OBSTRUCTIVE JAUNDICE- A review article

1. Introduction/Definition
Jaundice (derived from French word ‘jaune’ for yellow) or icterus (Latin word for jaundice) is a yellowish staining of the skin, sclera and mucous membranes by deposition of bilirubin (a yellow orange bile pigment) in these tissues.(1) Jaundice was once called the "morbus regius" (the regal disease) in the belief that only the touch of a king could cure it.
Jaundice indicates excessive levels of conjugated or unconjugated bilirubin in the blood and is clinically apparent when the bilirubin level exceeds 2mg/dl (34.2 μmol per L). It is most apparent in natural sunlight. In fact, it may be undetectable in artificial or poor light. In fair-skinned patients, jaundice is most noticeable on the face, trunk, and sclerae; in dark-skinned patients, it’s noticeable on the hard palate, sclerae, and conjunctivae. Pseudo jaundice may be found in black patients with pigmented sclera, from carotinemia, uremia (a sallow yellowish pallor), and quinacrine (a yellow-green color).
Causes of jaundice can be classified into pre-hepatic, hepatic or post hepatic.
In this review, our focus is on post hepatic causes of jaundice (obstructive or surgical cholestasis) as this is more relevant to surgeons.
Obstructive jaundice is not a definitive diagnosis and early evaluation to establish the etiology of the cholestasis is crucial to avoid secondary pathological changes (e.g. secondary biliary cirrhosis) if obstruction is not relieved.(2)
2. Surgical Anatomy of the Hepatobiliary system
An accurate knowledge of the anatomy of the liver and biliary tract, and their relationship to associated blood vessels is essential for the performance of hepatobiliary surgery because wide anatomic variations are common. The classic anatomic description of the biliary tract is only present in 58% of the population.(3)

The liver, gallbladder, and biliary tree arise as a ventral bud (hepatic diverticulum) from the most caudal part of the foregut early in the fourth week. This divides into two parts as it grows between the layers of the ventral mesentery: the larger cranial part (pars hepatica) is the primordium of the liver, and the smaller caudal part (pars cystica) expands to form the gallbladder, its stalk becoming the cystic duct. The initial connection between the hepatic diverticulum and the foregut narrows, thus forming the bile duct. As a result of the positional changes of the duodenum, the entrance of the bile duct is carried around to the dorsal aspect of the duodenum.(4)

The biliary system can be broadly divided into two components, the intra-hepatic and the extra-hepatic tracts. The secretory units of the liver (hepatocytes and biliary epithelial cells, including the peribiliary glands), the bile canaliculi, bile ductules (canals of Hering), and the intrahepatic bile ducts make up the intra-hepatic tract while the extra-hepatic bile ducts (right and left), the common hepatic duct, the cystic duct, the gallbladder, and the common bile duct constitute the extra-hepatic component of the biliary tree. (5;6)

The cystic and common hepatic ducts join to form the common bile duct. The common bile duct is approximately 8 to 10 cm in length and 0.4 to 0.8 cm in diameter. The common bile duct can be divided into three anatomic segments: supraduodenal, retroduodenal, and intrapancreatic. The common bile duct then enters the medial wall of the duodenum, courses tangentially through the submucosal layer for 1 to 2 cm, and terminates in the major papilla in the second portion of the duodenum. The distal portion of the duct is encircled by smooth muscle that forms the sphincter of Oddi. The common bile duct may enter the duodenum directly (25%) or join the pancreatic duct (75%) to form a common channel, termed the ampulla of Vater.

The biliary tract is supplied by a complex vasculature called the peribiliary vascular plexus. Afferent vessels of this plexus derive from hepatic arterial branches, and this plexus drains into the portal venous system or directly into hepatic sinusoids.

3. Physiology/Biochemistry of Bilirubin production and transport
Bile is a substance produced in the liver and contains bile salts, water, cholesterol, electrolytes, and bilirubin, which is a breakdown product of hemoglobin.

