APPROACH TO
PATIENTS WITH LIVER DISEASE

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I. INTRODUCTION:

A patient with liver disease may present with a variety of clinical features. The patient may be totally asymptomatic and the disease may be an incidental finding during routine work up. Laboratory investigations may reveal elevated liver enzymes or increased levels of serum bilirubin. On the other hand the patient may be morbidly ill with all the possible features of liver cell failure (Table 1) and its complications e.g. hepatic encephalopathy. Common liver diseases are shown in Table 2. The role of anaesthesiologists in liver disease patients may be to manage the complications (e.g) acute variceal bleed or to provide anaesthesia for diagnostic (e.g. ERCP) and therapeutic (e.g. TIPS) interventions. Patients may present for endoscopic, laparoscopic or open surgical procedures. Surgery may be elective or
emergency. It may be a hepatic surgery e.g. hepatectomy or non-hepatic surgery e.g. hernia repair.

Table: 1

<table>
<thead>
<tr>
<th>Jaundice</th>
<th>Alopecia</th>
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<tbody>
<tr>
<td>Parotid enlargement</td>
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<td>Feter hepaticus</td>
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<td>Spider neavae</td>
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<td>Gynaecomastia</td>
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<td>Prominent dilated veins over the abdomen</td>
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<td>Caput medusa</td>
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<td>Hydrothorax</td>
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<td>Ascites</td>
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<td>Hyperdynamic pulse</td>
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<td>Widened pulse pressure</td>
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<td>Paper money skin</td>
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<tr>
<td>Palmar erythema</td>
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<td>Duputyren’s contracture</td>
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<td>Clubbing</td>
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<td>Muscle wasting</td>
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<tr>
<td>Altered distribution of pubic hair</td>
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<td>Testicular atrophy</td>
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<td>Flapping tremors</td>
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<td>Tendon xanthematosis</td>
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</table>

Table: 2
## I. Acute liver diseases

1. Viral hepatitis
   - Viral hepatitis A
   - Viral hepatitis B
   - Viral hepatitis C
   - Viral hepatitis D
   - Viral hepatitis E
   - Cyto-megalo virus
   - Ebstein-Barr virus
2. Drug induced hepatitis
   - Acetaminophen overdose
   - Volatile anaesthetics (e.g) halothane

## II. Chronic liver diseases

1. Autoimmune hepatitis
2. Chronic hepatitis B
3. Chronic hepatitis C
4. Drug induced chronic hepatitis
   - e.g. methyl dopa

## III. Cirrhosis of liver

## II. PRE-OPERATIVE APPROACH
When a patient with liver disease presents for anaesthesia, a thorough work-up is done so that a definitive diagnosis is made. Patient should be categorized as acute or chronic liver disease; whether the patient is in compensated or decompensated state should be identified; involvement of other physiological systems should be looked for; Whether the surgery is elective or emergency should be considered; Pre-operative optimization of correctable conditions should be attempted; Risk stratification should be made to predict the peri-operative morbidity and mortality. Only life threatening problems requiring emergency surgery should be accepted for anesthesia in the presence of acute liver cell failure.

(i) **Pre-operative assessment:**

Pre-operative evaluation includes not only the hepato-biliary system but also the other physiological systems which are prone to get involved in liver diseases.

**Anaemia:** Chronic liver disease patients are usually anaemic. This is because of chronic gastro-intestinal blood loss, nutritional deficiencies, hypersplenism and bone marrow depression by alcohol.

**Coagulopathy** is commonly seen in CLD patients, since most of the coagulation factors are synthesized in liver.
CVS: Hyper dynamic circulation is seen in patients with cirrhosis of liver. There is increased cardiac output due to peripheral and splanchnic vaso dilatation, increased blood volume, decreased blood viscosity (due to anemia) and arterio-venous communications. Cirrhotic cardio myopathy may be seen in these patients. Cardiac function may appear normal during rest as the cardiac output is maintained due to decreased systemic vascular resistance. However, the function decompensates during exercise or stress. These patients have reduced sensitivity to sympathomimetics. Hypertension, cardiac failure and cardiac arrhythmias may also be present.

