

Acute Liver Failure (ALF)

Definition

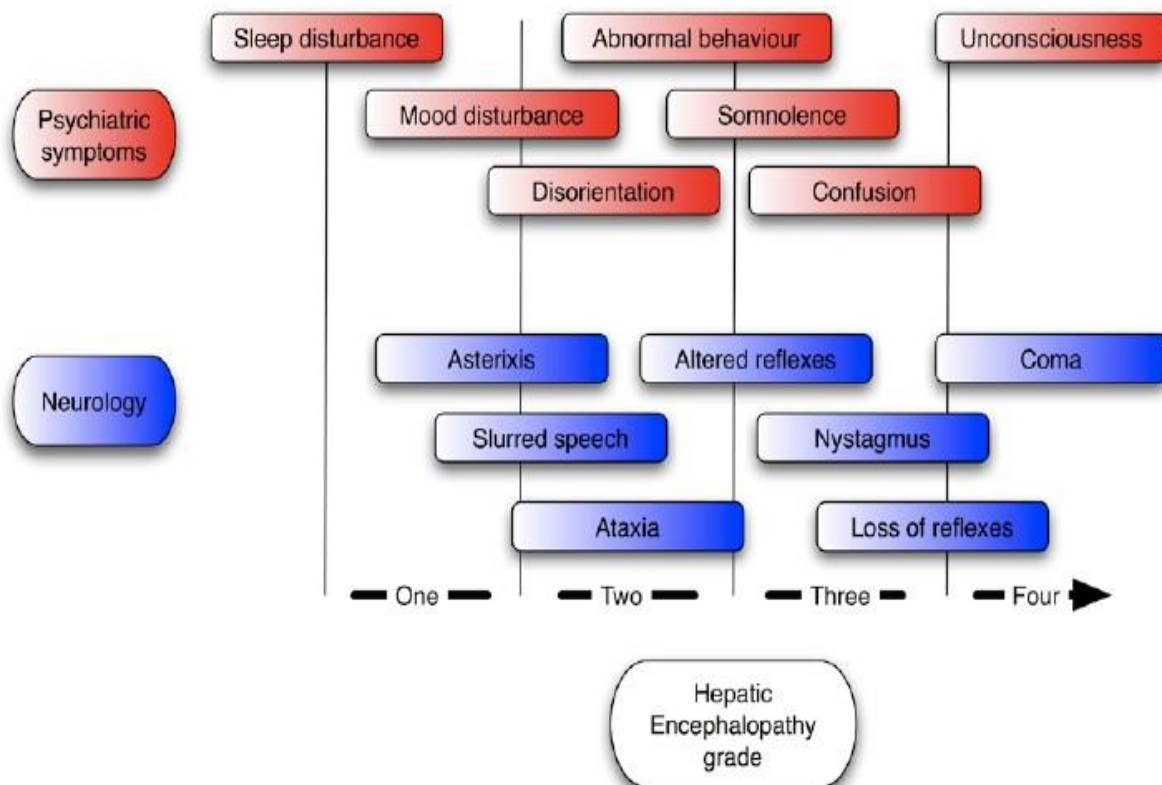
A potentially reversible condition, the consequence of **severe liver injury**, with onset of **encephalopathy** within days to few weeks of the appearance of the first symptoms (usually jaundice) and in the **absence of pre-existing liver disease**.

Synonyms

Fulminant hepatic failure

There are several definitions of ALF but the most widely accepted is O'Grady definition:

- Hyper-Acute liver failure: Encephalopathy within 7 days of onset of Jaundice
- Acute liver failure: Encephalopathy 8 to 28 days from onset of Jaundice
- Sub-acute liver failure: Encephalopathy 4 weeks to 12 weeks from the onset of Jaundice



Recognition and immediate actions

The presence of synthetic dysfunction (prolonged INR+/- low albumin) in a patient with an acute severe liver injury (usually significantly elevated ALT present) but with no evidence of previous liver disease or cirrhosis should ring alarm bells that the patient is at risk of developing ALF and should be considered for super urgent liver transplantation according to the Kings criteria (appendix 1).

- **Obtain a specialist hepatology / gastroenterology opinion as soon as practicable. Discuss with Liver transplant registrar in Queen Elizabeth, Birmingham. Ideal management is to transfer to their unit prior to the onset of encephalopathy or meeting the Kings criteria.**

If encephalopathy +/- hypoglycaemia are present the patient is at high risk of mortality within 24 hours unless action is taken.

