Consequences of Liver Injury & Acute Liver Failure in Children

DEIRDRE KELLY
ESPGHAN GOES TO AFRICA
CAPETOWN
October 2013
Functions of the Liver

- Regulation of uptake/processing of nutrients from GI tract
- Synthesis/bio-transformation of proteins, carbohydrates and lipids
- Excretion of bile and elimination of hydrophobic compounds
- Regulation of energy metabolism
- Endocrine functions/mediation of growth and development
- Immunological function
- Drug metabolism
- Regulation of fluid balance
Complications of Liver Failure

Liver Failure

- Brain Edema
- Hypoglycemia
- GI-Bleeding Intracranial Bleeding
- Hypovolemia
- Infection

Hypoglycemia

- Bloodsugar Monitoring
- Supplementation of FFP, Vit K, Cryo, F VII

GI-Bleeding Intracranial Bleeding

- Glucose-Homeostasis
- Endoscopy Substitution of Factors

Multiorgan Failure

- Hyperventilation Detoxification
- CT-Scan
- Detoxification
- Homeostasis

Supplementation of FFP, Vit K, Cryo, F VII
Acute Liver Failure

Hepatic necrosis with coagulopathy & encephalopathy within 8 weeks of onset of liver disease

Late-Onset hepatic failure:
Liver failure - 8-24 weeks

Acute on Chronic Failure:
Underlying liver disease

Infants: Coagulopathy without encephalopathy
Acute Liver Failure

Pediatric Acute Liver Failure Study Group Definition

• Acute onset of liver disease without chronic liver disease
• Biochemical and/or clinical severe liver dysfunction:
  • Coagulopathy (PT ≥ 20 sec or INR ≥ 2.0) not corrected by IV Vitamin K
  • and/or hepatic encephalopathy if PT ≥ 20 or INR ≥ 2.0

Squires, 2006
Pathogenesis of FHF

1. Acute hepatic necrosis
   - ? Virus
   - ? Toxin
   - ? Immune

2. Failure of hepatic regeneration

3. Hepatic encephalopathy
   - ? Cerebral oedema
Pathogenesis of Hepatic Necrosis

**Attack**
- Viruses
- Anoxia
- Toxins
- Immune

**Loss of**
- pl. membrane
- organelles
- RNA
- Ca++ homeostasis
- Protein thiols

**Defence**
- “Scavengers”
  - eg. glutathione
- Growth factors
  - eg HGF
- ? NAC
- ? Immune
Pathogenesis of Hepatic Necrosis

Host susceptibility
  - Age
  - Maturation (GST)
  - Genetic susceptibility

Extent of injury

Immune response
Pathogenesis of Hepatic Necrosis

Host immunophenotype
Soluble interleukin 2 receptor (sIL2rα)

77 patients PALF:
sIL2rα : normal: 37 survived (30 recovered)
   high: 15 – 5 recovered/ 8 Tx / 2 died

Bucuvalas et al, 2012
FHF - Pathology

- Massive hepatocyte necrosis
- Collapse of reticulin framework
- Loss of lobular architecture
- Variable inflammation
- Areas of regeneration
Mechanism of Hepatic Encephalopathy

Abrupt loss of hepatic function
- Toxic neuractive products
- ammonia/glutamine
- Short chain fatty acids
- mercaptans/octopamine
- false neurotransmitters
- GABA

Development of cerebral oedema
Reversible
Mechanism of Hepatic Encephalopathy

- Magnetic Resonance Spectroscopy:
  - 11 children with ALF and cerebral oedema
  - 8 healthy controls
  - MRS: increased glutamine
decreased choline
- Serum: increased inflammatory cytokines
decreased thiamine
- Srivasta et al, 2012
Aetiology of Neonatal Acute Liver Failure

Infection
- Hepatitis B, Herpes simplex, sepsis

Metabolic liver disease
- Tyrosinemia
- Niemann-Pick C

Mitochondrial disease

Neonatal Hemochromatsis (GALD)

Poisoning (acetaminophen)

Erythrophagocytic syndrome
Aetiology of Acute Liver Failure

148 neonates < 90 days

Infection

Herpes simplex: 13%

Indeterminate: 38%

Neonatal Hemochromatsis: 14%

Outcome: 60% recovered

24% died without Tx

16% transplanted

PALF study group, Sundaram, 2011
Aetiology of Acute Liver Failure in the Older Child

