Overall in all patients: investigation for cause limited to 3 colonoscopies and 1 ERCP, follow up inadequate in 15 (38%), mortality 8%.
Conclusion Management of this serious condition was remarkably poor, with limited use of cultures, inconsistant radiologic intervention, no search for cause, and scanty follow up. Despite this confirmed mortality was just 8%.Guidelines for future management have been drawn up including recommendation that all patients are looked after by the Gastro team.
Disclosure of Interest None Declared

PTU-105 OUTCOME OF CIRRHOTIC PATIENTS ADMITTED TO INTENSIVE CARE UNITS AT HOSPITALS WITHOUT SPECIALIST LIVER SERVICES

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Introduction Patients with liver cirrhosis admitted to an ICU are believed to have a poor prognosis with high mortality despite significant use of resources. Most of the literature to date on this topic has been collected at hospitals with Specialist Liver Units and these results may not be representative of the outcome at general ICUs. A recent prospective study of cirrhotic patients admitted to a tertiary Liver ICU in the UK demonstrated an overall hospital mortality of 59%. The aim of this study was to determine the outcome of cirrhotic patients admitted to non-specialist ICUs.
Methods Data was retrospectively collected from four hospitals in the NW region of the UK without specialist liver ICUs. Patients were identified using the Intensive Care National Audit and Research Unit (ICNARC) database. 61 patients with liver cirrhosis admitted to a general ICU between January 2010 and January 2012 were included in this study.
Results Age range was 30 to 79 years (average 51 years). 80% of patients were male and alcohol was the commonest aetiology for liver cirrhosis (90%). The main reason for admission to ICU was for gastrointestinal bleeding (38%). 51% of patients had a Child Pugh score of C on admission to ICU. 46% of patients had a MELD score between 10 and 19 and 28% had a score between 20 and 29. 79% of patients required invasive ventilatory support, 49% required vasopressors and 21% needed renal replacement therapy. 51% developed further decompensation of their liver disease during their ICU stay. These included GI bleeding (21%), hepatic encephalopathy (15%), HRS (11%) and SBP (3%). 67% of patients had an ICU stay of < 5 days. A 49% inpatient mortality rate was observed in our study with sepsis and multi-organ failure being the most common causes of death.
Conclusion Patients with liver cirrhosis admitted to general ICUs have similar rates of mortality compared to those in tertiary liver ICUs. Therefore, admission to such units should not be deemed futile in cirrhotic patients and earlier admission may improve outcome.
Disclosure of Interest None Declared

PTU-106 PATIENT IMPACT OF INFLAMMATION IN PRIMARY BILIARY CIRRHOSIS (PBC): INFLAMMATORY CYTOKINE LEVELS ARE ELEVATED BUT UNRELATED TO FATIGUE SEVERITY

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Introduction PBC is characterised by loss of small intrahepatic bile ducts, and in a significant proportion of patients by persistent fatigue. Genes regulating inflammatory pathways have been strongly associated with PBC in population-scale genetic studies, implicating inflammation in disease pathogenesis. Animal models of cholestasis, a biological process in PBC, have demonstrated fatigue-like behaviour appearing to result from responses to inflammatory cytokine release in the brain. Elevation of inflammatory cytokines has therefore, unsurprisingly, been postulated as an underlying mechanism for fatigue in PBC as well as other chronic inflammatory conditions. However, more recently data demonstrating that fatigue is not proportional to liver disease severity in PBC has questioned this presumed correlation between inflammation and fatigue. This study aimed to explore the serum cytokine profile in PBC compared to healthy controls, and to correlate this picture of inflammation status with fatigue severity.
Methods 68 patients from the Newcastle sector of the UK-PBC cohort and 9 healthy controls provided a morning peripheral blood sample and completed the PBC-40, a validated disease-specific quality of life measure with a fatigue domain. Sera were derived using standard protocols and stored at –80°C prior to multiplex cytokine quantification using the MSD platform.
Results PBC patients showed significant elevation of IFN-γ (median 2.4pg/ml[IQR 1.6–15.4] v control 0.7[0.2–1.5], $p < 0.0005$), IL-6 (1.0pg/ml[0.4–3.3] v 0.5[0–1.5],$p < 0.005$) and TNF-α (7.1pg/ml[5.5–10.5] v 4.3[3.6–5.9],$p < 0.001$). IL-1β was elevated in patients but fell short of significance (2.3 pg/ml [0.2–2.3] v 0.5[0.1–0.8],p = ns). Within the PBC group cytokine levels were compared between 21 patients reporting mild fatigue (established using published cut-offs for PBC-40 fatigue domain severity) and 24 patients with severe fatigue. No significant differences were seen between mildly and severely fatigued patients, and for three of the four pro-inflammatory cytokines (IFN-γ,IL-1β and TNF-α) levels were in fact lower in severely fatigued patients.
Conclusion Serum inflammatory cytokine levels are significantly elevated in PBC, in keeping with inflammation playing a key role in disease pathogenesis. Although the study protocol cannot exclude central nervous system-specific inflammatory mechanisms, no evidence was found to implicate inflammation in the pathogenesis or expression of fatigue in PBC, suggesting a further factor independent of inflammatory disease pathogenesis predisposes certain patients to fatigue.
Disclosure of Interest None Declared.

