UNIT 3 DISORDERS OF LIVER, BILIARY SYSTEM AND PANCREAS

Structure

3.0 OBJECTIVES

After going through this unit, you should be able to:

- describe the physiological and biological alterations;
- discuss the clinical features of liver, gall bladder and pancreatic infections and diagnose them; and
- detect liver and gall bladder tumours including pancreas.

3.1 INTRODUCTION

In the previous two units, you have learnt about the diseases of upper and lower gastrointestinal tract. In this unit, you will learn about common diseases of the liver, the biliary tree and

pancreas as seen in the elderly. Liver is the largest solid body organ. It plays an important role in maintenance of body homeostasis. In elderly, there is reduced ability to adjust to metabolic, infectious and immunologic insults and therefore presentation of disease may be different.

3.2 PHYSIOLOGICAL AND BIOLOGICAL ALTERATIONS

There is decrease in liver mass and liver blood flows with aging. Liver perfusion (liver blood flow per unit liver volume) is also decreased. Decrease is more in portal blood as compared to hepatic artery flow. Portal venous blood velocity and flow are inversely related to age. It also may be related to Atherosclerotic changes in mesenteric circulation.

The common biochemical indicators of liver disease include serum bilirubin, transaminases(SGOT/SGPT) and serum alkaline phosphatase These parameters do not alter with age, serum albumin may be altered because of co-existent malnutrition or due to co-existence of other diseases. However, this is an age-related loss of functional liver cell mass. The clinical significance of these tests is shown in Table 3.1.

Table 3.1 : Clinical Significance of Common Liver Tests

Test	Associated liver diseases
Aminotransferases	Hepatitis (viral, autoimmune, toxic, ischemic)
Alkaline phosphatase	a) Extra and intrahepatic cholestasis
	b) Infiltrating disease of liver
Bilirubin	a) Inherited hyperbilirubinaemia
	b) Hepatocellular disease
	c) Extrahepatic biliary obstruction
Prothrombin time	a) Acute or chronic liver failure
	b) Biliary obstruction
Albumin	a) Chronic liver failure

3.3 LIVER INFECTIONS

The infections affecting the liver may be either due to hepatotrophic viruses or bacterial, parasitic and fungal infections. Of these, hepatophilic virus infections are most prevalent.

Various viruses have been identified that appear to target the liver and produce liver disease. Most of them are RNA viruses and one is a DNA virus. These viruses include Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis E and Hepatitis G virus. The virology and clinical features of these agents are shown in Table 3.2. Viral hepatitis presents in three forms : Icteric illness, anicteric illness and subclinical asymptomatic infection. The spectrum of severity of illness varies from uncomplicated self-limiting acute viral hepatitis to acute liver failure manifesting with encephalopathy and loss of hepatic function. Progression to chronic hepatitis, cirrhosis of liver and even hepatocellular carcinoma can occur in case of infections with hepatitsis B,C viruses. These long term complications are not observed in hepatitis A and E virus infections. In the older age group, the disease severity also depends on the co-existent illness like diabetes, renal failure and immuno deficiency states.

Hepatitis A

The prevalence of hepatitis A is related to the quality of water supply, the level of sanitation and age. It is a common infection in the paediatric age group in the developing countries. It causes acute viral hepatitis in older group in developed countries. Illness is most frequently associated with cholestasis and recovery is slower than in younger patients The severity of illness is age dependent. Two atypical clinical causes are cholestatic hepatitis and relapsing

hepatitis. Overall the prognosis in acute HAV infection is excellent and chronic hepatitis does not occur.

Table 3.2 : Salient Features of Infection Caused by Hepatitis Viruses

	HAV	HBV	HCV	HEV
1) Family	Picornaviridae	Hepadnaviridae	Flaviviridae	Caliciviridae/alpha
2) Size	27-32 nm	42 nm	55 nm	32 nm
3) Shape	Icosahedral	Spheric	Spheric	Isosahedral
4) Envelope	No	Yes	Yes	No
5) Antibodies	Anti-HAV IgM	Anti-HBs, Anti-Hbe Anti-Hbe, IgG, IgM	Anti-HCV IgG, IgM	Anti-HEV IgG, IgM
6) Transmission				
Oral	Yes, common	Not likely	Not likely	Yes, common
Percuteneous	Rare	Common	Common	Unknown
Sexual	No	Common	Yes, common	No
Perinatal	No	Common	Yes, ? frequency	Yes, ? frequency
7) Incubation period (days)	15-49 (average 25)	60-180	14-160	15-60
8) Clinical illness	5% pediatric 70-80% adults	10-15%	5-10%	70-80% adults
9) Jaundice	Adults 30% Children < 5%	5-20%	5-10%	Common
10)	Fulminant	< 1%	<1%	Unclear <1%, higher in pregnant women.

Hepatitis B

Hepatitis B is caused by a DNA virus parenterally transmitted in a blood or blood products, sexual contract or perinatal exposure. Clinical presentation is an asymptomatic HbsAg carrier, acute hepatits, acute liver failure, chronic hepatitis or as long term complications of chronic liver disease: such as portal hypertension, variceal bleeding, ascitis, hepatocellular carcinoma. Risk of chronic infection is related to age and immune status of the host. Fatality increases with advancing age Risk of infection is high in haemodialysis patients, subjects on immunosuppressive therapy and concomittent HIV infection.

Treatment of acute infection is largely supportive and antiviral therapy is not indicated. Interferon alpha is used as the antiviral agent for therapy of actively replicating virus in chronic HBV infection. Lumirudine is a nucleoside analogue with anti HBV activity. However, this treatment is associated with a poorer efficacy and a higher risk of complications.