The formation of bilirubin from heme is essential for mammalian life, because it provides the body with the main means of elimination of heme. Eighty percent of the circulating bilirubin is derived from heme of hemoglobin from senescent red blood cells destroyed in the reticuloendothelium of the bone marrow, spleen, and liver. Ten to twenty percent of the bilirubin comes from other sources such as myoglobin, cytochromes, and other heme-containing proteins processed in the liver. Initially, heme is oxidized at the alpha position to the green pigment biliverdin, which is then reduced at the gamma position to bilirubin. Bilirubin is virtually insoluble in aqueous solutions. In blood it is reversibly but tightly bound to plasma albumin at a 1:1 ratio. Newly formed bilirubin is removed from the circulation very rapidly by the liver.
The processing of the serum bilirubin load by the hepatocytes occurs in four steps. These are: uptake, cytosolic binding, conjugation, and secretion. Hepatic uptake of bilirubin occurs with the dissociation of the albumin-bilirubin complex facilitated by plasma membrane proteins with subsequent translocation of bilirubin into the hepatocyte through a saturable protein carrier, which also binds other organic anions, but not bile salts. In the hepatocytes, bilirubin binds to two cytosolic proteins: ligandin and Z protein. The binding limits the reflux of bilirubin back to the plasma and delivers it to the endoplasmic reticulum for conjugation. Conjugation of bilirubin involves its esterification with glucuronic acid to form, first, a monoglucuronide, then a diglucuronide. The principal enzyme involved is uridine diphosphate (UDP)-glucuronyl transferase. Conjugation renders bilirubin water-soluble and is essential for its elimination from the body in bile and urine. Most of the conjugated bilirubin excreted into bile in humans is diglucuronide with a lesser amount of monoglucuronide. Secretion of conjugated bilirubin from the hepatocyte to the bile canaliculi involves a specific carrier and occurs against a concentration gradient. Conjugated bilirubin is excreted in bile, as a micellar complex with cholesterol, phospholipids, and bile salts, through the biliary and cystic ducts to enter the gallbladder, where it is stored; or it passes through Vater’s ampulla to enter the duodenum. Inside the intestines, some bilirubin is excreted in the stool, while the rest is metabolized by the gut flora into urobilinogens and then reabsorbed. The majority of the urobilinogens are filtered from the blood by the kidney and excreted in the urine. A small percentage of the urobilinogens are reabsorbed in the intestines and re-excreted into the bile through the enterohepatic circulation. Recent findings in the field of molecular biology and the human genome project have highlighted various proteins and genes responsible for the metabolism of bilirubin and some of these are being exploited in the treatment of cholestasis.

4. Pathophysiology of obstructive jaundice

Bile is a multipurpose secretion with an array of functions, including intestinal digestion and absorption of lipids, elimination of environmental toxins, carcinogens, drugs, and their metabolites (xenobiotics), and serving as the primary route of excretion for a variety of endogenous compounds and metabolic products, such as cholesterol, bilirubin, and many hormones. In obstructive jaundice, the pathophysiological effects reflect the absence of bile constituents (most importantly, bilirubin, bile salts, and lipids) in the intestines, and their backup, which causes spillage into the systemic circulation. Stools are often pale because less bilirubin reaches the intestine. Absence of bile salts can produce malabsorption, leading to steatorrhea and deficiencies of fat-soluble vitamins (particularly A, K, and D); vitamin K deficiency can reduce prothrombin levels. In long-standing cholestasis, concomitant vitamin D and Ca malabsorption can cause osteoporosis or osteomalacia. Bilirubin retention produces mixed hyperbilirubinemia. Some conjugated bilirubin reaches and darkens the urine. High levels of circulating bile salts are associated with, but may not cause, pruritus. Cholesterol and phospholipid retention produces hyperlipidemia despite fat malabsorption (although increased liver synthesis and decreased plasma esterification of cholesterol also contribute); triglyceride levels are largely unaffected. The lipids circulate as a unique, abnormal, low-density lipoprotein called lipoprotein X.
Cholestatic liver diseases are characterized by accumulation of hepatotoxic substances, mitochondrial dysfunction and impairment of liver antioxidant defense. The storage of hydrophobic bile acids has been indicated as the main cause of hepatotoxicity with alteration of some important cell functions, such as the mitochondrial energy production. Both mitochondrial metabolism impairment and hydrophobic bile acids accumulation are associated with increased production of oxygen free radical species and development of oxidative damage. (13)

5. Etiology
Myriad of diseases can lead to extra hepatic biliary obstruction (Table 1)
The common ones include:
- Choledocholithiasis
- Cholangiocarcinoma,
- Ampullary cancers,
- Cancer of the Pancreas
- Biliary strictures.

