FULMINANT HEPATIC FAILURE
FULMINANT HEPATIC FAILURE

Definition

“A clinical syndrome characterized by encephalopathy and coagulopathy due to massive hepatocellular necrosis or sudden severe impairment of hepatocellular function, in a patient without any pre-existing liver disease. It develops within 8 weeks of the onset of first symptoms attributable to the liver disease”

Trey-Davidson (1970)
FHF IN CHILDREN

• Trey Davidson’s definition not always applicable in children.
• E.g.: Chronic liver diseases like Wilson disease, galactosemia, NH etc. may present acutely as FHF. Early stages of hepatic encephalopathy difficult to assess in infants and neonates.
PAEDIATRIC ACUTE LIVER FAILURE STUDY GROUP (PALFSG) CRITERIA

• Biochemical evidence of liver injury
• No history of known liver disease
• Coagulopathy not corrected by vitamin K administration.
• INR >1.5 if the patient has encephalopathy or > 2 if the patient does not have encephalopathy.
O’GRADY’S CLASSIFICATION OF FHF

Based on the time interval between jaundice and encephalopathy

• Hyperacute - with in 1 week
• Acute - between 8-28 days
• Subacute - between 29 days- 12 weeks
FHF: AETIOLOGY - THE ABCS

- **A** Acetaminophen, hepatitis A, autoimmune hepatitis
- **B** Hepatitis B; bacterial diseases- Weil’s disease; septicemia; liver abscess
- **C** Cryptogenic, hepatitis C, cardiac causes- CCF, CCHD, shock & myocarditis
AETIOLOGY – CONT..

• **D** Hepatitis D, drugs (acetaminophen, aspirin, NH, NSAIDs, valproate, halothane)
• **E** Esoteric causes - Wilson's disease, Budd-Chiari syndrome
• **F** Fatty Infiltration – Reye’s syndrome
• **G** Genetic diseases- galactosemia; HFI; Wilson
AETIOLOGY – CONT...

• $H$ – other Hepatitis viruses- HE, HG, TTV, Herpes simplex
• $I$ - Infiltration – leukemia, neuroblastoma, hepatoblastoma
• $I$ - Ischemic hepatitis- shock due to any cause
FHF – AETIOLOGY (CONT..)

- Toxins
- Aflatoxin
- Amanita phalloides
- Carbon tetrachloride
- Indigenous medicines
HISTORY IN FHF

- Consanguinity
- Sibling death due to liver disease
- Contact with VH
- Risk factors for HB
- Drugs
- Toxins
- Travel history
INFECTIVITY OF HB

1 ml blood contains-
1 trillion viral particles

Infective dose:
Just 0.00001 ml of blood!
RISK FACTORS OF VBH

• Blood & blood products
• Needle stick injury
• Resheathing of needles
• IV drug abuse
• Mouth pipetting
• Shared tooth brush/razors
• Ear/ nose piercing
PHYSICAL EXAMINATION

• Evidence of CLD
• Cataract: galactosemia, HFI, WD
• KF ring
• Liver span
• Ascites
• Grade of coma
• Complete CNS examination
DAWSON’S SIGN
(PALMAR ERYTHEMA)
MONITORING LIVER SPAN
GALACTOSEMIA
WILSON DISEASE
WHEN TO SUSPECT FHF IN A CHILD WITH VIRAL HEPATITIS

- Persistent anorexia
- Persistent vomiting
- Deepening jaundice
- Decreasing liver span
- Relapse of initial symptoms
- Development of ascites
- Neuropsychiatric changes
WHEN TO SUSPECT FHF: LAB CRITERIA

- S. bilirubin > 20 mg/dL
- Prolonged PT not corrected with vitamin K
- Very high ALT (> 3000 IU/L), beyond 2 weeks
- Sudden fall in ALT without clinical improvement
- Leukocytosis
- Thrombocytopenia
WHEN TO SUSPECT FHF (CONT..)

• Hypoglycemia
• Low BUN
• High ammonia
• Low albumin & fibrinogen
• Very low factor V levels
• Respiratory alkalosis
ENCEPHALOPATHY

- Essential component for diagnosis
- Effect of HC failure on function of brain
- Accumulation of neurotoxins: ammonia, glutamine, short chain fatty acids, mercaptans, octopamine, GABA.
- Absence of neuroregulatory substances
FHF – AETIOLOGY (CONT..)