- **Discuss with Liver transplant registrar in Queen Elizabeth, Birmingham.**
- **ITU review to consider immediate intubation to protect airway if grade III or IV or to allow safe transfer to the transplant unit**
- **III and IV require ITU admission and super urgent listing for liver transplantation if meet's the King's criteria.**

General Management

- Monitor for encephalopathy and conscious state.
- Administer N-acetylcysteine in all patients with acute liver failure, *regardless of aetiology* (appendix 2)
- Insert a urinary catheter and monitor urine output hourly.
- Blood glucose should be monitored by nursing staff every 2 hours for hypoglycaemia.
- Baseline tests depend on the history ie paracetamol levels following an overdose. (See appendix 3). All patients regardless of aetiology should have these bloods taken 12 hourly (those in bold are used in Kings Criteria for liver transplantation):
 - FBC
 - U&Es, **Creatinine**
 - **PT** (ask lab for Manchester rather than Innovan method can be used)
 - **ABG's**, including Lactate
 - **Bilirubin** and other LFTs
 - Phosphate, Magnesium
- Arrange USS abdomen with Doppler of hepatic veins.
- Avoid all sedating agents where possible (unless the patient is intubated), NSAIDs and benzodiazepines and intra-muscular administration of any agents.
- **It is very important not to correct the coagulopathy (as unable to use Kings criteria to judge whether super urgent transplantation is required).**

Specific management

- *Cardiovascular*

Patients are often intravascularly deplete due to previous vomiting etc, also low peripheral vascular resistance secondary to liver failure, this leads to a high-output state with systemic hypotension. Fluid resuscitation with:

 - 0.9% NaCl solution.
 - Infusions of concentrated Glucose (20% or 10%) to maintain normal serum glucose concentration.
 - Fluid resuscitation should not be done solely with 5% Glucose as likely to induce hyponatremia which may predispose to cerebral oedema.
- *Neurology*
 - Grade III or IV encephalopathy is indication for ITU transfer and elective intubation.
 - Elevate head to 30°, minimise stimulation, maintain normocapnia.
 - Maintain sodium at 145-155mmol/l by infusions of 30% saline at a rate of 5 - 20 ml per hour.
 - Monitor for haemodynamic changes (bradycardia/hypertension) that might suggest raised intracranial pressure (ICP).
 - A sustained (>5mins) raised ICP should be treated with:
 - Increase sedation with propofol.
 - A bolus of 100 mls of 20% mannitol
 - A bolus of 20mls of 30% saline if mannitol fails
 - Consider if cerebral blood flow could be increased with fluids and noradrenaline.
 - Cool the patient to 34°C.
 - Thiopentone bolus (125mg).
 - If seizures occurring terminate with lorazepam and load with phenytoin and give magnesium (40 mmol) in 100 ml N/S over 1 hour.
 - Use of an ICP bolt is restricted to the liver transplant unit.
- *Renal*
 - Pre-renal failure and ATN occur commonly in ALF.
 - Look for reversible causes of renal failure including nephrotoxic drugs => Renal USS.
 - CVVH (Bicarbonate buffered solutions are preferable to lactate) is the preferred modality of renal replacement therapy.
- *Haematology*
 - Vitamin K (10mg IV 1-2 doses) can be given but is unlikely to be effective.
 - Low platelets also common in ALF. Platelets can be given if less than $50 \times 10^9/L$ and there is bleeding.
- *Metabolic*
 - Monitor K, Na, Mg, PO₄ and Glucose, correct as necessary.

- *Gastrointestinal*
 - Commence either sucralfate 1g QDS or IV H2 Receptor antagonist (H2RA) prophylaxis of stress ulcers.
 - If major GI bleeding occurs (unusual), urgent OGD may be warranted.
 - Nutrition. Commence early via enteral route, caution with protein. Gastric stasis commonly occurs (prokinetics /NJ feeding may be required)
- *Respiratory*
 - Pneumonia, hypoxaemia and ARDS can all occur.
 - Early intubation and ABG monitoring.
- *Microbiology*
 - Sepsis very frequent cause of death in ALF.
 - Staphylococcus, Streptococcus and capsulated fungi commonest.
 - Empirical fluconazole and broad-spectrum antibiotic (e.g. Augmentin) started.
- *Psychiatry and social background*
 - In case of paracetamol overdose it is very useful to find out as much as possible about the circumstances of the overdose, whether there are previous episodes, whether the patient takes drugs or alcohol, whether they are known to the psychiatric services, whether they are on treatment and what he response to treatment has been and what social support network the patient has. This can be gathered from the patient prior to intubation, family, GPs and the patient's psychiatrist if they have one.
 - A psychiatric assessment of the patient's current mental state (not whether they are suitable for transplant) is also very useful and therefore ask a liaison psychiatrist to review prior to the onset of encephalopathy. Being on an N-acetyl-cysteine drip is not reason for this not to be performed.

