PRE AND POST PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE OUTCOMES AND COMPLICATIONS IN PATIENTS WITH OBSTRUCTIVE JAUNDICE AT MOI TEACHING AND REFERRAL HOSPITAL

KIPTOO KIPYATOR SAMMIN

THIS THESIS IS SUBMITTED TO THE SCHOOL OF MEDICINE COLLEGE OF HEALTH SCIENCES IN PARTIAL FULFILLMENT FOR THE AWARD OF MASTER OF MEDICINE IN RADIOLOGY AND IMAGING OF MOI UNIVERSITY

DECLARATION

Declaration by the Candidate

This thesis is my original work and has not been presented for a degree or any academic credit in any other University or examining body. No part of this thesis may be reproduced without the prior written permission of the author and/or Moi University.

KIPTOO KIPYATOR SAMMIN

Registration Number: SM/ PGR/12/2017

Signature ……. Date ……

Declaration by Supervisors:

This thesis has been submitted for examination with my approval as a University supervisor.

Dr. Loice Sitienei
Lecturer Moi University and Consultant Radiologist,
Department of Radiology and Imaging.
Moi University School of Medicine, Eldoret, Kenya.

Signature ……. Date ……

Dr. Cornelius Kipchirchir
Consultant Radiologist,
Department of Radiology and Imaging.
Moi Teaching and Referral Hospital, Eldoret, Kenya.

Signature ……. Date ……

DEDICATION

I would like to dedicate this work to God Almighty and All Knowing whom it has pleased to see me through this project. I would also like to acknowledge my wife Joyce Muthoni and my two sons Kigen Berur and Kalya Tilil for giving me the motivation to achieve always, and my father and my mother for the constant support. Finally, the Ministry of Health and Kilifi County government for facilitating my education.

ACKNOWLEDGEMENT

I wish to thank my supervisors, Dr. Cornelius Kipchirchir and Dr. Loice Sitienei for their contributions, corrections, and advice that was given to facilitate the successful completion of this thesis. I also wish to acknowledge Nehemiah Kosgei my biostatistician for his invaluable assistance.

LIST OF ABBREVIATIONS

ALP	Alkaline Phosphatase
CBD	Common Bile Duct
CT	Computed Tomography
ERCP	Endoscopic Retrograde Cholangiopancreatography
GGT	Gamma Glutamyl Transpeptidase
INR	International Normalized Ratio
IREC	Institutional Research and Ethics Committee
LFTs	Liver Function Tests
MTRH	Moi Teaching and Referral Hospital
PT	Prothrombin Time
PTBD	Percutaneous Transhepatic Biliary Drainage
SPSS	Statistical Package for Social Sciences

DEFINITION OF TERMS

Outcomes	this are the outcomes analyzed in this study:- (A) laboratory outcomes i.e AST, ALT, Total bilirubin (direct and indirect), ALP, and GAMMA GT (B) clinical outcomes i.e pruritus
Malignant obstructive jaundice	obstructive jaundice due to a malignant tumour.
PTBD	it refers to a radiological procedure where a tube is inserted into a dilated bile duct in the liver through the skin by an interventional radiologist to drain obstructed bile flow.
Complications	are post-procedure complications evaluated within two weeks. This was the optimum period as per the MTRH Interventional radiology standard practice. A longer period of 30 days saw the majority of the patients being lost to follow-up or transferring out to other facilities.

ABSTRACT

Background: Obstructive jaundice is a specific type of jaundice, where symptoms develop due to a narrowed or blocked biliary tree, preventing the normal drainage of bile from the liver into the intestines. It can have benign causes such as gallstones or malignant causes such as pancreatic cancer. Malignant causes are the majority and by the time of diagnosis, they are usually advanced with most patients exhibiting a poor clinical status. Percutaneous Transhepatic Biliary Drainage (PTBD) is an imaging-guided procedure performed by an interventional radiologist for biliary drainage in both benign and malignant cases including palliation. It is a relatively new specialty in Kenya and as such a study on PTBD and information on the clinical and laboratory parameters pre and post drainage as well as on the associated immediate complications, is due for Kenya and Sub-Saharan Africa.

Objectives: To evaluate outcomes pre and post PTBD and assess the complications from the PTBD procedure.