6. Clinical Features
A good history, physical examination and diagnostic tests are the requisites for the evaluation of the jaundiced patient. Jaundice, dark urine, pale stools and generalized pruritus are the hallmark of obstructive jaundice. History of fever, biliary colic and intermittent jaundice may be suggestive of cholangitis/choledocholithiasis. Weight loss, abdominal mass, pain radiating to the back and progressively deepening jaundice may be suggestive of pancreatic cancer. Deep jaundice (with a greenish hue) that appears to fluctuate in intensity may be due to a peri ampullary cancer. A palpably enlarged gall bladder in a jaundiced patient is also suggestive of an extrahepatic malignancy (Couvoissier’s statement).

7. Investigations
   a) Biochemistry/Hematology
   Elevated serum bilirubin level with a preponderance of the conjugated fraction is the rule. The serum gamma glutamyl transpeptidase (GGT) level is also raised in cholestasis. In general, patients with gallstone disease have less hyperbilirubinemia than those with extra-hepatic malignant obstruction. The serum bilirubin is usually less than 20 mg/dL. The alkaline phosphatase may be elevated up to ten times normal. The transaminases may abruptly rise about ten times normal and decrease rapidly once the obstruction is relieved. Elevated WBC may be present in cholangitis. In pancreatic cancer and other obstructive cancers, the serum bilirubin may rise to 35 to 40 mg/dL, the alkaline phosphatase may rise up to ten times normal, but the transaminases may remain normal. Tumor markers like CA 19-9, CEA and CA-125 are usually elevated in pancreatic cancers, cholangiocarcinoma and peri-ampullary cancers, but they are non specific and may be elevated in other benign diseases of the hepatobiliary tree. (14)

   b) Imaging
   The goals of imaging are:
   (1) to confirm the presence of an extrahepatic obstruction (i.e., to verify that the jaundice is indeed post-hepatic rather than hepatic), (2) to determine the level of the obstruction,
(3) to identify the specific cause of the obstruction, and (4) to provide complementary information relating to the underlying diagnosis (e.g., staging information in cases of malignancy).(15) A plain abdominal x ray may show calcified gallstones, porcelain gallbladder, air in the biliary tract or air in the gallbladder wall.

**Ultrasonography** shows the size of the bile ducts, may define the level of the obstruction, may identify the cause and gives other information related to the disease (e.g. hepatic metastases, gallstones, hepatic parenchymal change).(2) It identifies bile duct obstruction with 95% accuracy though results are largely operator dependent. It will also show stones in the gallbladder and dilated bile duct, but it is unreliable for small stones or strictures in the bile ducts. It may also demonstrate tumors, cysts, or abscesses in the pancreas, liver, and surrounding structures. In Africa, this is available in most centers and probably constitutes the main imaging modality available apart from X-ray.

**Computed tomography (CT)** of the abdomen provides excellent visualization of the liver, gallbladder, pancreas, kidneys, and retroperitoneum. It can differentiate between intra- and extra-hepatic obstruction with 95% accuracy. However, CT may not define incomplete obstruction caused by small gallstones, tumors, or strictures.

**Contrast-enhanced multi-slice CT** is very useful for assessment of biliary malignancies. Contrast agents given orally or intravenously are used and imaging done in unenhanced, arterial and venous phases.

**ERCP and PTC (Percutaneous transhepatic cholangiography)** provide direct visualization of the level of obstruction. However they are invasive and associated with complications like cholangitis, biliary leakage, pancreatitis and bleeding. These facilities are generally not available in most centers in Africa.

**Endoscopic ultrasound**: Endoscopic ultrasonography has various applications, such as staging of gastrointestinal malignancy, evaluation of submucosal tumors, and has grown to be an important modality in evaluating the pancreaticobiliary system. With regard to the biliary system, EUS is useful for the detection and staging of ampullary tumors, detection of microlithiasis, choledocholithiasis and evaluation of benign and malignant bile-duct strictures. It can further evaluate relationships to vascular structures. It may help define benign lesions mimicking cancer (e.g. sclerosing pancreatitis) if there is diagnostic doubt. Endoscopic ultrasound enables the aspiration of cysts and biopsy of solid lesions, but is operator-dependent.(16) Unfortunately, this is not readily available in most centers in Africa.

**Magnetic resonance cholangiopancreatography (MRCP)** is a newer, noninvasive technique for visualization of the biliary and pancreatic ductal system. It is especially useful in patients who have contraindications for endoscopic retrograde cholangiopancreatography (ERCP). Excellent visualization of biliary anatomy is possible without the invasiveness of ERCP. Unlike ERCP, it is purely diagnostic. Other imaging tests include Cholescintigraphy, radionuclide scanning (Tc 99) angiography and staging laparoscopy.