Active immunization is one of the major strategies for prevention of H,B,V, infection. Hepatitis B vaccination has poorer efficacy in the elderly. Elderly patients are at a higher risk of becoming chronic carriers and are risk of development of cirrhosis and primary liver cancer.

Hepatitis C

The mode of transmission of HCV infection is chiefly percutaneous route (i.e. blood transfusion, needle stick inoculation). It forms a major chunk of post-transfusion hepatitis. Less than 25% of infected patient have icterus during the acute stage of infection. Once established it persists in the vast majority. Progression of disease is largely silent and patients are often diagnosed on routine biochemical screening or during the course of blood donation. 85% of the infected patients develop cirrhosis of liver over a 15-20 year period. Hepato-cellular carcinoma is also seen after 25 years of infection.

Response to interferon treatment is poorer in elderly patients. There is no vaccine available for hepatitis C infection.

Hepatitis E

It is the most common cause of epidemic enterically transmitted hepatitis in developing countries. HEV is the major cause of acute viral hepatitis in both sporadic and epidemic in the Indian subcontinent. It is transmitted mainly by the faecal oral route through contaminated drinking water. Clinical presentation and mortality appears to be no different from what has been observed among young adults. The infection is usually self-limiting and has a benign course. Supportive care is the corner stone of the therapy.

Check Your Progress 1

1) Name the transaminases and mention their importance.

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2) Hepatitis B virus belongs to which type of virus. Mention mode of transmission.

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3) Name antiviral therapy given to treat H.B.V. infection.

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4) What is the treatment of HEV infection?

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3.4 PARASITIC AND MYCOBACTERIAL INFECTIONS OF THE LIVER

The common parasitic and mycobacterial infections include:

- Amoebic liver abscess
- Pyogenic liver abscess
- Hydatid disease
- Tuberculosis
- Malaria.

Amoebic Liver Abscess

Amoebic liver abscess is caused by Entamoeba histolytica and liver is the most common extraintestinal organ involved. It occurs mostly in the age group of 20-40 years. However, when it occurs in an elderly person, it carries a poorer prognosis, even with aggressive management. The disease presents as fever, abdominal pain and hepatomegaly. Metronidazole is the drug of choice and if the patient does not respond to medical therapy and if abscess is more than 8 cm in size, or left lobe abscess is present then percutaneous aspiration of the abscess is indicated.

Pyogenic Liver Abscess

Most cases of pyogenic liver abscess occur in the elderly with underlying biliary tract disease. The disease results due to either ascending cholangitis or due to hematogenous seeding of infection from a primary source. These include gallstone disease and colonic diverticulosis, both of which are common among the elderly. In addition, malignancies of the colon and the biliary tree too can be associated with portal bacteremia, resulting in pyogenic liver abscesses. Elderly patients with liver abscess frequently present with non-specific symptoms like fever, epigastric pain, weight loss, dyspnea and malaise. High grade fever with rigors, a common presentation among younger patients, is relatively less frequently encountered. Examination may reveal tender hepatomegaly, and in some cases, jaundice. Upon investigation, low serum albumin, raised alkaline phosphatase, and elevated right hemidiaphragm and right sided pleural effusion on chest X-ray are the most frequent findings. Ultrasound is very useful. In some cases, CT scan may be required to confirm the diagnosis. In recent years however, increasing reliance is being placed on the use of antibiotics and general supportive measures. In elderly patients, if pus drainage is considered to be necessary, ultrasonic guided drainage of abscess is usually preferred over surgery; today the latter is resorted to in only a few patients. The underlying cause of abscess, for instance biliary obstruction, needs to be treated to prevent recurrence. Despite aggressive management, in-hospital mortality remains 18% to 20%. The differentiating features between an amoebic and a pyogenic liver abscess is shown in Table 3.3.

Table 3.3 : Pyogenic and Amoebic Liver Abscess : Clinical Distinctions

	Pyogenic Liver Abscess	Amoebic Liver Abscess
Number	Often multiple	Usually single
Location	Either lobe	Usually right hepatic lobe, near the Diaphragm
Presentation	Subacute	Acute
Jaundice	Mild, if present	Moderate, if present
Diagnosis	US or CT ± aspiration	US or CT and serology
Treatment	IV antibiotics + drainage	Metronidazole, 75mg tid for five days Orally or IV followed by diloxanide Furoate, 500mg orally tid for ten days, Or iodoquinol, 650mg orally tid for 20 Days.

Hydatid Disease

Hydatid disease is related to infection with the larval or cyst stage of a tapeworm (Echinococcus granulosus). Symptoms of liver hydatid cyst in the elderly are similar to those in the younger patients. These include fullness, discomfort and pain in the right upper abdomen. Examination reveals a palpable mass. In Ultrasound, the presence of single or multiloculated cyst with internal septae or membranes is characteristic. Serologic tests can be helpful in certain situations. Casonic test is positive in 90 percent cases.

Orally administered albendazole diffuses freely across the parasitic membrane and is an effective treatment modality for small, uncomplicated cysts. Treatment with ultrasound guided percutaneous aspiration and hypertonic saline injection has been found to be as effective though less invasive than surgical cystectomy. The high surgical risk in the elderly makes this option particularly attractive.

Tuberculosis

Abdominal tuberculosis is common in developing countries. A rise in number of patients with HIV infection in the recent past has further increased the importance of this disease. Usual presentation is with fever, hepatosplenomegaly and weight loss. Some patients have focal lesions in the liver on ultrasound or CT. Only 15-20% have accompanying pulmonary TB. Liver biopsy showing granulomas and presence of acid-fast bacilli is diagnostic. Treatment with anti-tubercular drugs is effective; a strict monitoring of compliance is essential to prevent the emergence of resistant strains. In patients infected with multi-resistant strains of the tubercular bacteria, newer drugs need to be used.

