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.

REFERENCES

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.

REFERENCES
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 54% of patients, GI bleeding in 24%, and encephalopathy in 12%. Mortality was 59% 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 ICU mortality was 19.4% for this period. CPR was 75%, 65%, 58% and 70% respectively. Overall all-cause mortality was 39% in ICU, 55% at 30 days and 59% at 1 year. 30-day mortality was 19.4% for this period.

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Area under the curve</th>
<th>95% CI</th>
<th>Range of previously reported area under the curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOFA</td>
<td>0.736</td>
<td>0.650 to 0.821</td>
<td>0.77–0.94</td>
</tr>
<tr>
<td>SAPS II</td>
<td>0.716</td>
<td>0.629 to 0.802</td>
<td>0.80</td>
</tr>
<tr>
<td>APACHE II</td>
<td>0.697</td>
<td>0.606 to 0.768</td>
<td>0.77–0.90</td>
</tr>
<tr>
<td>MELD</td>
<td>0.691</td>
<td>0.603 to 0.779</td>
<td>0.78–0.878</td>
</tr>
<tr>
<td>RIFLE score</td>
<td>0.626</td>
<td>0.533 to 0.720</td>
<td>0.837</td>
</tr>
</tbody>
</table>

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=0.05). 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 births1 and is commoner in primiparous women with male or twin pregnancies.2 It has features in common with HELLP syndrome, though coagulopathy, hypoglycaemia and polydipsia are commoner in AFLP and anaemia is not a feature.3 Liver biopsy confirms the diagnosis but a Swansea Score of 6 or above, in absence of another explanation, indicates AFLP.1 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 6–15). Commonest presentation was abdominal pain, malaise and vomiting. 60% had polydipsia, 25% had encephalopathy. 100% had raised transaminase, AST 12.8 ± 10.9, ALT 25 ± 15.8, 50% patients had abnormal urine urate. 61% had high ammonia, average 58 (range 28–127). 50% 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 (US) 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 hepatitis E. All bloods, where available, showed improvement in 7 days and normalised by 3 months. Complications occurred in 5 pregnancies; 2 intrauterine deaths and 1 prolonged ITU stay. No patients had recurrence of AFLP. No maternal deaths occurred.