These imaging facilities are hard to find in Africa and ultrasonography remains the only diagnostic test available in most centers.

### 8. Approach to the Jaundiced Patient
Barkun et al have written an excellent review on an approach to the jaundiced patient. I have summarized the approach with the following questions:

Question 1: Is Jaundice present? A skin discoloration suggestive of jaundice can be mimicked by a variety of conditions which include:
  a) consumption of large quantities of food containing lycopene or carotene
  b) use of drugs like rifampicin or quinacrine

It is therefore necessary to inspect not only the skin, but the mucous membranes of the mouth, palm, soles and the sclera.

Q2: Is it Direct or Indirect Hyperbilirubinemia? Dark urine, pale stools and other features of cholestasis, like pruritus, are suggestive of direct hyperbilirubinemia, while normal colored urine and stool reflect unconjugated hyperbilirubinemia. In majority of cases, clinical findings alone will be sufficient to differentiate conjugated from unconjugated hyperbilirubinemia.

Q3: Is it Hepatic or Post hepatic? Once direct hyperbilirubinemia has been confirmed, the next question to answer is whether the jaundice is from hepatic or post-hepatic lesions. Clinical features of hepatic jaundice include history of alcohol abuse, acute hepatitis, and stigmata of chronic liver disease like palmar erythema, caput medusae, ascites and Dupuytren’s contracture.

Post-hepatic jaundice usually present with abdominal pain, rigors, itching and palpable liver more than 2cm below the costal margin.

Using clinical approach and simple biochemical tests (total serum bilirubin, alkaline phosphatase and gamma glutamyl transferrase levels) will usually give a good judgment on whether the jaundice is hepatic or post-hepatic. However, this approach will not be able to identify the level of the obstruction.

Q4: What is the level of the obstruction? Imaging is the key to identifying the level of obstruction. Ultrasonography will be able to identify the level of obstruction in about 90% of cases. Other imaging facilities like MRCP, ERCP, PTC, and CT scan may be used where Ultrasonography can not determine the level of the obstruction.

Q5: What is the cause of the obstruction? The commonest cause of obstruction in the West is usually choledocholithiasis. However, if choledocholithiasis is excluded, pancreatic and peri ampullary cancers are the next common causes.

Q6: What is the extent of the disease (staging)/complications (cholangitis)? While obvious metastases may be present by a palpation of a nodular enlarged liver or other evidence of widespread disease, sophisticated imaging is required for more precise staging. Fever and elevated WBC are indicative of cholangitis.

Q7: If it is malignant, is it respectable? Assessment of the resectability of a tumor usually hinges on whether the superior mesenteric vein, the portal vein, the superior mesenteric artery, and the porta hepatis are free of tumor and on whether there is evidence of significant local adenopathy or extrapancreatic extension of tumor. Multislice spiral CT is the imaging of choice for assessment of respectability of pancreatic cancers. Optimal evaluation is achieved with a fine-cut dual-phase (arterial phase and portal venous phase) MRCP. EUS, CT angiography or duplex Doppler Ultrasonography are other imaging facilities that can be used in assessment of hepatobiliary malignancies in centers where they are available.
For unresectable malignancies, the choice is between surgical palliation/bypass and ERCP/PTC with drainage. In some cases, neither option may be feasible because of advanced disease; in such a case supportive care alone will suffice. For lesions that are respectable or amenable to surgical palliation, the choice of treatment will depend on the level of obstruction and the precise etiology. For this purpose, the lesions can be classified into three: (Table 2)

a) Upper third obstruction: Surgical palliation is best achieved with a left (segment 3) hepaticojejunostomy (The long extrahepatic course of the left hepatic duct makes it more accessible). For respectable lesions, the tumor is resected with a possible hepatectomy or segmentectomy and reconstruction achieved by hepaticojejunostomy or cholangiojejunostomy.

b) Middle third obstruction: Surgical palliation is easier and hepaticojejunostomy after the bifurcation is done. If tumor is resectable, reconstruction is achieved with hepaticojejunostomy.

c) Lower third obstruction: Surgical palliation done using a Roux en Y choledochojejunostomy. Cholecystojejunostomy carries a high risk of complications and subsequent jaundice. If tumor is respectable, a pancreatiduodenectomy (Whipple’s procedure) or local ampullary resection should be done.