Malaria

Liver involvement is not uncommon in patients with malaria. Cases of infection may be present with a clinical picture of fulminant hepatic failure; i.e. fever, jaundice, altered sensorium and/or renal failure. However, fever is frequently high grade, persists after the onset of jaundice and is often accompanied by hepatomegaly. Peripheral blood smear examination showing the presence of malarial parasites in red blood cells is diagnostic and must be performed routinely in such patients living in areas where this infection is endemic. Early treatment with antimalarial drugs is very rewarding in these cases.

3.5 DRUG INDUCED LIVER DISEASE

Liver injury at times irreversible can be caused by drugs and other chemicals. This is usually reflected in abnormalities of liver function tests. Further details of drug toxicities are given in Unit-4, Block-2 of Course-1. Elderly patients are particularly prone to drug induced liver disease because of advanced age, coexisting illnesses, alcohol abuse, use of many drugs for different illnesses at one time and often poor nutritional status.

Drugs causing hepatotoxicity in elderly include isoniazid, halothane, nonsteroidal antiinflammatory agents and nitrofurantoin.

Hepatotoxicity is liver injury caused by drugs and other chemicals. In general, liver injury is present when abnormalities of liver tests include an increase to more than twice the upper limit of normal of serum alanine aminotransferase (ALT) , serum alkaline phosphatase(SAP) or serum bilirubin. The severity of liver injury varies from minor non specific changes in hepatic structure and function to fulminant hepatic failure, cirrhosis and liver cancer. Many factors influence the risk of drug induced liver disease : age, sex, dose, genetic factors, excessive alcohol use, nutritional status, coexisting illnesses and concomitant use of other drugs. Elderly patients are particularly prone to drug induced liver disease because of advanced age, coexisting illnesses, use of many drugs for different illnesses at one time and often poor nutritional status. Further, altered pharmaco-kinetics and extra-hepatic drug metabolism may also increase the risk of adverse drug reactions in the elderly. Though it is uncertain whether aging leads to an increased susceptibility to drug reactions, it is clear that when reactions occur, they are more likely to be severe and carry a poorer prognosis.

Drugs causing hepatotoxicity in elderly include isoniazid, halothane, nonsteroidal antiinflammatory agents and nitrofurantoin. Isoniazid administration in the elderly is associated with an increased risk of liver injury. The risk and severity increase with age: in the third decade of life, the risk is 0.3% and it increases to 2% or higher after age 50. Halothane-related hepatitis in the elderly has been shown to be associated with a markedly increased mortality. Similarly, non-steroidal anti-inflammatory drugs are associated with an age related increase in frequency and severity of hepatic drug reactions. Drugs like alpha-methyldopa, dantrolene and benazoprofen too are associated with more severe liver damage with increasing age; whether this increase is related to accumulation of a drug metabolite, is mediated by Immunologic mechanisms or is due to some other age-related factor remains unknown. Other drugs commonly used in the elderly and associated with liver injury include antibiotics (sulfonamides, penicillin, erythromycin , tetracycline, ketoconazole, nitrofurantoin), oral hypoglycemics, psychotropic drugs (chlorpromazine and tricyclic antidepressants), anticonvulsants (diphenylhydantoin), estrogens, anabolic steroids, antineoplastic drugs and anesthetic agents.

With the exception of acetaminophen hepatotoxicity there is little effective treatment for drug induced liver disease. Hence the strategy is prevention and early detection of liver injury as well as prompt withdrawal of offending agent. The overall incidence of adverse hepatic reactions can be minimized only through avoidance of overuse of these drugs. Similarly, polypharmacy should be avoided where possible.

Check Your Progress 2

1) Fill in the blanks:

   a) Cause of amoebic liver abscess is ..... .

   b) Drug of choice in amoebic liver abscess is ..... .

   c) Hydatid disease of liver is caused by ..... .

   d) Diagnosis of hydatid disease is confirmed by ..... .

2) Name drugs causing hepatotoxicity in elderly.

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3.6 CIRRHOSIS AND PORTAL HYPERTENSION

You will understand the problems relating to cirrhosis if you know that clinically diagnosed cirrhosis signifies advanced disease. When symptoms occur, usually the structural changes of liver damage are so great that satisfactory recovery cannot be obtained.

Cirrhosis as you know is the end result of many disorders of the liver. These disorders are listed below in Table 3.4.

Table 3.4: Disorders Resulting in Cirrhosis

ı Toxic injury (alcohol)
ı Infection (viral)
ı Malnutrition
ı Biliary obstruction
ı Cardiac failure
ı Metabolic injury
ı Unidentified injury (Cryptogenic)

Whatever may be the cause the result is similar because liver's response is limited. There is hepatic cell destruction, regeneration, formation of connective tissue and distortion of architecture. These are changes of cirrhosis. You must note the clinical findings in establishing cirrhosis. These are ascites, jaundice, portal hypertension, oesophageal and gastric varices, neurological symptoms progressing to coma. There are two life threatening risks. These are bleeding from varices and hepatic coma. Your management of these requires skill and judgement.

You know already that haemorrhage from oesophagogastric varices is a major life threatening emergency. The cause of this high mortality is not only blood loss but also because the disease is already in advanced stage and there may be associated factors like:

- Electrolyte imbalance
- Defects of coagulation
- Nutritional deficiencies
- Risk of coma from blood in the gut
- Risks associated with emergent management.