Materials and Methods: A prospective study was conducted at the Moi Teaching and Referral hospital, in the Interventional Radiology section for a period of 12 months. All the patients with obstructive jaundice requiring PTBD who were sent to the interventional radiology unit for PTBD placement from the medical and surgical wards were recruited. Biodata and data on pruritus were collected using questionnaires whereas data on laboratory measurements were extracted from the patient records during the 2 week follow-up period. Analysis was done using Statistical Package for Social Sciences version 21. Descriptive statistics including mean, mode, and median, measures of dispersion, frequencies, and proportions were used for the analysis. The results are presented in form of tables, figures, and prose format.

Results: Among the 66 patients included in the study, 53% were male while the rest were female. The majority of the patients showed clinical improvement in pruritus post PTBD. There was a statistically significant reduction in aspartate aminotransferase (AST), alanine phosphatase (ALP), total bilirubin, and Gamma Glutamyl transferase (GGT) after PTBD with (A p value< 0.005). A total of 35 (53.0%) of the patients had major complications while 25 (42.4%) had minor complications after the PTBD procedure.

Conclusion: PTBD improved patient clinical and laboratory parameters and minor complications were mostly encountered in this study

Recommendations: PTBD uptake should be encouraged and further studies should be done to determine the quality of life post-PTBD procedure to relate whether improved laboratory and clinical outcomes translate to a better quality of life.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER ONE: INTRODUCTION

1.1 Background

Percutaneous transhepatic biliary drainage (PTBD) is a procedure done to decompress the biliary tree following an obstruction anywhere along the biliay system whether high or low.

Historically, PTBD was introduced in the early 1980s and has been used ever since. Early publications by Riemann and Faithfull demonstrated high technical success rates and low complication rates. They described the method as temporary or permanent depending on whether surgery was still an option for treatment or not.

Percutaneous transhepatic biliary drainage (PTBD) is a minimally invasive procedure for drainage of the biliary system (Yadav et al., 2018). PTBD is preferred as the primary procedure in patients who have had prior bilio-enteric anastomosis, or those who are unsuitable for endoscopic retrograde cholangiopancreatography (ERCP) due to other reasons.

Methods of biliary drainage include: bypass, minimally invasive imaging guided procedures; Percutaneous Transhepatic Biliary Drainage (PTBD), and Endoscopic retrograde cholangiopancreatography (ERCP).

Both ERCP and PTBD are well-established and effective means of biliary drainage for palliation in unresectable cases. With an increased technical success rate and expertise in these minimally invasive procedures, the recent time has witnessed an exemplary surge in the demand for such a procedure over surgical bypass. Selecting an option over another; however, is a multidisciplinary opinion, which not only involves the expertise of the operator and the site of obstruction but also takes into consideration other factors such as expected survival and the level of post-procedural

care provided to the patients. ERCP is usually performed in cases of distal CBD block (beyond hilum), while PTBD is preferred in proximal biliary obstruction (Covey & Brown, 2008).

Radical tumor resection is the primary means of treating a malignancy causing obstructive jaundice, but many patients (approximately 80%) lose radical surgery opportunities because of these features of tumors including insidious onset, and low early diagnosis rate, etc. So far, endoscopic retrograde cholangiopancreatography (ERCP) has become the best treatment choice for malignant obstructive jaundice. But even if operated by experienced endoscopists, there is still a 3% to 10% failure rate in the management of these patients with malignant obstructive jaundice (Shu *et al*., 2012) Percutaneous transhepatic biliary drainage (PTBD) or endoscopic ultrasonography guided biliary drainage (EUS-BD) has become the preferred treatment for malignant obstructive jaundice when ERCP failed. Several studies (Dhir *et al*., 2014; Ogura *et al*., 2016; Xu *et al*., 2015) have demonstrated that these procedures are effective and safe for palliative biliary drainage in patients with malignant obstructive jaundice. However, there have been few published studies on PTBD procedure locally, and the associated complications (Lee *et al*., 2016).

PTBD is performed by an interventional radiologist and the technique is as follows;

The patient is placed in a supine position. Sterile preparation and draping are performed.