• Viral hepatitis non A-E (Indeterminate)
• Drugs
  acetaminophen
  TB/anti-epileptic
  Herbal/Recreational
• Autoimmune Hepatitis
• Metabolic:
  Wilson’s
  Alpers
• Juvenile Rheumatoid Arthritis + MAF
Hepatotoxicity; herbal medications

- Perceived safe because “natural”
- No formal evaluation or regulations
- Exposure often not disclosed
- Unpurified mixtures of various compounds
- Common interactions with other medications
- Indirect exposure (transplacental or lactation) could induce liver injury in a child
Hepatotoxicity; recreational drugs

- Cannabis
- Cocaine
- Heroine
- Amphetamine derivatives ("Ecstasy")
- Slimming tablets (ephedrine derivatives combinations)

- Increasingly popular amongst teenagers
- Confounding factors (alcohol, viruses, malnutrition)
- Clinical picture of hepatitis, but could progress to ALF
# Aetiology of Acute Liver Failure

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Age (y)</th>
<th>HAV</th>
<th>HBV</th>
<th>Metab</th>
<th>Indet</th>
<th>AIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>PALF</td>
<td>348</td>
<td>-</td>
<td>1%</td>
<td>-</td>
<td>10%</td>
<td>49%</td>
<td>6%</td>
</tr>
<tr>
<td>Phillipines</td>
<td>26</td>
<td>17</td>
<td>19%</td>
<td>4%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Turkey</td>
<td>74</td>
<td>-</td>
<td>18%</td>
<td>-</td>
<td>35%</td>
<td>21%</td>
<td>-</td>
</tr>
<tr>
<td>India</td>
<td>130</td>
<td>7.5</td>
<td>53%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Argentina</td>
<td>40</td>
<td>5.3</td>
<td>42%</td>
<td>-</td>
<td>-</td>
<td>35%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Squires 2006; Braro 2012; Baris 2012; Srivasta 2011; Sanchez 2011
Age distribution of 103 children with FHF

- 103 cases; 51 males, 52 females
- median age 24 mths (1 d – 17 y)
Underlying causes of 103 children with FHF according to age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1m</td>
<td>1</td>
</tr>
<tr>
<td>1-12m</td>
<td>5</td>
</tr>
<tr>
<td>1-6y</td>
<td>10</td>
</tr>
<tr>
<td>&gt;6y</td>
<td>15</td>
</tr>
</tbody>
</table>

- Metabolic
- Infective
- Drug-related
- Other
Incidence of Drug Related Acute Liver Failure in Children

<table>
<thead>
<tr>
<th></th>
<th>NIH</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>348</td>
<td>97</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>Other drugs</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>49%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Squires, 2006; Lee, 2005
## Drug Related Acute Liver Failure in Children

<table>
<thead>
<tr>
<th></th>
<th>Age &gt;3yrs</th>
<th>Recovery</th>
<th>Tx (% surv)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIH</td>
<td>94%</td>
<td>36%</td>
<td>29% (100%)</td>
</tr>
<tr>
<td>UK</td>
<td>100%</td>
<td>40%</td>
<td>40% (50%)</td>
</tr>
<tr>
<td><strong>Acetam</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIH</td>
<td>96%</td>
<td>94%</td>
<td>4% (50%)</td>
</tr>
<tr>
<td>UK</td>
<td>85%</td>
<td>50%</td>
<td>14% (50%)</td>
</tr>
<tr>
<td><strong>Indeterm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIH</td>
<td>58%</td>
<td>42%</td>
<td>47% (91%)</td>
</tr>
<tr>
<td>UK</td>
<td>64%</td>
<td>22%</td>
<td>61% (73%)</td>
</tr>
</tbody>
</table>
Acetaminophen Hepatotoxicity

- Outcome and Prognosis
- Dependent on:
  - Dose
    - Time to therapy (NAC)
    - Concomitant drug therapy
    - Age

Children/Adolescents: 90% recovery
Transplantation: 5%
- Severe Poisoning/concomitant drugs/alcohol
Acetaminophen Related Hepatotoxicity

- **Overdose**: - suicide
  - accidental
  - chronic accumulation*

- **Prevention**
- Reduce pack size
- Education about chronic effects
- ? Regular monitoring for chronic use

- **Therapy**
- Early treatment with NAC
Indeterminate Acute Liver Failure

Most frequent cause of ALF
Diagnosis by exclusion:
- viral, metabolic, immune, genetic and toxic causes
- viral non A-E
- unknown toxin