Treatment of bleeding requires that you have to consider risks versus benefits in a high risk patient. Goals and principles of management are given in Table 3.5. Your patient is usually a high risk case with advance liver disease and significant blood loss. In such a case, operation is risky and further bleeding is even more risky. The question of timing is therefore very important when you are faced with a high risk subject and you have to plan on major operation under from ideal conditions. Poor caval shunt reduces incidence of bleeding but does not influence the course of cirrhosis.

Table 3.5: Goals and Principles of Managing Variceal Hemorrhage

Goals of Management

- Prevent first bleed
- Control acute bleeding
- Prevent recurrent bleeding

Principles of Management

- Reduce portal pressure
  - Pharmacologic therapy
  - Surgical or interventional (TIPS) shunts
- Local control/obliteration of varices
  - Balloon tamponade
  - Endoscopic sclerotherapy
  - Endoscopic ligation/banding
  - Surgical devascularization (transection, Sugiura procedure)

Hepatic Coma

You might have seen patients of hepatic coma in the wards. Patients with advanced liver disease may have cerebral dysfunction. There may be mild personality disorder, confusion, disorientation, stupar and finally coma. Due to liver destruction, large amounts of portal blood reach general circulation without passing through liver. This causes cerebral intoxication from unmetabolised blood direct from intestine reaching general circulation. Ammonia resulting from intestinal bacterial action on nitrogenous material disrupts metabolic cycles of CNS. Disturbances of carbohydrates, aminoacids, fat, electrolyte metabolism, acid/base balance may also be important in producing coma.

When a patient presents with bleeding, you have to find the source of bleeding. Even if the patient has signs of cirrhosis, the bleeding may not be from varices. The patient may have gastritis, peptic ulcer or gastric tumours. Expert and immediate endoscopy if available should be used for confirming the diagnosis.

Emergency treatment includes control of bleeding and supportive therapy. Ample fresh blood/fresh frozen plasma is needed. Patient may be referred if facilities are not available.

To control bleeding skill experience and judgement is needed.

a) You may control bleeding by Tamponade by Sengstaken-Blakemore tube (complication risk—air way obstruction, regurgitation, aspiration, pneumonia, oesophageal tear rupture).

b) Oesophagogastric cooling with hypothermic apparatus.

c) Vasopressin (Pitresin) IV 20-30 units in 5% glucose in 10-15 minutes. To be repeated after 1-2 hours (causes abdominal cramps and diarrhoea in some). It is associated with risks in coronary disease because it is a vasoconstrictor. It can be given in very small amounts directly into superior mescentric artery under angiographic control.

d) Ligation of transoesophageal varices.

e) Portacaval shunt.

Coma can be precipitated by:

- Excessive intake of protein/ammonia salts
- Massive haemorrhage in the gut
- Diuretics: Chlorothiazide
  Acetozolamide
- Potassium depletion
- Acute infections
- Surgical operations (Therapeutic procedures adding metabolic burden).
- Paracentesis
- Azotemia
- Morphine.

Best treatment is early recognition (of toxicity) and its treatment to avoid rapid deterioration leading to death. Warning state is brief in fulminating hepatitis but if you are alert you could recognise early danger signals i.e. slight changes in personality and behaviour slurred speech, and diminished mental acitivity. Confusion and restlessness should not be treated with a sedative because it can lead to coma and death.

3.7 LIVER TUMOURS

Primary malignant tumours of the liver occus in adults and elderly, however hepatic metastaris are more common.

3.7.1 Primary Liver Cancer

The incidence of hepatocellular carcinoma generally rises progressively with age although it tends to level off in the oldest age groups. Hepatocellular carcinoma (HCC), is the most common primary liver malignancy in adults in general, and in the elderly in particular. It is more common in Asia and sub-Saharan Africa and is about 2 to 7 times more common among men than women in different populations. Its increased incidence among the elderly is related mainly to its occurrence in patients with long standing cirrhosis. The higher prevalence rate in the developing world is related to a higher prevalence of chronic HBV and HCV infections, which predispose the development of this cancer.

When far advanced, hepatocellular carcinoma usually presents with typical symptoms of anorexia weight loss, abdominal pain and signs of cirrhosis. In the elderly, particularly it manifests with underlying cirrhosis investigations. In some cases, the clinical features are attributable directly to HCC; abdominal pain, right upper quadrant abdominal mass, friction rub or a bruit over the liver, blood tinged ascites, etc. may be present. The occasional patient may present with paraneoplastic manifestations like erythrocytosis, hypercalcemia, hypoglycemia, hypercholesterolemia, fever, etc. In most cases, diagnosis is made by imaging studies like US, computed tomography (CT) and magnetic resonance imaging (MRI), which reveal a single or multiple focal space occupying lesions in the liver. Diagnosis is confirmed by fine needle aspiration cytology (FNAC) or biopsy of liver lesions. The presence of increased serum alpha-fetoprotein levels is a useful adjunct for diagnosis and may be the major confirmatory evidence in patients in whom FNAC and biopsy are not possible.

The treatment options for hepatocellular carcinoma include : i) surgical resection which offers the best chance for cure but seldom is possible when disease is symptomatic; ii) liver transplantation may be useful in selected patients; iii) alcohol injection is the palliative therapy for small and multiple tumours that cannot be resected; iv) chemoembolization is used to shrink large tumours to the point where they become resectable; v) chemotherapy is again palliative and can be used as an adjunct to surgical resection and transplantation. The

usual life span of these patients after diagnosis is 3-6 months. Surgical resection, whenever possible, offers the best chance of cure. Unfortunately, however, most tumors are already unresectable at the time of diagnosis because of the multifocal nature of the disease and co-existent cirrhosis of the liver, and hence a poor liver reserve. Bony metastases are also more common in older patients.