9. Treatment
Extrahepatic biliary obstruction requires mechanical decompression. Other goals include treatment of the underlying cause, symptoms, and complications (e.g., vitamin malabsorption). Decompression of extrahepatic biliary obstruction can be achieved by any of these three methods: surgical bypass, resection of obstructing lesions, percutaneous insertion of stents, and endoscopic insertion of stents.(17)

9.1. General Considerations
Pruritus usually subsides with correction of the underlying disorder or with 2 to 8 gm. orally of cholestyramine bid, which binds bile salts in the intestine. However, this is ineffective in complete biliary obstruction. Unless severe hepatocellular damage is present, hypoprothrombinemia usually subsides after use of (vitamin K1) 5 to 10 mg sc once/day for 2 to 3 days. Ca and vitamin D supplements, with or without a bisphosphonate, slow the progression of osteoporosis only slightly in long-standing irreversible cholestasis. Vitamin A supplements prevent deficiency and severe steatorrhea can be minimized by replacing some dietary fat with medium-chain triglycerides.

Jaundiced patients undergoing surgery for large bile duct obstruction (from any cause) are subject to specific risks that require prophylactic measures. These include
- infections (cholangitis, septicaemia, wound infections)
- bleeding (non-coagulant acarboxyl derivatives of vitamin K dependent factors)
- renal failure
- liver failure
- fluid and electrolyte abnormalities

Preparation for surgery is important because of the associated perioperative morbidity previously discussed. The specific measures required in all patients are:
- parenteral administration of vitamin K analogues – to normalise prothrombin time
- intravenous hydration and catheterization of the urinary bladder
9.2. Specific Treatment based on causes
9.2.1. Choledocholithiasis (bile duct stones)
There are various options available. The best option should be individualized and based on the following factors:

- Physical condition of the patient including co morbidity and medical history
- Previous attempts at intervention or previous cholecystectomy
- Availability of equipment/theatre/anesthetist/expertise of Interventionist
- Patient preference.

Open exploration of the common bile duct: involves
- Cholecystectomy, if present.
- supraduodenal longitudinal choledochotomy
- Extraction of calculi by Fogarty balloon trawl, Desjardins forceps or Dormia basket and irrigation with saline.
- Confirmation of duct clearance superiorly and inferiorly by choledochoscopy and/or cholangiography.
Where facilities for choledochoscopy and intraoperative cholangiogram are not available, to avoid the risk of leaving retained duct stones, a T tube is usually inserted to confirm clearance of the duct by a postoperative cholangiogram after at least five days. The T tube is removed after two weeks, when an epithelialized tract has formed to avoid bile leak into the peritoneal cavity.

Several trials however have shown that primary closure of the bile duct without T tube is as safe as using T tube and is associated with less complications like sepsis, tube migrations and bile peritonitis.(18;19). In Africa and other developing countries where there may be no facilities for intraoperative cholangiogram or intraoperative Ultrasonography, T tube placement will be a pragmatic approach. Unfortunately, in most centers, T tubes are hard to find.

Other procedures in difficult cases:
Removal of common bile duct calculi may prove difficult by any of the above methods, for example:
- impacted stone when all efforts to remove it have failed
- multiple large stones
- inaccessible duct (e.g. previous surgery, unfit patient).

Surgical or percutaneous drainage procedures may be useful. Choledochoduodenostomy may be done by anastomosis of a dilated common bile duct to the duodenum. Alternatively, particularly in a non-dilated duct, a transduodenal sphincteroplasty is undertaken by first carrying out an open sphincterotomy and stone extraction, then suturing the mucosa of the duct and duodenum together to keep the lower end patent; these procedures are rarely undertaken. Percutaneous stenting or naso-biliary drainage may be done in an unfit patient with common bile duct stones that cannot be removed by ERCP.
**ERCP±sphincterotomy**: A cholangiogram is done after the ampulla of Vater has been identified and cannulated to confirm anatomy and the presence of stones. An adequate sphincterotomy is undertaken and the duct cleared using a balloon catheter or Dormia basket. Confirmation of duct clearance should be established with a radiograph. If the stones are too large, they can be crushed in situ using a mechanical lithotripter; however care should be exercised to avoid damage to the duct lining. Other techniques described in the literature include extracorporeal shockwave lithotripsy, contact lithotripsy, laser under direct vision. These are however time consuming, resource intensive and are limited to few specialized centers.

Endoscopic placement of a stent, or temporary naso-biliary drainage can be a good option if the stones are multiple or too large for extraction. This relieves obstruction and prevents impaction of stones at the ampulla of Vater.

Success rate after ERCP±sphincterotomy is about 90% with low complications in experienced hands. Complications include perforation, acute pancreatitis, and bleeding from damage to a branch of the superior pancreatico-duodenal artery.