It begins with the performance of percutaneous transhepatic cholangiography (PTC). Once the needle is in the bile duct, a 0.018-inch wire is advanced. After the wire is passed to a secure position in the biliary tree, the needle is removed. A sheath of the coaxial system can be passed over the 0.018-inch wire, and the inner two components

(wire and inner coaxial dilator) can then be removed to allow passage of the larger wire.

The assembly set, consisting of an outer fluoropolymer sheath and an inner fluoropolymer sheath, and a metal cannula, is advanced over the wire. After the tip is in the bile duct, the two outer fluoropolymer sheaths are advanced over the wire. Once the sheaths are in position, the inner sheath and stiffener are removed, leaving the outer sheath behind. This outer sheath has a 4-French inner diameter and a 4-French catheter through which a 0.035- or 0.038-inch wire can be passed.

A 4-French catheter with a distal curve and a 0.035-inch hydrophilic guide wire is usually used to cross the obstructing lesion. When the obstruction is high-grade and the bile ducts are severely dilated, crossing the obstruction may not be possible. In these cases, external drainage can be tried for a few days to decompress the biliary system, and another attempt can be made later.

After the catheter is advanced to the duodenum, the wire is exchanged for a stiff guide wire. The catheter and sheath are removed, and a biliary drainage catheter is advanced.

The end of this catheter is reformed after the catheter tip is in position in the duodenum and after the inner stiffener is removed. The proximal side-hole location is checked by injecting contrast material to ensure that it is in the bile duct and not intraparenchymal; malpositioning may lead to pericatheter leakage or hemobilia. The internal fixation is achieved by using a loop-retaining suture. Catheters are also secured to the skin by using sutures such as nylon 2-0.

Jaundice is an important clinical entity associated with a wide variety of differential diagnoses for problems that occurs when there is an obstruction to the passage of conjugated bilirubin to which the prognosis differs depending on etiology. Obstructive jaundice as the name suggests is the obstruction of the flow of bile from liver cells to the intestines. It is among the most challenging conditions managed by doctors and contributes significantly to high morbidity and mortality. Given that patients with obstructive jaundice have high morbidity and mortality, early diagnosis of the cause of obstruction is essential, especially in malignant cases, as resection is only possible at the early stages (Saddique & Iqbal *et al*., 2007).

Recent studies of patients with jaundice have included a limited number of patients with jaundice due to biliary obstruction and provided no analysis of the clinical characteristics and prognosis of these patients.

Obstructive jaundice is not a disease per se but is the manifestation of some underlying disease process. It can present with acute symptoms or gradually progressive indolent course depending upon the underlying cause (Padhy et al., 2018)

Jaundice due to biliary obstruction may be caused by a heterogeneous group of diseases that include both benign and malignant conditions (Roche & Kobos *et al*., 2004). Moreover, the prognosis of unselected patients with severe obstructive jaundice is unclear. The most common clinical presentation of malignant obstructive jaundice traditionally has been considered silent jaundice (Björnsson et al., 2008).

Anatomy

The liver is a large and solid gland situated in the right upper quadrant of the abdominal cavity. It weighs about 1300g to 1600g.

The liver occupies the whole of the right hypochondrium, the greater part of the epigastrium, and extends into the left hypochondrium albeit to a lesser extent. It is the largest gland in the body. It secretes bile and performs various other metabolic functions.

The biliary tree is divided into intra- and extra-hepatic bile ducts.

Intrahepatic bile ducts

Bile canaliculi unite to form segmental bile ducts which drain each liver segment. The segmental ducts then combine to form sectoral ducts with the following pattern :

- segments 6 and 7: right posterior sectoral duct, coursing more horizontally
- segments 5 and 8: right anterior sectoral duct, coursing more vertically
- right posterior and anterior sectoral ducts unite to form the right hepatic duct
- segmental bile ducts from 2-to-4 unite to form the left hepatic duct

The left and right hepatic ducts unite to form the common hepatic duct whereas bile duct(s) from segment 1 drain into the angle of their union.

Extrahepatic bile ducts

The common hepatic duct is joined by the cystic duct from the gallbladder to form the common bile duct. The common bile duct travels initially in the free edge of the lesser omentum, then courses posteriorly to the duodenum and pancreas to unite with the

main pancreatic duct to form the ampulla of Vater, which drains at the major duodenal papillae on the medial wall of the D2 segment of the duodenum.