3.7.2 Metastatic Liver Tumours

The liver is the most frequent site for metastatic spread of tumours. Hepatic metastases commonly originate from primary sites in the portal system. Outside this site, the lung and the breast are the most common organs of origin. Metastatic tumours of the liver rank second to cirrhosis as a cause of liver disease among the elderly.

Symptoms and signs are usually related to the primary tumour. In many patients, however, the primary tumour may be asymptomatic and clinical presentation is primarily hepatomegaly, anorexia and weight loss. Diagnosis is made with the help of Ultrasound or CT, which usually reveal multiple space-occupying lesions in the liver, and is further confirmed by guided fine-needle aspiration cytology. At times it is difficult to distinguish a primary liver tumour from metastatic liver tumour. Metastases usually present with multiple small lesion, whereas primary liver cancers often have one dominant large mass with multiple small satellite nodules. The presence of clinical or laboratory features suggestive of liver cirrhosis tends to favour a diagnosis of primary liver tumour.

The extent of replacement of liver tissue by metastases generally determines the patient's prognosis. Successful treatment is possible in a minority of patients only. Most metastatic tumours represent an advanced stage of disease, have poor prognosis and respond poorly to all forms of treatment. Treatment is at best palliative. Occasionally surgical resection may be possible if metastases are limited to one lobe of the liver and Diseases of the gallbladder and bile ducts.

Check Your Progress 3

1) What is cirrhosis of liver?

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2) What are the clinical features of cirrhosis of liver?

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3) Enumerate two life threatening complications of cirrhosis of liver.

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4) What is hepatic coma? Enumerate risk factors responsible for coma.

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5) Which is most common primary malignancy of liver?

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6) Which is useful adjunct for diagnosis of carcinoma besides FNAC?

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7) Enumerate treatment options for hepatocellular carcinoma.

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8) What are the common causes of Metastasis in liver?

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3.8 PHYSIOLOGY OF BILE PRODUCTION AND FLOW

Bile formed in the hepatic lobules is secreted into a complex network of canaliculi, small bile ductules, and larger bile ducts that run with lymphatics and branches of the portal vein and hepatic artery in portal tracts situated between hepatic lobules. The total daily basal secretion of hepatic bile is approximately 500 to 600 ml. The primary bile acids, cholic acid and chenodeoxycholic acids, are synthesized from cholesterol in the liver, conjugated with glycine or taurine and excreted into the bile. Secondary bile acids including deoxycholate and lithocholate are formed in the colon as bacterial metabolites of the primary bile acids. The

normal capacity of the gall bladder is 30 to 75 ml of bile. In elderly, there is a decrease in the fasting volume of gall bladder as well as decreased contractility of gall bladder.

3.9 DISEASES OF THE GALL BLADDER

The gall bladder and bile ducts are most commonly affected by two disorders i.e. stones and inflammation.

Gall Stones

Gall stones are crystalline structures formed by concretion or accretion of normal or abnormal bile constituents. These stones are divided in to three major groups. Cholesterol and mixed stones account for 80% of the total with pigment stones comprising the remaining 20%. The important mechanisms in the formation of lithogenic bile are : increased biliary secretion of cholesterol, reduction in bile acids pool, defective micelle formation, nucleation of cholesterol monohydre crystals and hypomotility of the gall bladder. Hence, the sequence of events is saturation of bile with cholesterol, nucleation followed by biliary sludge formation and subsequently gallstone formation. The most specific and characteristic symptom of gallstone disease is biliary colic. Ultrasound of the gallbladder is very accurate in the identification of cholelithiasis. In asymptomatic gallstone disease no treatment is required. Laparoscopic cholecystectomy has become the gold standard for treating symptomatic cholelithiasis. In patients who are unfit for surgery, gallstone dissolution therapy in the form of ursodeoxycholic acid is given. The best results are seen in patients with small (< 5 mm) floating radiolucent stones.

Cholecystitis

Inflammation of the gall bladder (cholecystitis) could be acute chronic or emphysematous. Acute inflammation of the gallbladder wall usually follows obstruction of the cystic duct by a stone. It often begins as an attack of biliary colic that progressively worsens. Deep inspiration or cough during subcostal palpation of the right upper quadrant usually produces increased pain (murphy's sign). Ultrasound demonstrates gall bladder thickening with presence of gall stones.

Emphysematous Cholecystitis

This condition occurs most frequently in elderly men and in patients with diabetes mellitus. This condition begins with acute cholecystitis followed by ischaemia and gangrene of the gallbladder wall and infection by gas producing organisms. Treatment involves prompt surgical intervention coupled with appropriate antibiotics.

Chronic Cholecystitis

Chronic cholecystitis is due to persistent mechanical irritation of the gallbladder wall by gallstones. Chronic cholecystitis may be asymptomatic for years and may progress to acute cholecystitis or symptomatic gall stones disease.

3.10 DISEASES OF THE BILE DUCTS

Under this section, you will learn about common bile duct stones, biliary parasites and sclerosing colangitis.

Common Bile Duct Stones

Passage of gallstones into the CBD occurs in approximately 10-15% of patients with cholelithiasis. The incidence of common bile duct stones increases with increasing age of the patient so that upto 25% of elderly patients may have calculi in the common duct at the time of cholecystectomy. Cholangitis and obstructive jaundice are complications of these stones. They may also produce acute pancreatitis. The diagnosis is made by endoscopic retrograde cholangiography. This procedure also facilitates removal of CBD stones.

Biliary Parasites

The biliary tract may be involved by intraductal migration of adult Ascaris lumbricoides from the duodenum or by intra biliary rupture of hydatid cysts of the liver produced by Echinococcus species. The diagnosis is made by cholangiography and the presence of characteristic ova on stool examination.