- Complications:
  - sepsis
  - Acute renal failure
  - Bone marrow depression
  - Multiorgan failure
  - Neurological symptoms late and inconsistent feature
Sodium Valproate in Acute Liver Failure

• Risk of liver failure in children:
  < 2 yrs : 1 in 8,000 on valproate alone
  1 in 550 with other anti-epileptics
  3-10 yrs: 1 in 6,000 - 12,000
  > 10 yrs: 1 in 50,000

• Neurodevelopmental delay
• Fatty acid oxidation defects/urea cycle disorders
• Mitochondrial diseases
Sodium Valproate in Acute Liver Failure

Presenting symptoms are:

• Diminished consciousness
• Jaundice; vomiting; bleeding;
• Increased frequency of convulsions;
• Anorexia; oedema, pancreatitis
• ? Stimulated by intercurrent infection
Sodium Valproate in Acute Liver Failure

- Routine monitoring may not be predictive
- Asymptomatic abnormal LFTs are common
- ALF may occur without previous abn LFTs
- Progress despite discontinuation of valproate
- Onset of hepatotoxicity within 5 mths of Rx
- Hepatocellular necrosis with macro/microvesicular fatty change in the liver.
Treatment of Sodium Valproate in Acute Liver Failure

- Discontinue valproate
- Supportive therapy/IV l-carnitine
- Liver dysfunction resolves in 50%
- Transplantation is controversial:
  - Contra-indicated: multi-system disease
  - Underlying metabolic or mitochondrial disorder
- 82% children with VPA-AL died < 1yr post Tx

Thomson, 1992; Lheureux, 2009; Mindikoglu, 2011
Acute Liver Failure in Children

Clinical Presentation

Jaundice: Variable

Coagulopathy: (PT>50 secs)

Encephalopathy: Irritable
  Day/night reversal
  Vomiting
  Poor feeding
  Aggressive behaviour

Diagnosis: EEG/CT
Clinical Presentation of 103 Children with FHF – Birmingham data

% of patients

Coag | Enceph | Jaundice | Hepatomegaly | Splenomegaly | Ascites

100 | 90 | 80 | 60 | 40 | 20

Degree of enceph. at presentation

Lee et al, JPGN, 2005
Biochemical Features of Acute Liver Failure

Elevated ammonia

Abnormal coagulation

Transaminases x 20-80

Rising bilirubin
Investigations in Acute Liver Failure

**Serum:** Hep A,B,C,E, EBV,CMV
- Cu, Caeruloplasmin,Amino acids, Fe, ferritin
- Autoantibodies, immunoglobulins
- Acetaminophen or other drug

**Urine:** drug screen
- succinylacetone
- metabolic screen

**DNA:** for mitochondrial/NPC/Wilson’s

**Muscle Biopsy +/- Lumbar Puncture:**
for mitochondrial disease
Management of Fulminant Hepatic Failure

1. Assess prognosis with reference to need for liver transplantation.

2. Anticipate and prevent complications while awaiting regeneration /donor liver

3. Hepatic support
Management - Specific Aspects

- Coagulopathy
- Hypoglycaemia
- Sepsis
- Respiratory failure
- Renal failure
- Acidosis
- Hepatic encephalopathy
Management of Acute Liver Failure

1. Abd U/S for liver size
2. EEG/CT scan
3. LFT, PT, PTTK
4. Glucose, lactate
5. Blood gases
Management of Acute Liver Failure

NO SEDATION
Nurse at 10-20 degrees
10-50% glucose
Vitamin K
Ranitidine 1-3 mg/kg TDS
Lactulose 2-4 ml/kg TDS
Low protein diet for encephalopathy
Management of Acute Liver Failure

1. Fluid restriction/high calorie feeds
2. H$_2$ antagonists/PPI and sucralfate
3. Coagulation support and vitamin K
4. Broad spectrum antibiotics
5. N-acetylcysteine
6. Specific medical therapy
Management of Cerebral Oedema

Critical
1 Restriction of fluids
2 IV mannitol 1-2g/kg/1 hour
3 Intracranial pressure monitoring
4 Elective ventilation and hyperventilation
5 Phenobarbitone coma
Prevention of Sepsis in Acute Liver Failure