Role of PTBD

The treatment modalities available for the management of malignant biliary obstruction can be categorized into surgical, endoscopic, and percutaneous. Each approach has its benefits and drawbacks. The choice of the method of treatment depends on the local protocols and expertise, type of biliary obstruction, and patients' condition and choice.

When considering PTBD in isolation it has four main roles. The first is in pre-surgery preparation, where a suitable candidate for surgery has been identified and the team is seeking to stabilize the patient first before going in to perform the surgery. In this case, the patient can have a percutaneous tube inserted to correct the deranged liver functions or even treat sepsis before surgery.

The second role is where the tumour is determined to be unresectable therefore PTBD is done as a palliative measure.

The third role is as a post-surgical intervention when cases of re-obstruction following surgery occur, most commonly due to recurrence of malignancies and cases of multiple segment strictures.

Lastly as an alternative for failed endoscopic drainage.

PTBD is not a procedure that by itself can be considered final for patients with obstructive jaundice, but rather just one of many complementary methods available for the treatment of obstructive jaundice.

A case in point is surgical palliation which comprises of a biliary bypass (usually hepaticojejunostomy) and a gastric bypass (gastrojejunostomy), which are usually done for advanced cancers of the head of pancreas, or duodenal and biliary stenting which are very effective in the treatment of mid and distal malignant biliary strictures.

This goes to show that obstructive jaundice has several options available for treatment and each intervention depending on the specific needs of the patient is chosen. In some instances all three, that is; surgery, endoscopic and percutaneous interventions are used on one patient.

1.2 Problem Statement

In Kenya majority of the cases of obstructive jaundice are due to malignancy with the burden of gallbladder tumour and pancreatic head cancer being about 2.8% as per the WHO international agency for research on cancer 2020 statistics. Most of these patients will undergo surgery or endoscopic drainage to relieve the obstruction but for those who don't meet the criteria for surgery or endoscopic drainage then the imaging guided radiological procedures such as percutaneous transhepatic biliary drainage (PTBD) is the remaining option and this study seeks to focus on those patients.

Moreover; the radiological procedure (PTBD) is a relatively new procedure in sub-Saharan Africa and a paucity of data on its complications and outcomes exists which will be addressed by this study.

1.3 Study Justification

PTBD is an intervention in the management of patients who have developed obstructive jaundice. The patients indicated for PTBD fall into the category of patients who need stabilization before surgery or chemo and those who need palliative drainage, especially in cases where the disease is advanced. We also have those patients that have developed re-obstruction after surgery for one reason or the other.

Given that this procedure is still fairly new in our setup and it is not as widely performed in our country's public hospitals; a study needed to be done on this procedure. This was done by assessing the outcomes and the complications. This gave us knowledge of the procedure's benefits which could be defended and therefore encouraged for uptake among the local physicians. The studies that had been done on PTBD had been done mostly in the western world and Asia where the populations and their environment are different from ours. East Africa was due a study that focuses on the local population and would be adding knowledge to what was already known from around the world as well as generating new data for our setup.

In Kenya we have many non-surgical candidates that are usually left without any viable alternatives, PTBD could be an option. Therefore the addition of data on the outcomes and complications of this relatively new procedure could lead to increased adoption that will invariably lead to a reduction in morbidity and mortality rates.

Of additional benefit is PTBD with the faster recovery period means the initiation of medication whether chemotherapy or otherwise will be done sooner, therefore, improving the outcomes for patients diagnosed with cancer, and also acts as a bridge to definitive management, so that patients with benign causes of obstruction can be stabilized before initiation of therapy.

1.4 Research Question

What are the pre and post PTBD clinical and laboratory outcomes and complications from this procedure?

1.5 Objectives

1.5.1 Broad objective

To evaluate the pre and post PTBD clinical and laboratory outcomes, as well as look at the complications related to PTBD among patients with obstructive jaundice within a 2 week period at MTRH.

1.5.2 Specific objectives

1. To evaluate the pre and post PTBD clinical and laboratory outcomes within two weeks of percutaneous transhepatic biliary drainage .
2. To assess the complications related to percutaneous transhepatic biliary drainage within two weeks post procedure.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

In this chapter, I present a review of literature on the study based on peer review journal articles and grey literature from students' thesis and organization reports. This chapter is organized in sections according to the study objectives. At the end of the chapter, a summary of the review anthe d research gap identified are presented.

