age 51 (14) years and, median (range) Child-Pugh Turcotte (CPT) score 11 (9–11) were prospectively assessed for 10 days or until AKI, developed. Baseline iothexol clearance was performed to calculate GFR and urine underwent PCR analysis. Daily urine and serum samples were collected for determination of novel serum and urine biomarkers of kidney injury, including Cystatin C. Biomarkers were assessed by area under the receiver operating curve (AUROC) for predicting AKI stage 1, renal replacement therapy (RRT) and death.

**Results** 16 (47%) patients developed AKI defined by an increase of >26.4  $\mu\text{mol/l}$  from baseline serum creatinine (median 73 range 37–120  $\mu\text{mol/l}$ ). Estimated GFR overestimated GFR with median eGFR 95 (47–181)  $\text{ml/min/1.73 m}^2$  compared to a median iothexol