• Toxins
• Aflatoxin
• Amanita phalloides
• Carbon tetrachloride
• Indigenous medicines
FACTORS PRECIPITATING HE

• Constipation
• GI bleed
• Excess protein intake
• Hypokalemia, hyponatremia
• Hypoglycemia, hypoxia
• Uremia
• Sepsis
FACTORS PRECIPITATING HE (CONT..)

• Sedatives
• Tranquilizers
• Diuretics
• Paracentesis
• Surgical procedures
COAGULOPATHY

• All clotting factors low except VWF & VIII
• Malabsorption of vitamin K
• Dysfibrinogenemia
• Thrombocytopenia
• Disseminated intravascular coagulation
• Prolonged PT, PTT
ACID-BASE IMBALANCE

• Resp alkalosis - hyperventilation in early HE
• Metabolic alkalosis - furesemide; hypokalemia
• Respiratory acidosis:
  ▪ Respiratory failure
  ▪ Cerebral edema
  ▪ Obstructed ET tube
  ▪ Pneumonia
ACID-BASE IMBALANCE

Metabolic acidosis

- Metabolic failure - accumulation of org. acids
- Hypotension, poor perfusion - lactic acidosis
- Renal failure
- Mechanical ventilation
- Citrated blood
BASE LINE ESSENTIAL INVESTIGATIONS

• CBC, Platelet count
• Blood group, Cross match
• PT, PTT, Factors V & VII
• LFT, RFT
• Electrolytes, Glucose
• Sepsis screen
• CXR, USS, EEG
DIAGNOSTIC INVESTIGATIONS

• Urine sugar- galactosemia, hereditary fructose intolerance
• Serum paracetamol levels
• Wilson disease work up
• Metabolic work up
• Auto antibodies- LKM, ANA, SMA
• High urine/serum succinyl acetone – type I tyrosinemia
VIRAL MARKERS

• IgM anti HAV
• HBsAg
• IgM anticore Ab
• Anti-delta, anti-HCV
• PCR for HCV RNA
• Ig M anti HEV
GENERAL MEASURES

• Blood, all secretions/excretions potentially infective
• Protective gowns, mask
• IV, radial artery& central venous catheters
• Nasogastric tube, saline lavage
• Bladder catheterization
• Fluid chart, vital signs, daily weight
• Cardio-respiratory monitor
HEPATIC ENCEPHALOPATHY

• Protein restriction - 0.5g/kg/day

• Ampicillin / neomycin / rifaximin / metronidazole

• Lactulose / lactilol

• Bowel wash

• Prevention of GI bleed

• Flumazenil
LACTULOSE
MANAGEMENT OF HYPOGLYCEMIA

• Frequent monitoring (every 2-4 hrs)
• IV glucose 25%-2ml/kg
• Maintain glucose 40-60 mg%
COAGULOPATHY

- Mild (PT <18 seconds)
- Moderate (PT 18-25)
- Severe (PT >25)
FHF – AETIOLOGY (CONTD)

• Toxins

• Aflatoxin

• Amanita phalloides

• Carbon tetrachloride

• Indigenous medicines
COAGULOPATHY

• Vitamin K: 0.2-0.3 mg/kg - max 10 mg
• **Mild coagulopathy** - no treatment
• **Moderate**: FFP(10 ml/kg 6 hourly) to reduce PT to 16-18 seconds
• **Severe**: FFP(15-20 ml/kg 6 hourly) to reduce PT to 18-25
• Cryoprecipitate, platelet transfusion
PREVENTION OF GI BLEED

• Ranitidine 1-2 mg/kg/dose IV 2-4 times/day

• Omeprazole 0.5mg/kg/dose NG 1-2 times/day

• Sucralfate 10-20 mg/kg/dose NG 4-6 hourly
RENAL DYSFUNCTION IN FHF

• Pre-renal failure

• Acute tubular necrosis

• Hepatorenal syndrome - commonest
HYPOKALEMIA

• Injudicious diuretics

• Secondary hyperaldosteronism

• Excessive vomiting

• Nasogastric aspiration
HYPONATREMIA

• Decreased water excretion by kidneys
• Increased ADH
• Excess use of hypotonic fluids
• Frusemide
• Restrict fluids to 75% of maintenance
• Do not correct with saline
INFECTION IN FHF

