the virus remains a combination of pegylated interferon (PegIFN) alpha and ribavirin. In this specific genotype 4 population, there is a major medical need for studies on natural history, new treatments, and predictors of response.

We performed a study in a well-characterized cohort of HCV-4 patients, to investigate the association of IL28B polymorphism with response to treatment or liver disease severity [2]. In our article, our well-characterized unique large cohort was defined based on its ethnic origin. In this cohort, three different ethnic groups were represented with 70 (43%) Egyptians, 53 (32%) Europeans, and 37 (23%) Sub-Saharan Africans. A liver biopsy was performed in 160 patients, of whom 78 (49%) had a mild fibrosis (F0–F1) and 82 (51%) a moderate to severe fibrosis (F2–F4).

We did not observed an association between fibrosis stage and response to treatment; however, the proportion of patients with cirrhosis (F4) was relatively small (17.1%). Eighty-two patients received 48 weeks of PegIFNα and ribavirin. Among these, 43 patients (52%) obtained an SVR and 39 failed treatment (28 (32%) obtained a non-response and 11 (16%) were relapers). Among our treated patients, the proportion of rs12979860 CC was 26.8%; CT was 52.4%, and TT was 20.8%. Since in genotype 4 patients the treatment will remain PegIFN and ribavirin for several years, IL28B polymorphism may remain an important associated factor with response. Another study performed in Italy gave similar results with an association between IL28B polymorphism and SVR [3]. Of 112 treated patients (98 males, 75 of Egyptian descent, 26 with cirrhosis) 103 were included in the final analysis; five discontinued treatment for non-virologic reasons and four did not consent to genetic testing. Twenty-four (23%) were genotype CC, 65 (63%) CT, and 14 (14%) TT. Overall, 50 (49%) achieved an SVR. 21 (88%) CC patients versus 29 (37%) CT/TT.

Further studies will be needed to demonstrate whether genotype 4-infected patients with good predictors of response, including IL28B CC, may benefit from shorten therapy.

Conflict of interest

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References


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The impact of organ dysfunction in cirrhosis: Survival at a cost?

To the Editor:

We were delighted to read the recent study from Shawcross et al. which has reported the findings of a large and robust prospective dataset examining the outcomes of patients with cirrhosis and acute organ dysfunction admitted to the Liver ICU at King’s College Hospital, London over a 7-year period (2000–2007) [1]. The study population of 563 first admissions represents the largest cohort described in the literature to date. The reported ICU (51%) and hospital (59%) mortality rates are comparable to those quoted in the majority of published datasets in recent years. Whilst unarguably higher than the ICU and hospital mortality rates of unselected general ICU admissions nationally (20% and 30%) [2], they are still notably lower than those reported by some of the earlier publications in this field [3].

This complex and challenging patient cohort held too frequently find themselves the focus of negative clinical bias and prognostic pessimism due to entrenched anecdotal experiences and healthcare provider perceptions regarding ‘self inflicted’ illness. It is therefore important that studies such as these examine current trends in outcome, after all, the incidence of chronic liver disease related hospital admissions and overall mortality is rising in the UK [4] and is a growing area of significant public health concern.

Despite the quantitative success of this dataset, by virtue of its specialist setting it represents a tertiary transplant centre experience. More relevant to non-transplant critical care centres, we would like to draw your readers’ attention to the results of a study performed in 2010, which reported on the outcomes of patients with cirrhosis and critical illness from the general intensive care units of two large non-transplant centres in London [5]. It suggested the hypothesis that the patient population seen outside of transplant centres present with a different clinical phenotype, and hence would demonstrate even better outcomes from their critical illness episode. The study population of Shawcross et al. was composed largely of in-patients already on the tertiary liver wards (50%) or cases referred acutely from external secondary care centres (44%) who were deemed to require specialist input. Only 6% (35/563) were admitted de novo via the emergency department or ‘general’ wards from elsewhere within King’s College Hospital. Table 1 shows the descriptive cohort data from both studies.

Differences can be observed in the degree of hyperbilirubinemia and serum creatinine level between groups. CPS, MELD, APACHE and SOFA were also more extreme in the tertiary centre cohort. This could conceivably account for the observed
difference in mortality between the two studies. A categorical Chi square comparison shows that outcome was significantly better in the non-transplant centre (Hospital mortality 47% vs. 59%, \( p = 0.02 \)), which also experienced a higher proportion of alcohol related liver disease (85/118 (72%) vs. 263/563 (47%), \( p < 0.001 \)).

Regarding the provision of renal replacement therapy, often regarded as a harbinger of doom in secondary care ICUs, more patients received this during their transplant centre ICU stay (50% vs. 31%, \( p < 0.001 \)) but with identical outcomes (81% vs. 81% mortality, NS). Whether the use of this particular organ support represents the highest observed incidence of renal failure or a more aggressive standard of care is difficult to say.

The apparent disparity in CPS and SOFA between the studies could be accounted for by differences in the assessment and calculation of the encephalopathy and GCS score components. Anecdotally, this is a difficult area to reliably assess during data collections such as these, more so when receiving tertiary transfers who have already been intubated.

Overall, the clinical presentation and individual phenotype of patients with cirrhosis and acute organ dysfunction remains a highly variable field. As more datasets are published, it seems clear that these patients continue to have very significant levels of mortality but perhaps not as severe as once thought. Care should be taken when comparing different datasets and consideration should be given to the patient cohort under scrutiny before necessarily applying the results to individual local practice.

**Conflict of interest**

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**References**


