

**PTU-037** **ENDOTHELIAL INJURY AND OXIDATIVE STRESS IN PATIENTS WITH SCHISTOSOMAL HEPATIC FIBROSIS: RELATION TO RENAL DYSFUNCTION AND HAEMODYNAMICS**

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**Introduction** Endothelial injury plays an important role in the pathogenesis of chronic renal diseases and may be related to oxidative stress. The present work was designed to study markers of endothelial injury and oxidative stress in patients with schistosomal hepatic fibrosis (SHF) in relation to renal dysfunction and haemodynamics.

**Methods** 45 patients with SHF and 15 healthy subjects were included in the study. The severity of liver disease was assessed using Child-Pugh scoring system. According to urinary albumin excretion rate, patients with SHF were classified into 15 patients with normoalbuminuria, 15 patients with microalbuminuria and 15 patients with persistent albuminuria. Endothelial injury was assessed by plasma von Willibrand factor (vWF) activity and serum ACE levels. Serum malondialdehyde (MDA) levels were also measured as a marker for oxidative stress. Tubular damage was determined by measuring 24-h urinary levels of leucine aminopeptidase (LAP). Renal haemodynamics were assessed using Duplex-doppler ultrasonography by calculating the diastolic/systolic renal flow velocity ratio (d/s), intrarenal renal resistive index (RI) and hilar renal blood flow (RBF).

**Results** Compared to healthy subjects, patients with SHF showed significant increases in plasma vWF activity, serum levels of ACE and MDA and urinary LAP levels ( $p < 0.05$ ). Serum MDA and urinary LAP levels were significantly higher in patients with microalbuminuria and persistent albuminuria than in patients with normoalbuminuria while serum ACE level was significantly higher in patients with persistent albuminuria than in those with normoalbuminuria or microalbuminuria ( $p < 0.05$ ). Patients with SHF also showed a significant increase in RI and significant decreases in d/s ratio and RBF compared with healthy subjects regardless of the severity of glomerular injury ( $p < 0.05$ ). No statistically significant correlations were found between the severity of liver disease on one hand and plasma vWF activity, serum ACE levels, urinary LAP levels and renal haemodynamics on the other hand in patients with SHF ( $p > 0.05$ ), while there was a significant positive correlation between serum MDA levels and Child-Pugh score in these patients ( $p < 0.05$ ).

**Conclusion** Endothelial injury, possibly due to oxidative stress, may play an important role in the pathogenesis of renal dysfunction and increased renovascular impedance in SHF and in the initiation of schistosomal nephropathy in this disease.

**Competing interests** None declared.

**PTU-038** **LONG TERM FOLLOW-UP OF PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS**

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**Introduction** Non-alcoholic steatohepatitis (NASH) is an increasingly common cause for liver disease. More evidence is needed to

determine the natural history and prognosis of this condition. The aim of the study was to conduct a prospective follow-up of a group of patients with NASH confirmed on liver biopsy over a period of up to 26 years.

**Methods** A study of 62 patients who had NASH on liver biopsy performed during the period 1985 to 1994 was published in 2002.<sup>1</sup> Biopsies were scored according to Brunt's system<sup>2</sup> by a single pathologist. 59 of these patients were now traceable. Information on long-term outcome was obtained by review of case notes, electronic patient records and data from NHS Information Services Division and the Registrar General for Scotland. Follow-up duration was defined as the time between diagnosis by initial liver biopsy and last hospital attendance or death. 1 patient subsequently tested positive for hepatitis C and was excluded from further analysis.

**Results** 17 of the 58 patients were male, with an overall mean age at diagnosis of 44 (range 17–74 years). 56 were Caucasian and 2 Asian and mean follow-up in years was 15 (range 0–26). Mean body mass index at diagnosis was 27.6 (range 21.1–41.3). At diagnosis, 6 (10.3%) had diabetes mellitus (DM), 14 (24.1%) hypertension (HTN) and 4 (6.9%) ischaemic heart disease (IHD). On follow-up a total of 21 (36.2%) patients had a diagnosis of DM and 30 (51.7%) HTN. On initial biopsy none of the patients had cirrhosis. During follow-up 15 (25.8%) patients developed cirrhosis (3 biopsy proven and 12 clinical). 5 (8.6%) patients developed hepatic decompensation with jaundice (2), ascites (2), encephalopathy (1), variceal haemorrhage (1) and hepatoma (1). 28 (48.3%) of the patients have died at a mean age of 70.4 years (range 33–97). Time to death from diagnosis was 0.5 to 24 years (mean 14). Two patients died of liver failure (7.1%), 4 from non-hepatic malignancy (14.3%), 6 from IHD (21.4%), 3 of infectious causes (10.7%), 3 of cerebrovascular disease (10.7%) and 10 of "other causes" (2 chronic obstructive pulmonary disease, 1 DM, 1 alcohol, 1 pancreatitis, 5 unknown).