Prophylactic antibiotics

- Cefuroxime
- Amoxil
- Metronidazole
- Fluconazole
Hepatic Support

• Nutrition: glucose, TPN

• Vit K, FFP

• N-acetylcysteine
Nutrition in FHF
Role of Parenteral Nutrition

Negative nitrogen balance

Increased catabolism

Increased protein turnover
Acute Liver Failure

Coagulation problems

DIC:  
- \( \uparrow \) FDP
- \( \downarrow \) Fibrinogen
- \( \downarrow \) Factor VIII C

Hepatic necrosis:  
- \( \downarrow \) Factor levels
- \( \uparrow \) Factor VIII C

Therapy:  
- FFP, cryoprecipitate,
- Recombinant Factor VII
- Platelets
Acute Liver Failure

Electrolytes
- Hyponatremia
- Hypokalemic alkalosis
- Hypocalcaemia:
- Pancreatitis
- Hypoalbuminemia
Acute Liver Failure

Renal Failure:

Acute Tubular Necrosis:
- sepsis
- haemorrhage

Urinary sodium >20 mmol/l

Functional renal failure:
- renal vasoconstriction
- reduced renal perfusion

Urinary sodium <20 mmol/l
Management of Renal Failure in FHF

1. Maintain volume with colloid

2. Frusemide 2mg/kg IV or infusion

3. Haemofiltration/haemodialysis
Convulsions in Acute Liver Failure

Phenytoin 10 mg/kg IV
Paraldehyde 50% solution PR
Phenobarbitone 10-15 mg/kg
Ventilation
Poor prognostic sign
Artificial Liver Support

Haemodialysis/haemoperfusion/plasma exchange/cross circulation/plasmapheresis
Absorption columns (charcoal)
MARS
Hepatocyte transplantation
Poor Prognostic Features in Neonatal Liver Failure

Coagulopathy  PT>50 secs
Rising bilirubin
Failing transaminases

Older Child:
Encephalopathy (Grade III)
Aetiology (Non A-G)
## Prognostic Features in Acute Liver Failure

<table>
<thead>
<tr>
<th>Feature</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>45%</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>23%</td>
</tr>
<tr>
<td>Hepatitis non A, non B</td>
<td>9%</td>
</tr>
<tr>
<td>Age &lt; 10 years</td>
<td>10%</td>
</tr>
<tr>
<td>Onset &gt; 7 days</td>
<td>7%</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>34%</td>
</tr>
</tbody>
</table>

(N=588, O’Grady et al 1989)
Prognostic Scores in Acute Liver Failure

• King's College Criteria:
  • Arterial pH < 7.3
  • INR > 6.5
  • Creatinine > 300 micromoles per litre
  • Encephalopathy Grade III or IV
Prognostic Scores in Acute Liver Failure

• Endpoint:
  • Recovery/ Death/ Liver Transplantation
• King's College Criteria:
  – Not specific for PALF
  – PPV=33%; NPV = 88%
• PELD Scores > 40 indicated poor outcome & Tx
• PRISM > PELD in identifying mortality

Sundaram, 2012; Sanchez 2012; El-Karaksy, 2011
# Prognostic Factors in Acute Liver Failure

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Bilirubin &gt; 2.0 mg</th>
<th>PT&gt;40</th>
<th>Enceph 2-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PALF</td>
<td>163</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>India</td>
<td>130</td>
<td>&lt;3.5yrs</td>
<td>&gt;16</td>
<td>&gt;40</td>
<td>+</td>
</tr>
<tr>
<td>BCH</td>
<td>103</td>
<td>Duration</td>
<td>NS ALT&lt;2000</td>
<td>&gt;55</td>
<td>+</td>
</tr>
</tbody>
</table>

Survival without liver transplantation vs death at 21 days

Sundaram 2012; Srivasta, 2012; Way Leah, 2005
Selection for Transplantation

- Aetiology: Indeterminate Hepatitis
- Prognostic factors
  - Severity of liver disease
  - No response to specific therapy
  - Persistent Encephalopathy
  - Increasing Coagulopathy
- Reversible brain disease
Contraindication for Liver Transplantation

Exclude: Multi-organ disease
  eg mitochondrial disease
  Sodium valproate poisoning
  Irreversible brain damage
  Sepsis

Age/size: No contraindication
BCH Experience Patients Presenting with Acute Liver Failure 2000 - 2012