PTU-107 NAFLD IN PATIENTS WITH SEVERE ASTHMA

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Introduction NAFLD is a spectrum of liver disease that encompasses Nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). The pathophysiology is not fully understood, but is believed to be a combination of insulin resistance leading to steatosis and subsequent oxidative injury. Known risk factors include obesity, diabetes and dyslipidaemia.

Severe asthma may entail frequent corticosteroid use and a sedentary lifestyle; both predispose to risk factors implicated in NAFLD. As such we hypothesised a link between asthma and NAFLD, and a possible under detection of NAFLD amongst patients with severe asthma.
Methods We audited the investigation and management of NAFLD amongst patients under the care of the Difficult Asthma Team at the Royal Brompton Hospital. We conducted a retrospective

study of patients who were entered into the National Asthma Database following investigations under the Difficult Asthma Protocol (DAP) between 2007 and 2011. The following were included: Age at diagnosis, liver function (at initial assessment and most recent), liver imaging, glucose and lipids at initial investigation, and medication history.

Results 209 subjects were included in the audit, all of whom entered into the National Asthma Database between 2007 and 2011. Mean age was 45 at presentation to RBH.

Abnormal Liver Function 20% (n = 41) patients had abnormal liver function tests either at first presentation to RBH or on their most recent blood tests. Only 14 (34%) were further investigated with liver imaging. Of those with deranged liver function who were imaged, 79% (n = 11) had radiological evidence of NAFLD.

Management of patients with confirmed NAFLD Of the patients with confirmed NAFLD only 27% (n = 3) had their fasting lipids and glucose measured. 18% (n = 2) were prescribed a statin and a similar number were prescribed metformin.

Asthma medications of patients subsequently diagnosed with NAFLD 81% of patients were prescribed aminophylline. 54% were prescribed montelukast and 81% patients were prescribed oral corticosteroids. 36% of patients were treated with omalizumab (anti-IgE).

Conclusion Amongst our cohort of wevere asthmatics a substantial proportion have deranged liver function. Of those with abnormal LFT who underwent imaging, a high proportion (79%) had radiological evidence of NAFLD. However 66% of patients with deranged LFT did not proceed to liver imaging. This suggests that NAFLD is currently under diagnosed and managed in this patient population

Disclosure of Interest None Declared

PTU-108 AZATHIOPRINE PHARMACOGENETICS IN AUTOIMMUNE HEPATITIS

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Introduction Azathioprine (AZA) is widely used to treat autoimmune hepatitis (AIH). However, 20% of patients are intolerant of AZA and a further 18% are unresponsive. AZA metabolism is complex and in childhood leukaemia, genetic polymorphisms in thiopurine methyltransferase (TPMT) and inosine triphosphate pyrophosphatase (ITPA) have been associated with AZA toxicity and differences in active metabolite production. This has been little studied in AIH. We aimed to assess the association of these polymorphisms with AZA toxicity and with accumulation of AZA derived thioguanine nucleotide (TGN) and methylmercaptopurine metabolites (MeMPNs) in AIH.