Sclerosing Cholangitis

This is a disorder characterized by progressive, inflammatory, sclerosing and obliterative process affecting the extrahepatic and often the intrahepatic bile ducts. These patients present with symptoms of chronic or intermittent biliary obstruction. Ursodeoxycholic acid is the drug of choice.

3.11 TUMOURS OF BILIARY TRACT

3.11.1 Carcinoma of Gall Bladder

The two common conditions encountered in the elderly are: Carcinoma of gall bladder and cancer of extrahepatic biliary duct.

Gall bladder cancer has a median age of diagnosis of 70 years with a female predominance of 3-5:1. It presents as obstructive jaundice. The patient has abdominal pain, a GB mass palpable and jaundice with pruritus and cholestasis. Diagnosis is by ultrasound and a fine needle aspiration cytology. The treatment depends upon the extent of spread, presence of hepatic metastases and functional status of the patient. The only curable lesions are those removed incidentally during cholecystectomy. In 90% of the cases the diagnosis of cancer of the gall bladder is made after the tumour has become unresectable. The treatment is either resection with surgery or palliative. Palliative therapy involves placement of endoscopic placement of biliary prosthesis to drain bile ducts. Age by itself is not a contraindication to the extent of surgical resection and the risks of surgery are determined by the stage of tumour and the coexisting illnesses.

3.11.2 Extrahepatic Bile Duct Cancer

Cholangiocarcinoma is a disease of the elderly, with a median age of presentation between 60-65 years.The distribution of cholangiocarcinoma in the elderly is not different from the younger patients. The patient presents with pruritus and obstructive jaundice. Surgical resection is possible only in less than 50% of cases and if palliative treatment is required then endoscopic placement of stents is done.

Ampullary cancer also presents with obstructive jaundice and is the most amenable to surgical therapy. In presence of metastases, endoscopic pallliative therapy is done.

Check Your Progress 4

1) Enumerate types of gall stones.

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2) What are the mechanisms of formation of gallstones?

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3) What are the features of emphysematous cholecystitis?

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4) How will you diagnose the presence of stones in common bile duct?

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3.12 DISEASES OF PANCREAS

Pancreas is situated posteriorly in the upper abdomen and produces an external secretion – pancreatic juice and an internal secretion – insulin. The head of the pancreas lies within the duodenal loop in close approximation. The common bile duct passes through the head of pancreas. Being deeply placed, the lesions of the pancreas may remain without producing clinically demonstrable local physical signs for long periods.

Inflammation of the pancreas may be acute or chronic, its incidence varies in different states. It is usually associated with alcoholism, biliary tract disease trauma, infections, metabolic disorders, connective tissue disorder, tumour, pancreatic duct obstructions and with certain drugs.

3.12.1 Acute Pancreatitis

It results from autodigestion of the pancras by its own enzymes. The proenzymes are activated as a result of inection, trauma, or toxins, or by the chemical substances in the bile. Obstruction to ampulla by tumor, spasm or enchanced secretion by the gland as in alcoholism may lead to pancreatitis as a result of disruption of the ducts. The digestion of the tissue causes oedema, haemorrhage, vascular damage, coagulation necrosis and fat necrosis. The two most commonest causes of actue pancreatitis are cholilithiasis and alcoholism. Aetiology is obscure in about 30 percent of patients.

Clinical Features

The onset is suaully sudden with pain in the upper abdomen and may radiate to the chest, precordium, back or lower abdomen. It often precipitated by a large meal or a bout of alcohol. The patient adopts a stoping posture with pressure on the abdomen to get relief. Pain is often accompanied by nausea, and vomitting and later by abdominal distension. In severe cases, three may be features of paralytic ileus, hypotension and shock. Rigidity and guarding of the upper abdomen develop later in the stage of the disease. Mild jaundice may be seen in few cases. Mild to moderate fever, tachycardia, ascitis, pleaural effusion may appear. Presence of bluish discolorations around the umbilicus or on the flanks indicate a severe form of the disease. A mass in the epigastric region due to pseudo-cyst may be felt. prognosis is very poor in older age group.

Serum amylase estimation is the most important test in the diagnosis of acute pancreatitis (levels greater than 130u/l) and value more than three times the normal vitually clinch the diagnosis. lately the serum lipase and trypsin level is the best measurement for diagnosis of acute pancreatitis.

Leucocytosis is common and haematocrit values are raised in early stages. Raised glucose level in blood and low calcium level also may be observed in severe pancreatitis. Serum bilirubin (4.0 mg/dl) occurs in 10% of the cases.

Plain X-ray abdomen might show biliary or pancreatitic calculi, absence of gas in transverse colon and also helps to exclude perforation of the bowel. Ultra sonography, CT Scan and MRI will confirm the diagnosis and also helpful in assessing the severity of the acute pancreatitis.

Treatment

First step in the treatment is to correct fluid and salt balance and haemoconcentration. I.V. saline and plasma should be given at once and to be monitored by the pulse rate, blood pressure and urinary output, hypocalcemia is corrected by the administration of calcium gluconate. I.V. Anagesics like methadone 10 mg or pethidine 100 mg are given to relieve the pain. In severe cases, Morphine 10-20 mg combined with atropine 0.5 mg or propantheline bromide 15-30 mg may be given. Anthicholinergic drugs are not indicated.

