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Causes& Management of Postoperative Jaundice

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- **ACE:** Angiotensin converting enzyme.
- **ALT:** Alanine tranasaminase.
- **ASA:** American society of anaestheologists.
- **AST:** Aspartate transaminase.
- **ATP:** Adenosine triphosphate.
- **BMJ:** British Medical Journal.
- **CBD:** Common bile duct.
- **CPDA:** Citrate-phosphate-dextrose-alanine.
- **CT:** Computerized tomography.
- **CTP:** Child-Turcotte-Pugh.
- **ETOH:** Ethyl alcohol.
- **ERCP:** Endoscopic retrograde cholangiopancreatography.
- **GGT:** Gamma glutamyl tranferase.
- **HABF:** Hepatic artery blood flow.
- **HMG-CoA:** Hydroxy-methyl-glutaryl coenzyme A.
- **IBDI:** Iatrogenic bile duct injuries.

- **IL:** Interleukin.
- **INR:** International normalized ratio.
- **LC:** Laparoscopic cholecystectomy.
- **MAC:** Minimum alveolar concentration.
- **MAP:** Mean arterial pressure.
- **MARS:** Molecular adsorbent recirculating system.
- **MELD:** Model for end stage liver disease.
- **MODS:** Multi-organ dysfunction syndrome.
- **MRCP:** Magnetic resonance cholangiopancreatography.
- **NADP:** Nicotinamide adenine dinucleotide phosphate.
- **NSAIDs:** Non-steroidal anti-inflammatory drugs.
- **PBF:** Portal blood flow.
- **PMNs:** Polymorph nuclear leukocytes.
- **PN:** Parenteral nutrition.
- **PSE:** Portosystemic encephalopathy.
- **PT:** Prothrombin time.
- **PTC:** Percutaneous transhepatic cholangiography.
- **RBC:** Red blood cell.

- **THBF:** Total hepatic blood flow.
- **TIPS:** Transjugular intrahepatic portosystemic shunt.
- **TMP-SMZ:** Trimethoprim- sulfamethoxazole.
- **TNF:** Tumour necrosis factor.
- **TPN:** Total parenteral nutrition.

Introduction

Postoperative jaundice is one of the main concerns of many anaestheologists allover the world. It can occur during the immediate postoperative period up to multiple weeks postoperatively according to the cause. Postoperative jaundice is multifactorial &it may present itself in many clinical forms. So, a good understanding of liver functions which in turn leads to understanding the pathophysiolgy of jaundice is quite important for establishment diagnosis& good management of this critical postoperative condition **(Faust and Reddy, 2004).**

Liver Functions

The liver conjugates bilirubin, produced from the degradation of the haemoglobin of red cells that are at the end of their normal life span. This now water-soluble form of bilirubin is then excreted into the bile ducts and thence into the small intestine. Also passed to the gut are the bile salts produced by the liver and necessary for the absorption of the fat-soluble vitamins A, D, E and K. Vitamin K is essential for the production of prothrombin and some other protein factors that are essential for the normal clotting of blood. Synthesis of many proteins takes place in the liver including most clotting factors and many carrier proteins, such as albumin, which to a varying degree bind drugs used during anaesthesia. The liver is also central in lipid metabolism with cholesterol and triglycerides synthesised here. The synthesis and breakdown of glycogen in the liver is pivotal in carbohydrate metabolism. It stores glycogen and releases glucose into the blood when the blood glucose falls for any reason. The liver is also responsible for the biotransformation of drugs either by oxidation or conjugation in order to render them water-soluble and therefore more easily excreted in the urine or bile **(Cotran et al., 2004).**

The term jaundice refers to the yellowish discolouration of skin, sclera, and mucous membranes that results from excessive deposition of bilirubin in tissues. It is generally held that jaundice develops when serum bilirubin levels rise above 2 mg/dl (34.2 μmol/L) ; however, the

appearance of jaundice also depends on whether it is conjugated or unconjugated bilirubin that is elevated and on how long the episode of jaundice last **(Sleisenger and Fordtran, 1998).**