Methods We studied 151 patients with AIH (123 female; median age at diagnosis 55 (range 2–81) years). Subjects were genotyped for the presence of *TPMT *3*, *TPMT *2* and ITPA (94C > A and IVS2+21A > C) variant alleles. TGNs and and MeMPNs were measured in patients who remained on AZA.

Results For TPMT, 138 patients were wildtype and 13 (9%) were heterozygous (1 *TPMT*2*, 11 *TPMT*3A* and 1 *TPMT*3C*). For ITPA, 95 were wildtype, 50(33%) heterozygous (10 94C > A and 40 IVS2+21A > C) and 6 homozygous/compound heterozygous. There were 57 adverse events (AE) in 54(36%) patients – in 32 (21%) AZA was withdrawn. TPMT wildtype and heterozygous patients had a similar incidence of leucopenia (18 vs 17%, p = 0.9) and of non-myelotoxic AEs (21 vs 8% p = 0.5). Likewise, ITPA wildtype, heterozygous and homozygous patients had a similar incidence of leucopenia (19, 10 and 16% respectively, p = 0.2) and of non-myelotoxic AEs (20, 39 and 15%, p = 0.2). Compared to wildtype patients, TPMT heterozygotes accumulated higher concentrations of TGNs (413 vs 212 pmol/8x10^{8}RBCs, p = 0.009) and lower MeMPNs (111 vs. 1000 pmol/8x10^{8}RBCs, p < 0.001), despite being a lower doses of AZA (1.0 vs. 1.7 mg/kg/day, p < 0.001). Comparing IPTA wildtype, heterozygous and homozygous patients, there was no difference in TGNs (222, 212 and 176 pmol/8x10^8 RBCs respectively, p = 0.76) and MeMPNs (957, 957 and 713 pmol/8x10^{8}RBCs respectively, p = 0.7)

Conclusion TPMT and ITPA polymorphisms do not predict the occurrence of adverse events in AIH. However, TPMT genotyping may be clinically useful as heterozygous patients may require a lower dose of AZA.

Disclosure of Interest None Declared

PTU-109 PLASMA HEAT SHOCK PROTEIN-32 LEVELS IN PATIENTS WITH HEPATITIS C VIRUS-RELATED CIRRHOSIS: RELATION TO RENAL FUNCTION AND HEMODYNAMICS

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Introduction Heat shock protein-32 (HSP-32) is a microsomal enzyme that has hemodynamic effects and may play a role in the pathogenesis of renal diseases. Therefore, the present work was designed to study the plasma levels of HSP-32 and its product carbon monoxide (CO) in patients with hepatitis C virus (HCV)-related cirrhosis in relation to renal function and hemodynamics.

Methods Thirty patients with HCV-related cirrhosis and 15 healthy subjects were included in the study. The severity of liver disease was assessed using Child-Pugh classification and The Model for End-Stage Liver Disease (MELD) score. Renal function was evaluated by serum creatinine (sCr) level, estimated glomerular filtration rate (eGFR) and urine sodium (UNa)concentration. Plasma HSP-32 levels were measured using commercially available enzyme-linked immunosorbant assay. Blood carboxyhemoglobin (COHB) concentration, an index of CO production, was assayed by spectrophotometry. Renal hemodynamics including renal artery peak systolic velocity (PSV), end-diastolic velocity (EDV), mean velocity (MnV), resistive index (RI) and pulsatility index (PI) and renal blood flow (RBF), were measured using Doppler ultrasonography.

Results Patients with HCV-related cirrhosis showed significant increases in plasma HSP-32 levels, blood COHB concentration and renal artery RI and PI and significant decreases in RBF and renal artery EDV and MnV compared with healthy subjects (P < 0.001) The plasma HSP-32 levels and blood COHB concentration showed positive correlations with Child-Pugh and MELD scores, sCr and renal artery RI and PI and negative correlations with eGFR, UNa concentration, RBF and renal artery EDV and MnV (P < 0.05). No correlations were found between plasma HSP-32 levels and blood COHB concentration on one hand and age of the patient, apparent duration of HCV infection and serum HCV RNA levels on the other hand (P > 0.05).

Conclusion The increased HSP-32 activity with enhanced endogenous CO generation may play an important role in renal dysfunction in HCV-related cirrhosis and could be a potential therapeutic target.

Disclosure of Interest None Declared