**Conclusion** This observational study shows that the outcome of NASH is not benign with a significant mortality over a mean of 15 years, largely due to vascular disease and malignancy as expected. Progression to cirrhosis occurred in 26% of patients causing considerable clinical morbidity, but death from liver disease over this time period was uncommon.

**Competing interests** None declared.

**REFERENCES**

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**PTU-039** **MORTALITY AND UTILITY OF PROGNOSTIC SCORING MODELS IN CIRRHOTIC PATIENTS ADMITTED TO A TERTIARY NON-TRANSPLANT INTENSIVE CARE UNIT (ICU) IN THE UK**

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**Introduction** Patients with liver cirrhosis admitted to ICU have a poor prognosis with reported ICU, in-hospital and 1-year mortality rates of 37% > 65%, 49–74% and 69–81% respectively. Prognostic models may enable accurate discrimination at admission of those who will benefit from ICU admission. Organ failure scoring models have been shown to be good predictors of ICU mortality, but there are few reports of their utility in non-transplant centres in Europe. We aimed to describe mortality and the prognostic value of commonly used predictors in patients with cirrhosis admitted to the ICU of a tertiary non-transplant London teaching hospital ICU.

**Methods** Retrospective analysis of the Intensive Care National Audit and Research Centre database of all patients with cirrhosis admitted to ICU from January 2006 to November 2010. Statistical analysis was performed with SPSS V. 19. The area under receiver operating curve (AUROC) was used to assess the prognostic accuracy of the scoring models.

**Results** 135 out of 4890 (2.8%) admissions had diagnosed cirrhosis. Mean age was 53. 77% were white, 16% were Asian, and 7% were black. 74% were male. Cause of cirrhosis was alcohol in 70.4%, HCV in 9.6%, HBV in 4.4% and NASH in 5.2%. Admission was for sepsis in 34% of patients, GI bleeding in 24%, and encephalopathy in 12%. Mortality was 39% in ICU, 55% at 30 days and 59% at 1 year. 30-day mortality in those who required renal replacement therapy (RRT), advanced cardiovascular support, mechanical ventilation or CPR was 75%, 65%, 58% and 70% respectively. Overall all-cause ICU mortality was 19.4% for this period.

**Conclusion** Mortality in this series compares favourably with published rates, particularly at 1 year. Mortality in patients who require CPR or RRT is high at 70% and 75%, but is appreciably better than the 100% and 89% mortality previously reported. SOFA score has the best predictive value for mortality, but is not strongly predictive. All predictive scores have a worse AUROC for mortality than previously seen suggesting a reduced prognostic validity in the non-transplant UK setting.

Abstract PTU-039 Table 1 Predictors of 30-day mortality

Variable	Area under the curve	95% CI	Range of previously reported area under the curve
SOFA	0.736	0.650 to 0.821	0.77–0.94
SAPS II	0.716	0.629 to 0.802	0.80
APACHE II	0.697	0.606 to 0.788	0.77–0.90
MELD	0.691	0.603 to 0.779	0.78–0.878
RIFLE score	0.626	0.533 to 0.720	0.837

**Competing interests** None declared.

**PTU-040 ALCOHOL: ALWAYS DETRIMENTAL TO THE IMMUNE SYSTEM? THE ROLE OF ACTIVE ALCOHOL CONSUMPTION ON NEUTROPHIL FUNCTION IN ALCOHOL-RELATED CIRRHOSIS**

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**Introduction** Neutrophil dysfunction has been reported in patients with alcohol-related cirrhosis (ARC) and is associated with increased risk of infection and mortality. There is a paucity of understanding regarding the mechanisms of immune dysfunction in patients with active alcohol consumption and ARC. This study aimed to characterise neutrophil phenotype, functionality and plasma cytokine profiles in abstinent patients with ARC (n=17) compared to those actively drinking (n=19), split by MELD score <15 vs >15 compared to healthy controls (n=12).