2.1.1 Obstructive jaundice and its causes

Obstructive jaundice is a specific type of jaundice, where symptoms develop due to a narrowed bile duct or pancreatic duct, preventing the normal drainage of bile from the liver into the intestines. Obstructive jaundice may be due to several causes, all of which narrow or block the bile ducts in some way. Commonly we can have gallstones which are the most common benign cause but pancreatic head cancer, swelling of lymph glands near the bile duct, and pancreatic cysts are some of the other causes of obstructive jaundice. (Covey & Brown *et al*, 2008) found that malignant causes such as carcinoma of the gall bladder, cholangiocarcinoma, pancreatic adenocarcinoma, metastasis, and lymph nodal compression of the common bile duct (CBD) constitute most cases

Any obstruction starting from the level of intrahepatic biliary radicles till the ampulla of Vater either intrinsic or extrinsic can cause obstructive jaundice. These can be divided into congenital causes like a choledochal cyst, postoperative strictures, and inflammatory causes like post inflammatory ampullary stricture, choledocholithiasis, neoplastic etiologies like carcinoma gallbladder, periampullary carcinoma, etc., and

It has been observed that the most common causes of surgical obstructive jaundice are malignant lesions (Selvasekaran Et al., 2017).

Obstructive jaundice is a cause of severe jaundice in one third of patients. Most cases of obstructive jaundice are as result of a malignancy, which carries a very poor prognosis, with a 2 year mortality rate of 95% (Björnsson et al., 2008).

Obstructive jaundice is a rising cause of mortality and morbidity worldwide, especially the malignant type. The same situation is seen in Kenya, where most patients present at the late stages of the disease, especially for malignant obstructive jaundice, due to the asymptomatic nature of the causative malignancy in the early stages. Biliary obstruction can be relieved surgically, via ERCP or percutaneously via PTC and external BD. PTBD is rapidly evolving as one of the primary treatment options for our patients due to the late stage at which patients present. No clinical study has been done in our population to evaluate these patients' clinical or technical outcomes.

2.1.2 Causes of biliary obstruction

From 1987 to 1988, a study carried out at the Kenyatta National Hospital (KNH) by Okoth et al. found that pancreatic head carcinoma accounted for 55% of cases of biliary obstruction. This was followed by gallstones at 10%, hepatocellular carcinoma at 10%, and gall bladder tumours at 10% (Okoth, Ogutu, Lule, & Wambugu, 1989). However, this was a limited study screening for causes of biliary obstruction on ultrasound. Another study by Bitta et al. in 2009, evaluating causes of malignant obstructive jaundice at KNH, found that the leading cause was carcinoma of the head of the pancreas at 65%, followed by cholangiocarcinoma at 21% and peri-ampullary tumours at 14% (Bitta, Githaiga, & Kaisha, 2014). According to the Eldoret Cancer Registry, 3 in 5 patients annually present with cholangiocarcinoma, similar to the incidence of gall bladder carcinoma (Ministry of Health, 2013).

Patency of the biliary tree and the related drainage of bile are crucial elements in the physiologic hepatic function (Levit et al., 2014); in biliary obstructions, bile ducts cannot deliver bile to duodenum resulting in hyperbilirubinemia, toxic accumulation of bile salts and jaundice (Sullivan and Rockey, 2017). If choledocholithiasis represents the leading cause of benign biliary obstruction, pancreatic head carcinoma represents the leading cause of malignant biliary obstruction. (Saluja et al., 2007).

Obstructions may arise at any level within the biliary tree and malignant obstructive jaundice can occur following primary cancers e.g. pancreatic cancer, cholangiocarcinoma, hepatocellular carcinoma, gallbladder cancer, lymph nodal compressions and liver metastases (De Lorenzo et al., 2018)

Given the deleterious effects caused by the gradual and inexorable increase of hyperbilirubinemia, biliary drainage is usually performed with the aim of relieving symptoms, improving quality of life and restoring serum biochemistry to normal. It is also an essential element for palliative systemic chemotherapy, palliative radiotherapy or surgical resection, when feasible (Crosara et al., 2013). Procedures of biliary drainage comprise surgical bypass and extensively used palliative techniques such as percutaneous transhepatic biliary drainage (PTBD) and endoscopic biliary drainage (EBD), each with its specific advantages and limits (Hiratani et al., 2019).