Transfer Criteria Guide

- The decision to, and the timing of the transfer to the transplant unit is an important one. This should be made by discussion between the transplant unit, Gastro/Hepatology consultant staff and ITU, as many patients, mainly following paracetamol toxicity, can be managed at UHL without transfer.

The patient must be resuscitated before any prognostic weight is attached to any blood test as these can often improve following fluids.

- The INR is > 3 in non-paracetamol aetiologies or the prothrombin time in seconds is greater than hours since paracetamol overdose for POD e.g INR 2.0 at 24 hours, 4.0 at 48 hours, 6.0 at 72 hours.
- If the INR is still rising on between day 3 and 4 following a paracetamol OD.
- If there is an elevated creatinine >200 with a significantly raised INR >3 or acidosis
- Significant hypoglycaemia
- Any evidence of encephalopathy
- Anyone who is hypotensive following fluids or requiring vasopressor support.

- Anyone who has evidence of a persistent metabolic acidosis (PH<7.3), a significant base deficit (<3), or a persistently raised lactate, following volume resuscitation.

Appendix 1

Kings Criteria for liver transplantation in ALF

Paracetamol	Non paracetamol
pH < 7.3 (irrespective of grade of encephalopathy)	Prothrombin time > 100 s (irrespective of grade encephalopathy)
Or Prothrombin time > 100 s and serum creatinine > 300 µmol/L (> 3.4 mg/dL) in patients with grade III or IV encephalopathy	Or Any three of the following variables (irrespective of grade of encephalopathy) <ul style="list-style-type: none"> • Age < 10 y or > 40 y • Aetiology hepatitis non-A, non-B, halothane hepatitis, idiosyncratic drug reactions • Duration of jaundice before onset of encephalopathy > 7 d • Prothrombin time 50 s • Serum bilirubin > 300 µmol/L

Appendix 2

N-acetylcysteine treatment

- Should be given in 5% glucose by IVI
- Loading dose:
 - 150mg/kg in 200ml over 15 minutes, followed by
 - 50mg/kg in 500ml over 4 hours, followed by
- Maintenance regime:
 - Dose 100mg/kg body weight, diluted in 1000ml 5% Glucose, given at 62.5ml/hr
 - At the end of 16 hours check INR, then repeat maintenance infusion as required.

Appendix 3

Diagnostic tests to be requested (depends on clinical situation):

- Viral screen (IgM HAV, IgM anti-HBc, HCV, HEV, CMV, EBV)
- Copper, caeruloplasmin
- Auto-antibodies (include LKM)
- Immunoglobulins
- Pregnancy test (where appropriate)
- Clotting studies (Budd-Chiari)
- Transjugular liver biopsy is often not very useful except if chronic liver disease suspected.

Appendix 4

Aetiology of Acute liver failure

<i>Infectious</i>	<i>Toxin/Drug</i>	<i>Other</i>
<i>Viral</i> <i>Hep A,B,C,E</i>	<i>Paracetamol</i> <i>Halothane</i> <i>TCAs / MAOIs</i> <i>Isoniazid</i> <i>NSAIDs</i> <i>Troglitazone / rosiglitazone</i> <i>Amanita (mushroom)</i> <i>CCI₄</i>	<i>Ischaemic Hepatitis</i> <i>Budd-chiari</i> <i>Venocclusive</i> <i>Malignant Infiltration</i> <i>Lymphoma</i> <i>Metabolic</i> <i>Wilson's</i> <i>hyperthermia</i> <i>Fatty Liver</i> <i>Reyes</i> <i>Pregnancy</i> <i>Drugs</i> <i>Autoimmune</i> <i>Sero-negative Hepatitis</i> <i>Surgery</i> <i>Hepatic Resection</i>

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