Jaundice can be prehepatic (haemolytic), hepatic (hepatocellular) or posthepatic (obstructive) in origin. An example of prehepatic jaundice is in the haemolysis that accompanies the breakdown of a large haematoma, or the jaundice that can occur when there is a massive intravascular haemolysis - as in some forms of malaria or in sickle cell anaemia. In these situations the hepatocellular function is normal but overwhelmed and so the increased bilirubin is for the most part unconjugated. Protein and carbohydrate metabolism is intact and there is no reduction in the absorption of Vitamin K or production of clotting factors. Hepatic (hepatocellular) jaundice refers to jaundice that is caused by actual hepatocellular dysfunction, as in hepatitis or cirrhosis, there may be evidence of decreased protein synthesis, with oedema and ascites, signs of delayed clotting only partly reversed by vitamin K administration, and even hepatic encephalopathy. Obstructive (posthepatic) jaundice is the most likely cause of jaundice to be encountered by the anaesthetist in many parts of the world. It can result from a stone in the common bile duct, pancreatic tumour or ascending cholangitis where the bile and biliary tree are infected. Hepatocellular function is normal (although it may deteriorate in prolonged obstruction) so the excess plasma bilirubin is chiefly conjugated. As conjugated bilirubin is water-soluble it will be excreted in the urine which becomes dark. Stools are pale as a result of poor lipid absorption. Although protein synthesis is normal, the production of vitamin K dependant clotting factors will be reduced, as the absorption of vitamin K is dependent on the excretion of bile salts into the small intestine. The clotting time can, therefore, be prolonged but this can be readily reversed by parenteral administration of vitamin K. Surgery in these cases is to remove or bypass the obstruction or to drain infected obstructed bile **(Feldman et al., 2002).**

Postoperative jaundice can be prehepatic, hepatic, or posthepatic. So, once postoperative jaundice is detected clinically a diagnostic approach to evaluate the case& identify its cause is so important. This includes many laboratory& imaging techniques. For example, a predominantly conjugated bilirubin suggests an obstructive cause, while unconjugated bilirubin points to a prehepatic problem. Hepatic disease may result in a predominantly unconjugated or a mixed pattern. Dark urine containing bilirubin suggests biliary obstruction **(Faust and Reddy, 2004).**

Imaging techniques include a wide spectrum of varieties including ultrasonogrphy, CT scans& MRI. Imaging usually plays an important role when direct hyperbilirubinemia is attained. The goals of which are to confirm the presence of an extrahepatic obstruction (i.e., to verify that the jaundice is indeed posthepatic rather than hepatic), determine the level of the obstruction, identify the specific cause of the obstruction, and provide complementary information relating to the underlying diagnosis (e.g., staging information in cases of malignancy) **(Briggs and Peterson. 2007).**

Postoperative jaundice can be avoidable in many cases. A good preoperative evaluation for patients undergoing surgery especially those patients who are at risk (e.g. patients with a history of liver disease) is a milestone for prophylaxis of postoperative jaundice Careful preoperative risk assessment, patient selection, and management of various manifestations of advanced disease might decrease morbidity and mortality from surgery in patients with liver disease **(Del Olmo et al., 2003).**

Whenever postoperative jaundice is noticed, efforts should be directed towards identification of its cause, whether this cause is related to anaesthesia or is of surgical origin. A proper establishment of the cause is the road for a proper management of the condition. So, treatment of postoperative jaundice is usually treatment of the underlying cause **(Faust and Reddy, 2004).**

Anatomy of the Liver

The liver is the largest organ of the human body (Figure 1), weighs approximately 1500 g, and is located in the upper right corner of the abdomen. The liver is divided macroscopically into the right and left lobe by the falciform ligament anteriorly. Inferiorly, this corresponds to the round ligament and umbilical fissure. The right lobe is further divided by the gallbladder fossa into the right hemiliver to the right of the gallbladder and the quadrate lobe to the left. The fourth lobe (caudate) is posterior and surrounds the inferior vena cava. Hence, anatomically the liver is divided into two main lobes and two accessory lobes. The liver was divided into three functional livers: the right, the left and the caudate. The separation between the right and left hemiliver is at Cantlie's line, which is an oblique plane extending from the center of the gallbladder bed to the left border of the inferior vena cava. In this plane runs the middle hepatic vein, which is an important radiological landmark **(Northover and Terblanche, 1998).**