RS: Arterial hypotension is common in cirrhotic patients. This could be due to (i) impaired diaphragmatic movement due to accumulation of ascetic fluid (ii) R-L intra pulmonary shunting due to portal HT. (iii) cigarette smoking (iv) COPD (v) Pnuemmonia (alcohol inhibits phagocytic activity in lungs. (vi) aspiration of regurgitated gastric contents due to alcohol induced decrease in the lower oesophageal sphincter tone. Atelectasis and pleural effusion may also be seen in liver disease patients. Hepato pulmonary syndrome includes pulmonary dysfunction, hypoxemia and intra pulmonary vaso dilatation. Porto pulmonary hypertension may also occur in these patients.
**Renal system:** Renal dysfunction may occur in liver disease patients due to contrast dye used for imaging studies, nephrotoxic medication, diuretic therapy and urinary tract interventions. Hepato renal syndrome may occur in these patients and is precipitated by GI bleed, spontaneous bacterial peritonitis, aggressive paracentesis and drugs.

**Nervous system:** Hepatic encephalopathy may results in changes in cognition, personality, motor function and consciousness. This may be precipitated by GI bleed, electrolyte abnormalities, acid base disturbances, sepsis, diuretic therapy sedatives, opioids, excess dietary protein intake and creation of porto systemic shunt.

**Hypoglycemia:** Hypoglycemia is commonly seen in patients with hepatic cirrhosis especially alcoholic cirrhosis. This is due to glycogen depletion (due to malnutrition) and alcohol induced interference with gluconeogenesis.

**Metabolic acidosis:** Liver is responsible for converting lactate to glucose. In CLD, this function is impaired leading on to accumulation of lactic acid and development of lactic acidosis.

**Alcohol:** Chronic alcohol consumption may increase the requirement of anaesthetics due to cross tolerance. Alcohol induced microsomal enzyme induction can also alter the anaesthetic requirements. Alcoholic cardio myopathy may
show increased sensitivity to cardiac depressant anaesthetic drugs and decreased sensitivity to inotropes.

(ii) Pre Operative investigations:

Following laboratory investigations are usually done when a liver disease patient is posted for surgery.

Hb, Complete haemogram, Peripheral smear - look for anaemia & its type.

WBC, TC, DC, ESR - rule out infections.

Platelet count.

Alanine aminotransferase, Aspartate aminotransferase - elevated levels indicate hepato cellular injury

Alkaline phosphatase, 5’ Nucleotidase, Gamma glutamyl transpeptidase - increased level indicates cholestasis.

Serum bilirubin –Total, direct, indirect.

Urine bile salts, bile pigments.

Serum Ammonia

Total proteins –Albumin, Globulin, A:G ratio

Prothrombin time & INR- coagulopathy

Serum electrolytes
Blood urea
Serum creatinine
Blood sugar
X-ray chest
ECG
Echo cardiography
ABG
Lipid profile
Serum Amylase
EEG
USG, CT- abdomen
Upper GI Scopy
Ascitic fluid analysis—cell count, Bacterial culture, Protein, Albumin, LDH, Glucose, AFB, Cytology
HBS Ag
HCV Ag
Liver biopsy.

(iii) Pre-operative optimization:
Preoperative optimization of co-existing problems may reduce the mortality and morbidity after major surgery.

* Abstinence from alcohol should be instituted

* Anaemia may require transfusion of blood

* Coagulation abnormalities should be corrected with inj. vitamin K and FFP.

* Platelet transfusion may be necessary for thrombocytopenia.

* Hypoglycemia should be corrected with IV glucose administration.

* Adequate hydration is maintained with IV fluids.

* Electrolyte abnormalities and acid-base disturbances should be corrected preoperatively.

* Adequate urine output should be maintained and renal function should be improved.