189 children with Acute Liver from January 2000 - August 2012

- 100F:90M
- Median (range) age at presentation years: 2.9 (0–16)
- 91/189 recovered spontaneously (48%)
- 37 died (not transplanted)
- 61 transplanted; 15 died
## BCH Experience Patients Presenting with Acute Liver Failure 2000 – 2012 (n=189)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
<th>Transplanted</th>
<th>Died</th>
<th>Overall survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic</td>
<td>56 (30)</td>
<td>24/56</td>
<td>15</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 post OLT</td>
<td></td>
</tr>
<tr>
<td>Infectious</td>
<td>36 (19)</td>
<td>11/36</td>
<td>16</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 post OLT</td>
<td></td>
</tr>
<tr>
<td>Drug induced</td>
<td>30 (16)</td>
<td>3*/30</td>
<td>1*no OLT</td>
<td>97</td>
</tr>
<tr>
<td>AIH</td>
<td>13 (7)</td>
<td>4/13</td>
<td>---</td>
<td>100</td>
</tr>
<tr>
<td>Other</td>
<td>24 (13)</td>
<td>13/24</td>
<td>9</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 post OLT</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>30 (16)</td>
<td>6/30</td>
<td>11</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 post OLT</td>
<td></td>
</tr>
</tbody>
</table>

* All acetaminophen
Comparison of survival post transplant ALF v elective BCH experience 1983 - 2012

Kaplan Meier Curve

ALF n= 118

Elective n=536

p <0.05
# Transplantation for Acute Liver Failure

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>% Survival 1 yr</th>
<th>% 5 yrs</th>
<th>% 10 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnon 2011</td>
<td>170</td>
<td>90</td>
<td>89</td>
<td>-</td>
</tr>
<tr>
<td>Miloh 2010</td>
<td>77</td>
<td>87</td>
<td>80</td>
<td>-</td>
</tr>
<tr>
<td>El Moghazy 2010</td>
<td>57</td>
<td>74</td>
<td>70</td>
<td>67 *</td>
</tr>
<tr>
<td>Faraj 2010</td>
<td>20</td>
<td>85</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>Farmer 2009</td>
<td>122</td>
<td>-</td>
<td>77</td>
<td>73</td>
</tr>
<tr>
<td>Mahabed 2009</td>
<td>33</td>
<td>-</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>Markewicz 2008</td>
<td>1/13</td>
<td>90</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Living donor      * Wilson
# Outcome of Fulminant Hepatitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>1980</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>&gt;70%</td>
<td>~ 30%</td>
</tr>
<tr>
<td>Cerebral oedema</td>
<td>54%</td>
<td>30%</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>45%</td>
<td>-</td>
</tr>
<tr>
<td>Renal failure</td>
<td>32%</td>
<td>-</td>
</tr>
<tr>
<td>Sepsis</td>
<td>16%</td>
<td>25%</td>
</tr>
<tr>
<td>MOF</td>
<td>-</td>
<td>19%</td>
</tr>
</tbody>
</table>

Pscharopoulons, 1980; Godbole, 2011; Lal, 2011; Tan, 2012;
Summary

- Childhood FHF uncommon
- Aetiology differs between neonate and older child
- Metabolic/Indeterminate commonest
- Overall survival 70%
- Spontaneous recovery rate 30-40%
- Future progress:
  - ?genetic susceptibility/Immune response
Acute Liver Failure in Childhood

Rare:
- Multisystem disease
- Metabolic liver disease
- Infection

Prognosis: Effective medical therapy
Availability of transplantation

Survival rate:
70% with transplantation
Prevention of GI Haemorrhage

Ranitidine  3-5 mg/kg/dose 8 hrly
Omeprazole  5-20 mg IV 12 hrly
Sucralfate  250-500 mg qds

? Beneficial effect
Grades of Hepatic Coma

Grade I : Minor drowsiness
Grade II : Drowsy, confused, responsive
Grade III : Marked drowsiness, agitated
Grade IV : Unrouseable
Approach to management of acutely ill Infants

Coagulopathy
+/-encephalopathy
+/-hypoglycaemia
+/-liver dysfunction

Yes

Liver Failure

No

Encephalopathy?

Yes

Hyperammonaemia

Yes

Metabolic acidosis or Lactate increased?

No

Hypoglycaemia?