Difficulties may arise as a result of technical problems in cannulating the ampulla of Vater or anatomical anomalies like duodenal diverticulum. ERCP may be considered the definitive treatment for some unfit patients, but most will proceed to cholecystectomy to remove remaining gallstones and prevent further complications. (2;20;21)

**Endoscopic balloon dilation** was introduced about three decades ago for elderly and frail patients as an alternative to sphincterotomy, because of the advantages of preserving the sphincter of Oddi. This has been abandoned in North America because of the risk of pancreatitis. It is still practiced in parts of Asia and Europe. A recent Cochrane review concluded that it is slightly less successful than endoscopic sphincterotomy in stone extraction and more risky regarding pancreatitis and probably has a clinical role in patients who have coagulopathy, who are at risk for infection, and possibly in those who are older. (22)

**Laparoscopic exploration of the common bile duct** may be done through the cystic duct (if the gall bladder has not been previously removed) or common duct via a choledochotomy. Stones are extracted under fluoroscopic guidance using balloon catheters or Dormia basket. Choledochoscopy and lithotripsy can also be done for larger stones. This technique requires considerable laparoscopic expertise and is time consuming, so it is rarely the first-line treatment for common bile duct stones; these are usually removed at ERCP preoperatively and a laparoscopic cholecystectomy done electively. Single stage laparoscopic cholecystectomy and ductal stone clearance has been shown in several studies to have the same efficacy and morbidity with the staged approach with the added benefit of reduced costs. (15;23;24)

Nevertheless, most centers still favor preoperative endoscopic ductal clearance because LECBD is technically demanding and sophisticated laparoscopic equipment may not be available in every surgical unit.

**Medical dissolution of common bile duct stones:**
Flushing with normal saline; infusion of bile salts, monoocanoin, methyl tert-butyl ether, or other solvents into the CBD through a Ttube are medical remedies for choledocholithiasis that have been described in the literature.
The efficacy of the surgical/endoscopic approaches to bile duct stones have made medical approaches unattractive. The principal disadvantages of bile acid infusion are the prolonged period of hospitalization required to carry out the treatment, the unsatisfactory handling of distal occluding stones and those on the hepatic side of the T-tube, the high incidence of side effects, and the rather unpredictable outcome. (25-29)

9.2.2. Cholangiocarcinoma
Cholangiocarcinomas are epithelial cancers of the cholangiocytes and they can occur at any level of the biliary tree. They are broadly classified into intra-hepatic tumours, (extra-hepatic) hilar tumours and (extra-hepatic) distal bile duct tumours. Majority arise in the absence of risk factors, however identified risk factors include age, primary sclerosing cholangitis, chronic choledocholithiasis, bile duct adenoma, biliary papillomatosis, Caroli’s disease, choledochal cyst, thorotrust, smoking, parasitic biliary infestation and chronic typhoid carrier state. (30) Hilar cholangiocarcinoma accounts for two thirds of all cases of extra-hepatic cholangiocarcinoma. Intra-hepatic and distal extra-hepatic cholangiocarcinomas are less common, but surgical resection remains the only chance of cure consisting of liver resection and pancreaticoduodenectomy, respectively. Unfortunately, the majority of these tumors are unresectable, Surgery is the only curative option for cholangiocarcinoma. The extent of spread, available surgical expertise and associated co-morbidities are important factors that will determine the treatment approach. Although several surgical series have been reported, recent trends are to advocate accurate preoperative staging with an aggressive onco-surgical approach involving en-bloc hilar or hepatic resections. Currently, cholecystectomy, lobar or extended lobar hepatic and bile duct resection, regional lymphadenectomy, and Roux-en-Y hepaticojejunostomy are the treatments of choice for hilar cholangiocarcinoma. Encouraging reports with the use of photofrin based photodynamic therapy have been reported in the literature.(31-34)

Systemic therapy/Palliative therapy: The majority of patients with cholangiocarcinoma present at an advanced stage or have associated co-morbidity that preclude surgery. For these patients, the goal of treatment is to obtain adequate palliation. Biliary endoprosthesis (stent) placement is a useful option for palliation of jaundice. The approach is usually by ERCP but for proximal lesions the transhepatic route may be used. Photodynamic therapy, radiation and chemotherapy are all available as palliative options. Several chemotherapeutic agents have been evaluated with limited results. Gemcitabine or 5-Fluorouracil are the two common agents used as a single agent or in combination with other drugs.(35;36)