Broad spectrum antibiotics (Carbapenem group of antibiotic) are given to treat the secondary infection. Oral feeding is avoided in acute stages. Food is gradually introduced when condition subsides. In the presence of biliary stones or other obstructive lesions, surgery may be carried out to prevent relapse of pancreatitis. The severity of the pancreatitis is usually assessed by the prognostic signs enumerated in the table given below :

Table 3.6 : Factors adversely affect the survival

At admission or diagnosis
ı Age over 60 years
ı Leucocyte count over 16,000/mm^3
ı Blood glucose over 300 mg/100 ml
ı Serum lactic dehydrogenase (LDH) over 500 IU/L
ı Serum AST level more than 250 IU/L
During initial 48 hours
ı Haematocrit fall greater than 10% points
ı Blood urea rise more than 100 mg/dl
ı Serum albumin level less than 2.0 g/dl
ı Arterial PO_2 below 600 mm Hg
ı Base Deficit more than 4 meq/l
ı Estimated fluid sequestration more than 600 ml
ı Haemorhagic peritoneal fluid
ı Blood pressure <90 mm Hg or tachycardia >130 Beats/mt

3.12.2 Chronic Pancreatitis

It is characterised by continuing inflammatory disease of the pancreas, accompanied by irreversible morphological change and typically causing pain and/or permanent loss of function. Sometime acute exacerbation may occur and pain might be absent.

The commonest cause of chronic pancreatitis is Alcoholism. About 30% of cases are associated with gall bladder disease and infections spreading up the pancreatic duct. Abdominal surgery, trauma, stenosis or stricture of the sphincter of oddi are other causes of chronic pancreatitis. In certain proportion of patients, 25-40% no aetiological factor can be demonstrated and this group is termed as "idiopathic".

Clinical Features

It presents with recurrent upper abdominal pain following excess meal or a bout of alcohol. It is usually present in epigastric region, persistent and radiate to the back with pertial relief in

squating posture. It is usually of gradual onset and may be continuous or intermittent and may at times atypically located. Vomiting or analgesics may fail to relief the paint. In 10-20% cases, the disease may be asymptomatic. Anorexia, weight loss and diarrhoea are common. Frank steatorrhoea occurs in 20-35% of the patients over diabetes develop in 1/5th of the cases.

Except for vague tenderness over the epigastrium, physical examination may reveal palphable mass in the epigastrium indicative of pseudocyst or pancreatic abscess. Occassionally jaundice may occur due to obstruction to the common bile duct from a pseudocyst or malignancy. Ascites may also develop.

Serum amylase and lipase values are not helpful. Elevation of serum bilirubin and alkaline phosphatase level may indicate cholestasis secondary to chronic infection around the common bile duct. Stool fat estimation help to confirm steatorrhoea. Plain X-ray abdomen, demonstrate the presence of pancreatic calculi. Ultrasonograpnhy, CT Scan and MRI are useful to confirm the diagnosis.

Treatment

Abstinence from alcohol and smoking may improve the prognosis. The main objectives of the treatment are relief of pain, treatment of diabetes mellitus and steatorrhoea, maintenance of adequate nutrition and prevention and treatment of complications.

Analgesics include pentazocin, dextropropoxyphene or pethiddine are useful in relieving the pain. Reduction of dietary fat to 20-30g/day helps to reduce the abdominal discomfort and relieve steatorrhea. Diagnosis can be aided by the administration of pancreatic enzyme or enzymes derived from fungal or other plant sources given orally after food. Pancreatic extract (Pankereon, pancreatin) are useful which have to be given with meals to help in digestion corrects the steatorrhea and also emebiorates the pain.

In uncomplicated cases of chronic pancreatitis, the only indication for surgery is severe, persistent or recurrent pain. Other indications are complications such as psedocyst, pancreatic ascites, jaundice, pancreatic abscess or pancreatic malignancy.

3.12.3 Pancreatic Malignant Tumours

Primary cancer of the pancreas may occur in 60-70 years age group and is common in males. The head of the pancreas is usually affected but the disease sometimes starts from the body or tail.

Clinical Features

Pancreatic cancer has an insiduous onset and is usually missed in the early stages. Jaundice appears earlier with periampullary cancer and cancer of the head. Vague abdominal discomfort and loss of weight may be the early symptoms. Jaundice is usually progressive and accompanied by intractable itching, clay coloured stools, and dark coloured urine. Pain occurs in the epigastrium and is constant and decreased by sitting up initially and is associated with anorexia, nausea, vomitting, progressive dyspnoea, weakness and loss of weight.

Palpable lump in the epigastrium indicates the possibility of carcinoma. A firm liver with secondary nodules indicates advance stage of the disease. Diabetes is common with a growth in the body and tail of the pancreas. Ascites is a terminal feature.

Diagnosis is made by derainged liver function tests indicative of obstructive jaundice. Barium meal studies are helpful when cancer involves the head of the pancreas. CT Scan, MRI have now proved to be useful modalities in the diagnosis of malignancy of gastro-intestinal tract. Endoscopic retrograde cholangio-pancreatography (ERCP) and percutaneous trans hepatic cholangio-graphy (PTC) are useful to distinguish cancer from stones or strictures.

Treatment

Symptomatic and pallitative. Various ‘by-pass’ procedures are done to reduce jaundice. A radical pancreatoduodenectomy is done if the growth is at the distal end of the pancreas. Survival rate is less than one year.

Check Your Progress 5

1) What are the causes of pancreatitis?

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2) Enumerate salient clincal features of acute pancreatitis.

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3) Name the newer imaging modalities which are helpful in arriving at diagnosis.

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4) What is the value of stool fat estimation in a case of chronic pancreatitis?

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5) What is the indication of surgery in uncomplicated case of chronic pancreatitis?

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6) Mention clinical feature in a case of primary cancer of pancreas.

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7) What is the value of ERCP and PTC in diagnosis of pancreatic tumour?