No

Urea cycle disorders

No

Fat oxidation defects

Yes

Ketosis

No

Mitochondrial disorders

Yes

Organic acidaemias
Underlying Mode of Death in Fulminant Hepatitis (n=28)

- Multi-organ failure: 11 (39%)
- Cerebral oedema: 4 (14%)
- Cerebral haemorrhage: 2 (7%)
- Coagulopathy/bleeding: 3 (11%)
Percentage of Spontaneous Recovery in Major Causes of FHF

- Autoimmune
- Hep A
- Paracetamol
- N. haem
- nAnBnC
Overall Survival of FHF According to Age Groups

no significant difference between different age groups and spontaneous survivors, chi-sq for trend: 0.68
Outcome of FHF According to Age

Mortality rate with/without OLT according to age group:

- <6 m: 56%
- 1-6 m: 47%
- 7m-6y: 32%
- >6y: 38%
Conclusion

Liver transplantation is an effective treatment for children with fulminant hepatic failure.

Early referral for liver transplantation assessment is vital.
# Outcome of Fulminant Hepatitis

*(n=31, Pscharopoulons, 1980)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>Cerebral oedema</td>
<td>54%</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>45%</td>
</tr>
<tr>
<td>Renal failure</td>
<td>32%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>16%</td>
</tr>
</tbody>
</table>
# Prognostic index in ALF in Wilson’s Disease

<table>
<thead>
<tr>
<th>Score</th>
<th>Bilirubin µ/L</th>
<th>INR</th>
<th>AST IU/L</th>
<th>WCC X 10^6/L</th>
<th>Alb g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0-100</td>
<td>0-1.3</td>
<td>0-100</td>
<td>0-6.7</td>
<td>&gt;45</td>
</tr>
<tr>
<td>1</td>
<td>101-150</td>
<td>1.3-1.6</td>
<td>101-150</td>
<td>6.8-8.3</td>
<td>34-44</td>
</tr>
<tr>
<td>2</td>
<td>151-200</td>
<td>1.7-1.9</td>
<td>151-300</td>
<td>8.4-10.3</td>
<td>25-33</td>
</tr>
<tr>
<td>3</td>
<td>201-300</td>
<td>2.0-2.4</td>
<td>301-400</td>
<td>10.4-15.3</td>
<td>21-24</td>
</tr>
<tr>
<td>4</td>
<td>&gt;301</td>
<td>&gt;2.5</td>
<td>&gt;401</td>
<td>&gt;15.4</td>
<td>&lt;20</td>
</tr>
</tbody>
</table>
Treatment of Wilson’s Disease

Liver failure without encephalopathy
- Trientine and zinc
- Decision to list for transplant
  - Deterioration and encephalopathy
  - Recovery with chelation therapy
- Wilson Predictive Index
  - Score >11: transplant
  - Score stable or improving: medical therapy
Treatment of Wilson’s Disease

Presymptomatic cases
- All genotypically affected,
- Treatment with Zinc < 3 years
- Prevent liver and neurological damage

Pregnancy
- Penicillamine & Zinc: safe
- Risk for baby of WD is 1 in 300
- Breast-feeding is recommended
Liver transplantation

• Indications:
  – No response to therapy
  – Fulminant or advanced liver failure
  – Chronic liver failure + portal hypertension

• Post transplant
  – Normal copper metabolism
  – Neurologic abnormalities may improve

• Live related donation from heterozygote
  – 32 patients (Kyoto)
Poor Prognostic Features of Acute Liver Failure

Non A, Non B hepatitis
Shrinking liver
Raised bilirubin > 300 mmol/l
Persistent coagulopathy > 70 secs
Failling transaminases
Grade III encephalopathy
Kaplan Meier Curve: Comparison of survival post transplant
ALF v elective BCH experience 1983 - 2012

ALF n= 118
Elective n=536

p <0.05
Age Distribution of 103 Children with FHF – Birmingham data

- 103 cases; 51 males, 52 females
- median age 24 mths (1 d – 17 y)

Lee et al, JPGN, 2005
Underlying Causes of 103 Children with FHF According to Age Group – Birmingham data

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1m</td>
<td>1</td>
</tr>
<tr>
<td>1-12m</td>
<td>10</td>
</tr>
<tr>
<td>1-6y</td>
<td>15</td>
</tr>
<tr>
<td>&gt;6y</td>
<td>10</td>
</tr>
</tbody>
</table>

- Metabolic
- Infective
- Drug-related
- Other

Lee et al, JPGN, 2005