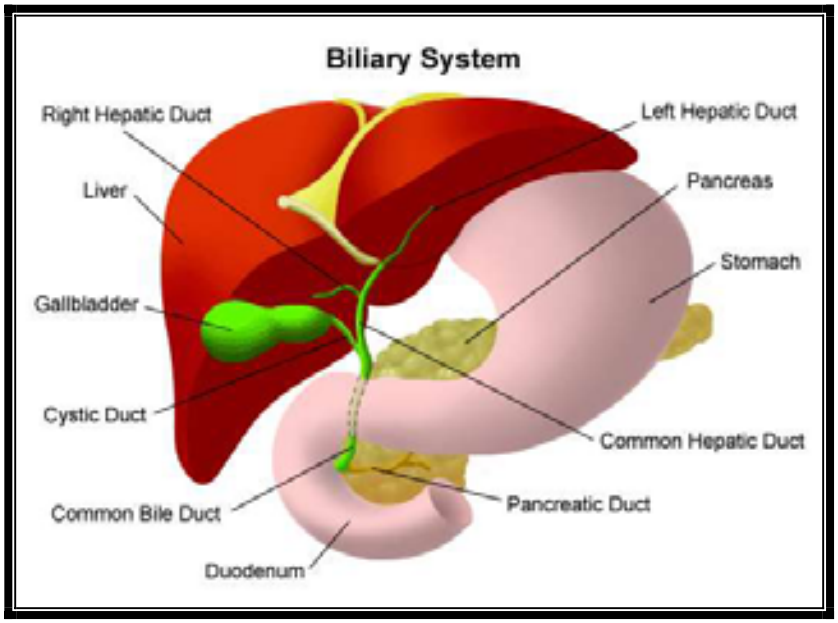

Fig.1. Liver, Pancreas, and Gall Bladder

(www.yalemedicalgroup.org)

Blood Supply and Venous Drainage

The arterial supply to the liver in early gestation life is from three main sources: the left hepatic artery from the left gastric artery; the middle hepatic artery (common hepatic artery) from the celiac trunk; and the right hepatic artery from the superior mesenteric artery. With further development, the blood supply assumes the adult pattern, with atrophy ofboth the right and left hepatic arteries and the common hepatic artery (middle hepatic) supplying the whole liver. It provides oxygenated blood at the rate of 400 to 500 mi/mm (about *25%* of the cardiac output). The hepatic portal vein, which receives deoxygenated blood from the inferior and superior mesenteric veins and the splenic vein, delivers about 1000 to 1200 mI/mm to the liver. Portal venous blood constitutes 70% of the blood supply to the liver. This blood carries some oxygen and is rich in nutrients that have been absorbed from the digestive tract **(Northover and Terblanche, 1998).**

Sinusoids

Sinusoids are the canals formed by the plates of hepatocytes. They are approximately 8-10 ¹m in diameter and comparable with the diameter of normal capillaries. They are orientated in a radial direction in the lobule. Sinusoids are lined with endothelial cells and Kupffer cells, which have a phagocytic function. Plasma and proteins migrate through these lining cells via so-called fenestrations (100-150 nm) into the Space of Disse, where direct contact with the hepatocytes occurs and uptake of nutrients and oxygen by the hepatocytes takes place. On the opposite side of the hepatocyte plates are the bile canaliculi situated (1 micrometer diameter). Bile produced by the hepatocytes empties in these bile canaliculi and is transported back towards the portal canal into bile ductiles and bile ducts, and finally to the main bile duct and gallbladder to become available for digestive processes in the intestine. The direction of bile flow is opposite to the direction of the blood flow through the sinusoids **(Cotran et al., 2004).**

Biliary Tree

a) Intrahepatic Bile Ducts

There are more than 2 km of bile ductules and ducts in the adult human liver. These structures are far from being inert channels, and are capable of significantly modifying biliary flow and composition in response to hormonal secretion. Bile secretion starts at the level of the bile canaliculus, the smallest branch of the biliary tree .They form a meshwork between hepatocytes with many anastomotic interconnection. The interlobular bile ducts form a richly anastomosing network that closely surrounds the branches of the portal vein. These ducts increase in caliber and possess smooth muscle fibres within their wall as they reach the hilus of the liver (**Mortelé and Ros, 2001).**

Furthermore, as they become larger, the epithelium becomes increasingly thicker and contains many elastic fibres. These ducts anastomose to form the segmental branches. These segmental branches anastomose together forming the right &left hepatic ducts. The right hepatic duct is usually short—approximately 9 mm in length. The left hepatic duct is generally longer and more surgically accessible than the right hepatic duct (**Sleisenger and Fordtran, 1998).**

b) Extrahepatic Bile Ducts

The right &left hepatic ducts unite to form the common hepatic duct. The accessory biliary apparatus, composed f the gallbladder and cystic duct, joins the common hepatic duct to form the common bile duct that drains bile into the duodenum. This comprises the extrahepatic biliary system. The confluence takes place at the right of the hilus of the liver, anterior to the portal venous bifurcation and overlying the origin of the right branch of the portal vein .The biliary confluence is separated from the posterior aspect of the liver by the hilar plate, which is the fusion of connective tissue enclosing the biliary and vascular structures with Glisson's capsule **(Lamah , 2001).**