* Cardio respiratory Function should be optimized.

* Nutrition should be improved.

* Ascites should be corrected with salt & water restriction, Diuretics (Spiranolactone 100-200mg/day up to 400-600mg/day; Frusemide 40-80mg/day up to 120-160mg/day). Large volume paracentesis (Less than 5Lit) with albumin replacement may be necessary. Leevann shunt (peritoneo-
venous shunt) may sometimes be necessary. Spontaneous bacterial peritonitis and secondary bacterial peritonitis should be treated with appropriate antibiotics.

- Acute variceal bleed: Fluid resuscitation with blood and blood products; Circulatory and ventilator support; Inj. Vasopressin 20 units in 200 ml over 20 min to produce splanchnic vaso constriction; Sengstaken Blackmore tube to produce direct pressure tamponade over the varices; Endoscopic variceal ligation.
- Hepatic encephalopathy: predisposing factors should be identified and corrected; Restriction of dietary proteins; Lactulose syrup 30- 40 mg orally; 300 ml retention enema; Oral non absorbable antibiotics like neomycin 4-12 g/day; metronidazole or vancomycin; Flumezanil, benzodiazepine antagonist.
- Portal hypertension; Non selective beta blockers e.g.propranolol to reduce portal venous pressure; Low salt diet; Diuretics: spironolactone/ frusemide; Vaso active drugs: somato statin or its analogues like octreotide; Porto-systemic shunt procedures-TIPS (Transjugular Intra hepatic Porto systemic Shunt).

(iv) Pre-operative risk stratification:
In liver disease patients, risk assessment can be done using several methods. The most common method is Child- Pugh classification (Table 3).

**Table: 3**

Child- Turcotte- Pugh classification

<table>
<thead>
<tr>
<th>No</th>
<th>Factor</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serum Bilirubin</td>
<td>&lt; 2mg/dl</td>
<td>2-3mg/dl</td>
<td>&gt;3mg/dl</td>
</tr>
<tr>
<td>2</td>
<td>Serum Albumin</td>
<td>&gt;3.5g/dl</td>
<td>3-3.5g/dl</td>
<td>&lt;3g/dl</td>
</tr>
<tr>
<td>3</td>
<td>Prothrombin time or INR</td>
<td>0-4 sec</td>
<td>4-6 s</td>
<td>&gt;6 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 1.7</td>
<td>1.7-2.3</td>
<td>&gt;2.3</td>
</tr>
<tr>
<td>4</td>
<td>Ascites</td>
<td>None</td>
<td>Easily controlled</td>
<td>Poorly controlled</td>
</tr>
<tr>
<td>5</td>
<td>Hepatic encephalopathy</td>
<td>None</td>
<td>Minimal</td>
<td>Advanced</td>
</tr>
</tbody>
</table>

Five factors are used for risk stratification. 1) Serum bilirubin; 2) serum albumin; 3) prothrombin time or INR; 4) ascites; 5) hepatic encephalopathy. Each factor is given score 1-3. Total score may range from 3-15. Depending on the total score the patient is divided into three grades; grade A,B,& C. Grade A(score 5-6) represents good risk with 5% mortality. Grade B score (7-9) indicates moderate risk with 10 % mortality. Grade C score >10 are at poor risk with
mortality >50%. Grade C indicates decompensated liver disease.

Another method to assess the severity of liver disease is MELD (Model for End stage Liver Disease). It is calculated by the summing up the following values.

\[3.78 \times \log_e \text{Serum Bilirubin mg/dl} +
11.2 \times \log_e \text{INR} +
9.57 \times \log_e \text{Serum albumin} +
6.43.\]

Maximum score is 40. More the score, more the risk of morbidity and mortality. More than 15 MELD patients are accepted for cadaveric liver transplantation.

III. INTRA-OPERATIVE APPROACH

(a) *Choice of anaesthesia* depends on the site and extent of surgery. Lower abdominal and lower limb procedures can be performed under central neuraxial blockade, provided the coagulation status is acceptable.

