A combination of medical therapy and liver transplantation save children with acute liver failure

Acute liver failure (ALF) in children is defined as a severe impairment of liver function characterized by biochemical evidence of acute liver injury, coagulopathy (INR ?2.0) regardless of the presence of hepatic encephalopathy (HE) and no history of chronic liver disease. ALF may be fatal and liver transplantation (LT) is often the only effective treatment. We performed a study to describe features and outcome of ALF in Italian children referred to the Paediatric Liver, Gastrointestinal, and Transplantation Unit of the Hospital Papa Giovanni XXIII, Bergamo (Italy), between 1996-2012.

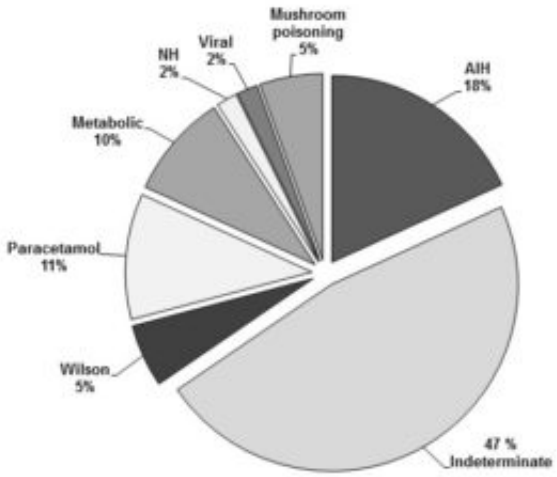

Fig. 1. Etiology distribution of a cohort of 55 Italian children presenting with acute liver failure. AIH: autoimmune hepatitis. NH: Neonatal haemochromatosis.

On admission all patients underwent investigations to identify any specify etiologies of ALF. Medical treatment was commenced in all to support the liver synthetic function but in presence of severe HE and/or progressive coagulopathy the patients were listed for LT.

To identify predicting factors associated with a worse outcome (need for LT or death) the analysis proceeded from dividing the patients into two groups and compared. Group 1 (G1): patients who survived without LT. Group 2 (G2): patients who underwent LT or died before LT.

Our results reported that 55 children with ALF (median age 2.6 years, range 0.1–15.1 years; M/F = 31/24) were included in the study. Etiologies of ALF were: autoimmune hepatitis (AIH) in 10 (18 %), metabolic disorders in 9 (17%), paracetamol overdose in 6 (11%), mushroom poisoning in 3 (5%), viral infection in 1 (2%), indeterminate (unknown) in 26 (47%) (Fig. 1). Twenty-five patients (45%)

were treated by medical therapy successfully, 28 (51%) underwent LT and 2 (4%) died on the transplant waiting list . All transplanted patients received a liver graft from a deceased donor. The median waiting time between admission and transplantation was 9 days (range 1–62 days) whereas the median waiting time between listing and transplantation was 5.3 days (range 1–48 days).

The median follow up time from the onset was 0.8 years (range 0.1–17.5), whereas the median follow up of the transplanted children was 5.7 years (0.2–17.5). The overall survival rate was 93%. On mulivariate analysis the severity of HE (grade 3–4) and bilirubin ?12 mg/dl were independent predictors of death or LTX (p less than 0.05).

In this study we demonstrated, once more, that identifying etiology and prognostic factors of ALF is crucial to institute disease-specific management and evaluate the correct indication to LT. We also found that AIH was a more common cause of ALF in children > 1 year compared to other studies, and 50% of patients with autoimmune ALF were successfully treated with medical therapy without requiring LT. These results suggest that AIH is likely an underdiagnosed and a potentially reversible cause of ALF.

To assess the correct indication to LT we retrospectively applied in our cohort of patients the redefined King’s criteria which are considered reliable parameters in predicting the outcome in children with ALF. We found that all 28 transplanted patients met King's criteria whereas among 27 patients who recovered with medical therapy, 16 (59%) met King’s criteria.

The survival rate of our cohort of patients was greater than previously reported, suggesting that there has been surely some improvements in the management of children with ALF. This may be also related to the very short waiting list we have at our institution, reflecting the efficient organ procurement process of the Italian organ sharing network.

In conclusion children with ALF can be managed successfully with combined medical treatment and transplantation but without requiring an over usage of LT. Nowadays the overall survival rate of children with ALF is over 90%, which is not different from that of children transplanted because of chronic liver disease.

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