9.2.3. Ampullary tumours
Peri-ampullary cancers can be broadly considered as tumors arising within 1 cm of the ampulla of Vater and include ampullary, distal bile duct, pancreatic, and duodenal cancers. However, without careful histological analysis, it is difficult if not impossible to differentiate the tumor type. Surgical excision is the mainstay of treatment for peri-ampullary cancers. Careful preoperative staging and assessment of respectability is crucial. If the tumor is resectable, the procedure of choice is a pancreaticoduodenectomy.
The classical approach (Whipple’s procedure or cWhipple) described by Kausch and Whipple remains the most popular technique in North America and Europe. The more conservative approach (pylorus preserving Whipple resection or ppWhipple) described by Watson in 1943 and later popularized by Traverso and Longmire is another technique that is gradually gaining more converts. Pylorus-preserving pancreaticoduodenectomy is reported to be an easier and less time-consuming operation with less blood loss, a shorter hospital stay, and better weight gain during follow-up care. Also, no differences in the recurrence rate and patient survival exist between pylorus-preserving pancreaticoduodenectomy and the standard Whipple procedure. (37;38)

For unresectable tumors, palliative treatment will depend on comorbidity factors, and availability of resources and expertise for endoscopic treatment. Biliary bypass procedures can be done operatively, laparoscopically, endoscopic stenting or by percutaneous transhepatic approaches. (39)

Gastric bypass procedures may also be indicated in patients with gastric outlet obstruction. The role of prophylactic gastric bypass procedures is controversial, however a prospective randomized clinical trial concluded that a prophylactic gastrojejunostomy significantly decreases the incidence of late gastric outlet obstruction and did not increase the incidence of postoperative complications or extend the length of stay. (40)

9.2.4. Pancreatic Cancer
Pancreatic ductal adenocarcinoma is one the most lethal GI malignancy with an overall 5-year survival rate of less than 4%. Factors influencing this grim prognosis are 1) clinical symptoms in the early stage are usually absent or non specific resulting in late diagnosis, with only 15–20% of tumors being respectable at presentation. 2) Clinically, aggressive growth, with retroperitoneal and perineural infiltration, angioinvasion, high rates of local relapse, formation of metastases, and 3) resistance to most of the available treatment regimens, makes patient management a complex and challenging task.(41)

The only hope for cure is surgery, but unfortunately less than 20% are respectable. There is now an acceptable operative mortality rate of less than or equal to 5% for resected patients when performed at experienced or dedicated centers with high volume of patients in the western world.

The treatment options are similar to peri-ampullary cancers.

The role of adjuvant therapy in advanced pancreatic cancer is controversial as most of the trials show limited benefits. Gemcitabine, 5FU are agents that show some promise. Pain Palliation: Patients who present with severe pain must receive opioids. Morphine is generally the drug of choice. Usually, the oral route is preferred in routine practice. Parenteral routes of administration should be considered for patients who have impaired swallowing or gastrointestinal obstruction. Percutaneous celiac plexus blockade can be considered, especially for patients who experience poor tolerance of opiate analgesics. (42)

9.2.5. Biliary Strictures
Biliary strictures can be benign or malignant. In this section of the review, our focus will be on benign biliary strictures as the common causes of malignant strictures have been treated earlier.
The majority of benign strictures are iatrogenic - as a result of operations on the gallbladder and the biliary tree. The introduction of laparoscopic cholecystectomy initially led to an increase in operative trauma to the bile ducts from 0.1-0.2% to 2%. This was not surprising considering the steep learning curve of laparoscopic procedures. However, after widespread adoption of lap cholecystectomy, the incidence of operative trauma still remains higher than what obtained in the era of open cholecystectomy at 0.2-0.7%.(43)

Non iatrogenic causes of benign strictures include inflammatory conditions and subsequent fibrosis related to chronic pancreatitis, cholelithiasis, choledocholithiasis, sclerosing cholangitis, stenosis of the sphincter of Oddi, or infections of the biliary tract. Three options for the management of benign biliary strictures are currently available: percutaneous dilation and stenting, endoscopic dilation and stenting, and surgical biliary drainage, most commonly by a Roux-en-Y hepaticojejunosotomy. All the options have comparable results, with stricture relapse rates reported between 15%–45% and mean follow-up times of 4–9 years. (43)

The choice of treatment modality must be individualized and should be based on the following considerations: the location and severity of the stricture, the presence of biliary-enteric continuity, the degree of infection, over-all health of the individual patient, the length of time anticipated for stenting, and the need for repeated dilation and stent exchange. It calls for a close collaboration between the surgeon and the interventional radiologist.