90% have clinical e/o bacterial infection

Factors predisposing to infections-

• Poor host defense
• Impaired Kupffer and polymorph function
• Low opsonins, fibronectin, complement
• Poor cough reflex
• ET tubes, catheters, venous lines
INFECTIONS IN FHF (CONTD)

• Pneumonia - commonest
• Urinary tract infection
• Septicemia
• Gram positive in 60%-staph/strep
• Gram negative bacilli
• Fungal infections in 30%
CEREBRAL EDEMA

• One of the most common cause of death
• ICP is above 30 mmHg
• Clinical detection difficult
• Sudden change in level of consciousness
• Anisocoria, hypertonia, seizures
• Decerebrate posturing, papilledema
• Bradycardia with rising BP
CEREBRAL EDEMA(CONT..)

• Seen in 80% of fatal cases
• Grade III-IV encephalopathy
• Raise head end 45°
• Fluid restriction, IV mannitol
• Avoid hyperthermia
• Ventilate if HE> grade III
  ▪ Extradural monitors - Ladd transducers
  ▪ Subdural monitors - Gaeltec monitors
BRAIN EDEMA FHF
SPECIFIC THERAPY IN FHF

- **N-acetylcysteine** in paracetamol poisoning
- **Benzyl penicillin & thioctic acid** in Amanita poisoning
- Acyclovir in herpes simplex
- D-penicillamine - Wilson disease
SPECIFIC THERAPY IN FHF

• Artificial liver support

• Hepatocyte transplantation

• Liver transplantation
ARTIFICIAL LIVER SUPPORT SYSTEM

• Molecular Absorbent Recirculating System (MARS)

• Albumin impregnated dialysis membrane and a dialysate containing 5% human albumin

• Removes water soluble toxins including NH₃
BIO-ARTIFICIAL LIVER SUPPORT

- Bio-reactors containing viable hepatocytes in culture
- Bio-artificial Liver (BAL)
- Extra-corporial Liver Assist Device (ELAD)
- Berlin Extracorporeal Liver Assist Device (BELS)
KING’S COLLEGE CRITERIA FOR LIVER TRANSPLANTATION

• Paracetamol induced FH
• pH < 7.3 (irrespective of grade of HE)

OR

• PT >100 sec
• Creatinine >300 micromol/L or >3.4 mg%
• Grade 3 or 4 HE
Non-paracetamol patients
PT >100 sec(INR>7) (irrespective of HE grade) Or any 3 of these, irrespective of HE grade:
• Age <10 or 40 years
• PT >50 seconds (INR > 3.5)
• SB >17.5 mg%
• Non- A-E hepatitis; halothane hepatitis; idiosyncratic drug reactions
• Duration of jaundice before onset of HE>7 days
GOOD PROGNOSTIC FACTORS

• Age: 10 - 40 years

• Hepatitis A

• Paracetamol poisoning if treated in time

• Presence of an obvious etiology

• Stage I/II HE

• Increased alpha-fetoproteins - as it is a sign of hepatocellular regeneration
## Survival Rate in FH

<table>
<thead>
<tr>
<th>Etiology of FH</th>
<th>Survival (%)</th>
</tr>
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<tbody>
<tr>
<td>Hepatitis A</td>
<td>70</td>
</tr>
<tr>
<td>Paracetamol poisoning</td>
<td>50</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>40</td>
</tr>
<tr>
<td>NA-G hepatitis</td>
<td>20</td>
</tr>
<tr>
<td>Halothane</td>
<td>10</td>
</tr>
</tbody>
</table>
CAUSES OF DEATH

• Cerebral edema
• Septicemia/fungemia
• Respiratory failure
• Hemorrhagic diathesis
• Complications of LT
Prevention of FHF

- Hepatitis B & A vaccination
- Monitoring of patients on ATT/NSAIDs
- Avoid paracetamol over dose
- Avoid aspirin- Reye syndrome
- Avoid Afla toxins, amanita
Thank You