2.1.3 Percutaneous transhepatic biliary drainage (PTBD)

Historically, PTBD was introduced in the early 1980s and has been used ever since. Early publications by Riemann and Faithfull demonstrated high technical success rates and low complication rates [7, 8]. They described the method as a temporary or permanent depending on wether surgery was still an option for treatment or not.

The PTBD procedure is usually performed under no sedation, minimal sedation or conscious sedation. The exception is usually for uncooperative patients who require general anaesthesia. An initial pre-procedure liver ultrasound is done to determine the access site. Doppler ultrasound is utilized to differentiate bile ducts and blood vessels. The skin is then cleaned and draped under the standard surgical skin cleaning procedures. Local anaesthesia is given under ultrasound guidance at the expected puncture site to the skin and subcutaneous tissue up to the liver capsule under ultrasound guidance, and a skin nick is made with a small blade size 11/15.

Using a 21G Chiba needle or micropuncture needle, the skin and liver are punctured under ultrasound guidance. A peripheral bile duct is then punctured using ultrasound guidance. The stylet is removed, and once bile is seen flowing out of the needle, contrast is given via the micropuncture needle, and a cholangiogram is done to confirm that the needle is placed within the biliary system. A 0.018' nitinol micro guidewire is then advanced into the bile ducts and the needle removed over it.