(b) For *regional anaesthesia*, prothrombin time should be less than 4 seconds of control and INR should be less than 1.4. Subarachnoid block to T4 level will reduce the hepatic blood flow by 20%. Spinal hypotension may decrease the hepatic arterial buffer response (HABR);
reduce the hepatic and renal blood flow. This may cause hepatic decompensation and renal failure. Administration of IV fluids and vasopressors may be necessary to maintain BP and thus the HBF.

(c) **Induction agents:**

Both thiopentone and propofol have been used safely in patients with liver diseases. Serum albumin level is decreased in chronic liver disease patients and thus the free fraction of thiopentone available in the blood is more. Hence the dose of thiopentone has to be reduced accordingly. Propofol can be used for induction as well as for maintenance of anaesthesia.

(d) **Muscle relaxants:**

Succinyl choline is metabolized by the enzyme pseudocholinesterase which is synthesized in liver. In chronic liver disease patients with hepatic dysfunction, the level of pseudo cholinesterase is less. However in the clinical set up the duration of action of succinyl choline is not prolonged because that happens only when the enzyme level becomes 50% of normal.

Initial dose of non-depolarizing muscle relaxants is higher due to increased volume of distribution. Subsequent doses are usually less because of the prolonged metabolism of drugs in the presence of CLD. Atracurium is the muscle relaxant of choice.
Atracurium is metabolized by Hoffmann degradation and ester hydrolysis. It is not dependent on liver or kidney for metabolism and elimination. Laudanosine, a metabolite of Atracurium is eliminated by hepatic clearance. In the presence of hepatic dysfunction and renal failure, accumulation of laudanosine occurs which may result in convulsions. Nevertheless, in the clinical doses of atracurium, significant level of laudanosine accumulation does not occur to cause convulsions.

(e) **Volatile anaesthetics:**

Isoflurane, Desflurane and Sevoflurane can be safely used in liver disease patients. Hepatic blood flow and hepatocyte oxygenation are maintained with these agents. Halothane is not preferred because it depresses the hepatic arterial buffer response (HABR) and it may also cause halothane hepatitis. Nitrous oxide can cause accumulation of gas in the bowel and surgical inconvenience during prolonged laparotomy. Hence, air may be used along with oxygen for maintenance of anaesthesia.

(f) **Benzodiazepines:**

All Benzodiazepines are metabolized in the liver. In the presence of severe hepatic dysfunction and hepatic encephalopathy, benzodiazepines especially long acting drugs should be avoided. However, small doses of midazolam can be used, provided there is no hepatic encephalopathy.
(g) **Opioids:** Opioids are metabolized in the liver. Long acting opioids are better avoided. Fentanyl and Remifentanil are usually preferred.

(g) **Maintenance of hepatic blood flow:**

Liver has got dual blood supply. Portal vein supplies 75% of total hepatic blood flow (THBF). Remaining 25% is through hepatic artery. However, 50-55% of hepatic oxygen supply is through portal vein and 45-50% is by hepatic artery. When the portal venous blood flow decreases, the hepatic arterial flow increases. This is an auto-regulatory mechanism and is called Hepatic arterial buffer response (HABR). In the presence of portal hypertension, portal venous blood flow is decreased and the total hepatic blood flow is maintained by compensatory increase in hepatic arterial flow. During anaesthesia in Cirrhotic patients decrease in hepatic arterial blood flow (due to surgical stimulation, hypotension, and volatile anaesthetics) will compromise the total hepatic blood flow.

(i) **Monitoring:**

Intra operative monitoring depends on the type, extent and duration of surgery. Noninvasive monitoring includes ECG, pulse oximetry, NIBP, ETCO2, temperature, peripheral nerve stimulator (for neuro-muscular monitoring), urine output and inspired concentration of volatile anaesthetics. Invasive monitoring includes intra-arterial BP, CVP, Pulmonary artery
occlusion pressure, ABG, serum electrolytes, CBG, Coagulation monitoring (Prothrombin time, INR, platelet count and Thromboelastography). In patients with esophageal varices unnecessary esophageal instrumentation (esophageal stethoscope, naso-gastric or oro-gastric tube) should be avoided.