10. Complications
Complications of obstructive jaundice include sepsis especially cholangitis, biliary cirrhosis, pancreatitis, coagulopathy, renal and liver failure. Other complications are related to the underlying disease and the procedures employed in the diagnosis and management of individual diseases. Cholangitis especially the suppurative type (Charcot’s triad or Raynaud’s pentad) is usually secondary to choledocholithiasis. It may also complicate procedures like ERCP. Treatment should include correction of coagulopathy, fluid/electrolyte anomaly, antibiotics and biliary drainage with ERCP where available or trans-hepatic drainage or surgery.

11. Conclusion
Obstructive jaundice is a clinical diagnosis that requires both clinical and diagnostic work up to elucidate the precise etiology. A multi disciplinary approach that requires the clinician, radiologist, endoscopist and interventional radiologist will lead to a better outcome.

12. Recommendations
1. Treatment should be individualized - based on patient factors and availability of resources and personnel.
2. To optimize treatment for pancreatic cancers, dedicated centers should be established.
3. Pylorus preserving resection is recommended instead of the Classical Whipple’s resection.
4. Extensive palliative procedures carry a significant degree of morbidity and mortality in advanced hepatobiliary malignancies and should be discouraged.
6. ERCP is preferred to trans-hepatic drainage for biliary decompression except for obstructions near the hepatic bifurcation.
7. Primary closure of the common bile duct after exploration for stones is as safe as leaving a T tube in situ and associated with fewer complications if confirmation of biliary clearance can be obtained.

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Table 1 Causes of Obstructive Jaundice

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<td>Idiopathic dilatation of common bile duct</td>
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<tr>
<td>Pancreaticobiliary malfunction(14)</td>
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<tr>
<td>Cystic fibrosis</td>
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<tr>
<td>Choledochal cysts</td>
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<table>
<thead>
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<th>Acquired</th>
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<tr>
<td>Cholecystitis - Mirizi Syndrome(15-17)</td>
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<tr>
<td>Common bile duct obstruction</td>
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<tr>
<td>Choledocholithiasis</td>
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<tr>
<td>Tumors (benign, malignant)</td>
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<tr>
<td>Gallbladder</td>
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<tr>
<td>Bile ducts</td>
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<tr>
<td>Ampulla of Vater</td>
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<tr>
<td>Pancreas</td>
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<tr>
<td>Lymphoma</td>
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<tr>
<td>Metastatic tumors</td>
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<td>External compression</td>
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<th>Trauma</th>
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<tr>
<td>Portal Biliopathy(18;19)</td>
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<th>Strictures</th>
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<tr>
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<tr>
<td>Sphincter of Oddi</td>
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<tr>
<td>Primary sclerosing cholangitis</td>
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<th>AIDS (Cryptosporidium)</th>
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<tr>
<td>Pancreatitis</td>
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<tr>
<td>Intra abdominal tuberculosis(20;21)</td>
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<tr>
<td>Parasites (Ascaris)</td>
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</table>
Table 2 Causes of post-hepatic jaundice

**Upper Third Obstruction**
- Polycystic Liver Disease
- Caroli Disease
- Hepatocellular carcinoma
- Oriental Choangiohepatitis
- Hepatic Arterial Thrombosis (e.g. after liver transplantation or chemotherapy)
- Hemobilia
- Cholangiocarcinoma (Klatskin tumor)
- Sclerosing Cholangitis
- Iatrogenic injury to the bile duct
- Papillomas of the bile duct

**Middle Third Obstruction**
- Cholangiocarcinoma
- Sclerosing Cholangitis
- Gallbladder cancer
- Choledochal cyst
- Mirizzi syndrome
- Intrabiliary Parasites
- Cystic fibrosis
- Iatrogenic bile duct injury
- Benign idiopathic bile duct stricture
- Extrinsic nodal compression (from breast cancer or lymphoma)
- Papillomas of the bile duct

**Lower Third Obstruction**
- Pancreatic tumors
- Ampullary tumors
- Chronic Pancreatitis
- Papillary stenosis
- Sphincter of Oddi dysfunction
- Duodenal diverticula
- Penetrating duodenal ulcer
- Retroduodenal adenopathy (carcinoids, lymphomas)
- Cholangiocarcinoma
- Sclerosing Cholangitis
- Papillomas of the bile duct

**Reference List**

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