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3.13 LET US SUM UP

Liver size and weight show a marked reduction with advancing age The liver function tests including serum bilirubin, transaminases (SGOT/SGPT),serum alkaline phosphatase do not alter with age. Viral hepatitis, protozal infections and pyogenic infections of the liver lead to a more severe disease in the elderly and the prognosis is also worse as compared to the young. The elderly are more prone to drug induced liver disease. HCV cirrhosis is commonly seen in the elderly. The mortality due to variceal bleed is higher in the elderly. Metastasis of liver is more common than hepatocellular carcinoma in the elderly. Gallstones are the most predominant of all diseases of the biliary tract. Their incidence increases steadily and persistently with advancing age. Cancer of gallbladder is the commonest biliary tumor affecting the aged and it presents with obstructive jaundice.

Inflamation of the pancreas may be acute or chronic. It is usually associated with alcoholism, bilary tract disease, trauma, infections, metabolic disorders and tumours etc. Pancreatic tumour is usally associated with progressive jaundice and palpable lump in the abdomen is poor.

3.14 KEY WORDS

Fulminant hepatic failure : Acute liver failure with main presentation as encephalopathy and jaundice within 4 weeks of the onset of prodromal symptoms and in absence of preexisting liver disease.

Hepatoxicity : Liver injury caused by drugs and other chemicals

Cirrhosis : Irreversible damage to hepatic architecture

Poral hypertension : Increased resistance to portal blood flow at various sites in the liver (pre-sinusoidal, simsoidal or post- sinusoidal).

3.15 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) The important transminases are SGOT and SGPT. These are raised in Hepatitis due to viral, autoimmune, toxic and ischaemic causes.

2) Hepatitis B virus (HBV) belongs to hepadna-viridae family (DNA virus). It is transmitted by blood or blood products, sexual contact or perinatal exposure.

3) Antiviral agents used are Interferon alpha and lumivudine.

4) The infection is self-limiting and has a benign course and supportive care is the corner stone of the therapy.

Check Your Progress 2

1) a) Entamoeba histolitica

   b) Metronidazole

   c) Cystic stage of tapeworm (Echinococus granulosus)

   d) Casoni Test

2) Drugs causing hepatotoxicity are

   – Isoniazid

   – NSAID

   – Nitrofurantoin

Check Your Progress 3

1) Cirrhosis of liver is characterised by hepatic cell destruction, regeneration, formation of connective tissue and distortion of liver architecture.

2) The clinical features are ascites, jaundice, portal hypertension, oeseophageal and gastric varices, neurological symptoms progressing to coma.

3) Two life threatening complications are bleeding, oesophageal varices and hepatic coma.

4) Hepatic coma is the result of liver cell failure and is characterised by mild personality disorder, confusion, disorientatin, stupor and finally unconsciousness. The risk factors include passage of portal blood goes to general circulation without passing through liver and unmetabolised blood causes cerebral intoxication. Ammonia is another intoxicant absorbed from intestine and causes dysfunction of CNS metabolism. Electrolyte metabolism and acid/base balance may also play important role in producing coma.

5) The most common primary liver malignancy of liver is Hepatocellular Carcinoma (HCC).

6) The presence of increased serum alpha-feto-protein levels is a useful adjunct for diagnosis of carcinoma besides FNAC or biopsy of liver.

7) The treatment options include 1) Surgical resection, 2) Liver transplantation, 3) Alcohol injection for small and multiple tumours that cannot be resected, 4) Chemoembolization, and 5) Chemotherapy.

8) The common causes are 1) Hepatocellular carcinoma, 2) Lung cancer, 3) Breast cancer.

Check Your Progress 4

1) Gall stones are crystalline, structures and are of three types viz., cholestrol, pigment stones and mixed stones.

2) The important mechanisms in the formation of stones are: 1) Increased biliary secretion of cholestrol, 2) Reduction in the bile acids pool, 3) Defective micelle formation, 4) Nucleation of cholestrol monohydrate crystals and hypomotility of the gall bladder.

3) It is characterised by acute manifestations of Inflammation of gall bladder followed by ischaemia and development by gangrene of gall bladder wall by gas producing organisms.

4) The presence of stones is made by endoscopic retrograde cholangiography (ERCP).

Check Your Progress 5

1) The comon causes includes alcoholism, biliary tract disease, cholilithiasis, trauma, viral infections, metabolic disorders including connective tissue disorder, tumour and certain drugs.

2) The salient clinical features include sudden onset of pain in upper abdomen, radiate to chest, precordium and back often aggravate by heavy meals and a bout of alcohol. Pain accompanied by nausea, vomitting and features of paralytic ileus, hypotension and shok. Rigidity and guarding may develop in later stages. Sometimes a mass can be felt in upper abdomen.

3) Ultra sonography, CT Scan and MRI are the newer modalities to arrive at diagnosis besides the presence of raised serum amylase lvel.

4) Stool fat estimation helps in confirming the presence of steatorrhoea in a case of chronic pancreatitis.

5) The only indication of surgery in uncomplicated case of chronic pancreatitis is severe, persistent or recurrent pain. Other indications ar pseudocyst, jaundice, pancreatic abscess or pancreatic malignancy.

6) Primary cancer of pancreas is associated with vague abdominal discomfort, weight loss and jaundice which is progressive in nature, accompanied by intractable itching. Palpable mass may be felt in the epigastrium.

7) ERCP (Endoscopic retrograde cholangio-pancreatography) and PTC (Percutaneous trans-hepatic cholangiography) are helpful to differentiate carcinoma from stones or stricture.

3.16 FURTHER READINGS

Fauci, Braunwald, Isselbacher, *et al., Harrison's Principles of Internal Medicine,* 14th edn., International edition McGraw Hill Publishers, 1998.

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