(j) Intra-operative fluid management should depend on the cardiac filling pressures (CVP, PAOP) and urine output. Urine output of 0.5 to 1 ml/kg/min should be maintained. Patients may require colloids like albumin and gelofusine. Excessive blood loss may occur intra operatively. Adequate replacement is done with blood and blood products like (packed RBCs, FFP, cryoprecipitate and platelets) and Coagulopathy should be corrected. Rapid infusion devices may be necessary. Active warming of fluids should be done. Citrate toxicity is a problem when a large volume of transfusion is done.

(k) Hypoglycemia is a frequent problem in these patients and glucose administration may be necessary to maintain normoglycemia. Sometimes patients may go in for hyperglycemia which may require insulin infusion.

(l) These patients are prone for arterial hypoxemia (for reasons mentioned earlier) which should be identified and corrected promptly.
Hypothermia is common in CLD patients due to convective heat loss when bowels are exposed as in laparotomy for a long time. Warming mattress, warmed IV fluids and air warmers should be used intra and post operatively.

Since these patients are prone for infection, antibiotics should be continued in the peri-operative period.

Standard precautions:

While handling patients with liver disease, all precautions should be taken for transmission of infections like Hepatitis A, B, C or HIV. Protective barriers like cap, mask, gown, gloves and goggles should be worn. Needles, blades and other sharps contaminate with body fluids should be disposed in the designated puncture resistant containers. Theatre personnel should wear heavy duty gloves when transporting sharps. Do not recap needles. Needle destroyer may be used to incinerate and melt the used needles. Disposables and consumables should not be reused. Reusable surgical instruments should be thoroughly disinfected.

Post-exposure Prophylaxis for Hepatitis B:

While handling a hepatitis B patient, if the operating room personnel sustain needle stick injury or exposed to infected material blood or body fluids, Post exposure prophylaxis should be undertaken. Hepatitis B antibody titre has to be estimated
immediately. If the antibody titre is adequate, immunization may not be necessary. If the antibody titre is inadequate, immunization should be done. Hepatitis B immunoglobulin should be administered within 24 to 72 hours after exposure. Three injections of recombinant vaccine are given on 0, 1-2 months and 3-6 months.

IV. POST OPERATIVE APPROACH:

Many of these patients would require postoperative ICU care. Postoperative ventilation is necessary after major surgery in severe liver disease patients. Parameters monitored per-operatively should continue to be monitored in the post-operative phase, with regular review of blood count, clotting profile and blood gases, chemistry and sugar. Inotropic support should be continued as long as is necessary. Bleeding is a frequent problem in the post-operative period. Coagulopathy needs to be corrected. Surgical reopening may be necessary. Adequate urine output should be maintained. Hypothermia should be prevented by warm mattress and air warmer. When removed, tips of arterial line, central venous line, peripheral venous line, urinary catheter etc. should be sent for culture and sensitivity and appropriate antibiotics given. Deep vein thrombosis may be prevented by pneumatic compression stockings.
Postoperative pain relief: regional nerve blocks and epidural analgesia may be considered when coagulopathy is not a problem. Inj. Bupivacaine 0.0625% is used as an infusion. Paracetamol may be used in smaller doses. NSAIDs like Diclofenac is added for synergistic effect. Fentanyl is used as an IV infusion in smaller doses.

V. CONCLUSION:
More and more patients are presenting for anaesthesia with liver diseases. Peri-operative morbidity and mortality in liver disease patients is high. A thorough pre-operative assessment, good understanding of the pathophysiology of the liver dysfunction and systematic & dedicated perioperative approach are essential for a better outcome of the patients with liver diseases.