**Methods** Neutrophils were isolated from patients with ARC. Phagocytic capacity was analysed by flow cytometry using FITC-labelled *Escherichia coli* and oxidative burst (OB) was determined by the percentage of neutrophils producing reactive oxygen species (ROS) at rest, and after stimulation with opsonised *E. Coli*. Neutrophils were stained with anti-CD11b (APC-Cy7), -CD16 (PE

and -TLR4 (biotin-conjugated PE-Cy7 Streptavidin). Plasma cytokine profiling was performed using cytokine bead array.

**Results** Phagocytosis was significantly reduced in the cirrhotic groups compared to controls (p=0.02) however this was not influenced by MELD score or abstinence. Spontaneous OB was significantly increased in the cirrhotic groups compared to controls (p=0.03). Median spontaneous OB in the abstinent patients with MELD <15 was 26% [IQR 8–42] compared to 10% (IQR 7–44) in those actively drinking. Median spontaneous OB in the abstinent group with MELD>15 was 31% (IQR 8–61) compared to 14% (IQR 4–29) in the active alcohol-drinkers. Stimulated burst was not impaired in the cirrhotic groups, with comparative values to controls. Plasma pro- and anti-inflammatory cytokine profiles were not discriminatory between the groups. Baseline TLR4 expression was increased in the MELD>15 abstinent group compared to active drinkers (p=0.004); alcohol attenuated resting TLR4 expression to values seen in controls.

**Conclusion** Active alcohol consumption did not impact on neutrophil phagocytic capacity but reduced spontaneous OB by 50% with a reduction in the generation of ROS and decreased resting TLR4 expression. This supports a paradoxical anti-oxidant role of active alcohol drinking in patients with ARC that may promote endotoxin tolerance and warrants further investigation.

**Competing interests** None declared.

**PTU-041 ACUTE FATTY LIVER OF PREGNANCY: A REVIEW OF 20 CASES**

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**Introduction** Acute Fatty Liver of Pregnancy (AFLP) is a life threatening condition occurring in the last trimester of pregnancy, its incidence is up to 1/1000 births<sup>1</sup> and is commoner in primiparous women with male or twin pregnancies.<sup>2</sup> It has features in common with HELLP syndrome, though coagulopathy, hypoglycaemia and polydipsia are commoner in AFLP and anaemia is not a feature.<sup>3</sup> Liver biopsy confirms the diagnosis but a Swansea Score of 6 or above, in absence of another explanation, indicates AFLP.<sup>1</sup> We aimed to review our experiences of AFLP to further our recognition and management of the condition.

**Methods** A retrospective review of 20 patients with suspected AFLP between 1993 and 2011, assessing patient demographics, Swansea score, biopsy results and complications.

**Results** Median age 26 (range 18–35), gestation age 36 (range 33–40), 3 twin pregnancies and 65% male births. Most were G1P0. Average Swansea score 9 (range 6–13). Commonest presentation was abdominal pain, malaise and vomiting. 60% had polydipsia, 25% had encephalopathy. 100% had raised transaminase, AST 231 u/l (range 84–4019), ALT 274 u/l (range 99–722). 95% had high urate 0.61 mmol/l (range 0.32–0.97), 85% had high bilirubin 62 umol/l (range 13–192) and 85% leucocytosis 19.4×10<sup>9</sup>/l (range 12.8–74.5). 65% had renal impairment, Creatinine 141 umol/l (range 40–305), 55% had coagulopathy, PT 15 s (range 10–57), 40% had hypoglycaemia, glucose 3 mmol/l (range 1–6). 20% patients had high ammonia, average 58 (range 28–67), 65% patients did not have ammonia checked. Ultrasound scan (USS) was performed on 4/20 patients, 2 had steatosis. 50% patients had biopsy, done 2–13 days post partum. All had microvesicular steatosis, 2 cholestasis, 1 centrilobular necrosis and 1 hepatocyte inflammation. All bloods, where available, showed improvement in 7 days and normalised by 3 months. Complications occurred in 3 pregnancies; 2 intrauterine deaths and 1 prolonged ITU stay. No patients had recurrence of AFLP. No maternal deaths occurred.