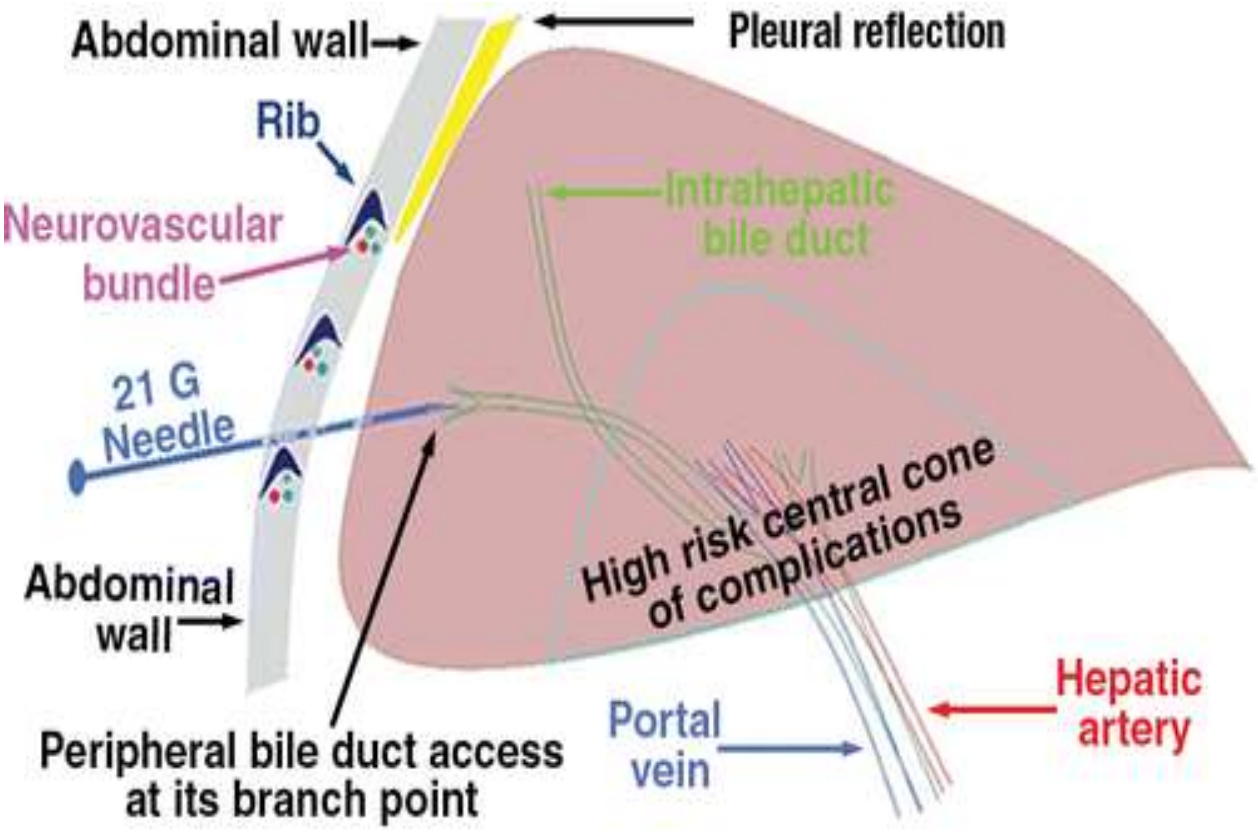


Figure 1: Coronal illustration of the right-sided biliary access technique in accessing a peripheral bile duct. The needle is traversing the soft tissues above the upper border of the rib but below the pleural reflection.[1]

Serial dilatation is done with the assembled dilators and then a 0.035 standard Teflon guide wire is advanced under fluoroscopic guidance into the confluence of the RH and LHD or CHD. Once the position is confirmed, an 8F or 10F biliary drainage tube is inserted over the wire and position confirmed on fluoroscopy. If an endo-exo or internal-external drain is required, a 0.035 or 0.038 hydrophilic wire is advanced through the dilator into the CBD, and up to the duodenum, under fluoroscopic guidance. A 40 cm 8F/10F drain is then advanced under fluoroscopic guidance with its end holes placed in the duodenum and the proximal side holes located above the level of obstruction, usually at the hilum. Final cholangiogram is then done using

[1] https://www.researchgate.net/profile/Karthikeyan-Damodharan/publication/314972115/figure/fig2/AS:731798682214400@1551485810123/Coronal-projection-illustration-of-the-technique-used-to-access-a-peripheral-bile-duct_W640.jpg

contrast injection through the newly placed biliary drain. The biliary drain or tube is secured to the skin using a suture and dressing done. The drainage tubes are attached to an external bag where the bile will drain.

Percutaneous transhepatic biliary drainage (PTBD) is a minimally invasive procedure for drainage of the biliary system (Yadav et al., 2018). PTBD is preferred as the primary procedure in patients who have had prior bilio-enteric anastomosis, or those who are unsuitable for endoscopic retrograde cholangiopancreatography (ERCP) due to other reasons. Imaging plays an essential role in the diagnosis of underlying etiology and provides a road map for the procedures (Patel et al., 2006). Imaging modalities for evaluation of biliary tree are ultrasonography (US), endoscopic ultrasound (EUS), computed tomography (CT), and magnetic resonance imaging MR cholangiopancreatography (MRCP) (Katabathina et al., 2014).

PTBD can be a lifesaving procedure in certain clinical conditions, especially in the setting of severe cholangitis. The technical and clinical success of PTBD depends on multiple factors including patient-specific, disease-specific, and technique-specific factors as well as the expertise of the interventional radiologist. In routine interventional radiology (IR) practice, the degree of peripheral biliary ductal dilatation is considered the most critical factor for the technical success of PTBD. Greater technical success can also be expected in cooperative patients who can follow breath-hold instructions (Das et al., 2021).

Percutaneous transhepatic biliary drainage (PTBD) may be performed for both benign and malignant causes (Yadav et al., 2018). It can be used as a palliative procedure in non-operable patients, a bridging procedure for further biliary stenting, or as an emergency procedure for clinically unstable patients presenting with acute severe

cholangitis. PTBD is indicated for biliary drainage, management of postoperative complications and biliary access route establishment for dilatation of biliary strictures, stent placement, stone removal, endoluminal therapy and tissue sampling (Gupta et al., 2020).

PTBD requires dilatation of the ductal system for the intervention radiologist to puncture the duct. For routine purposes, peripheral ductal dilatation of more than 2 mm is desirable. However, under expert hands, nondilated or minimally dilated systems can also be punctured using micropuncture sets and other techniques.

The presence of moderate to gross ascites has been reported to increase the risk of bleeding and biliary peritonitis (Bonshock et al., 2017). The presence of a distended gallbladder should be recorded as in some situations when all attempts to drain the biliary radicles have failed, and drainage may be achieved via percutaneous cholecystostomy (Gupta et al., 2015). Hence, detailed review of imaging is vital to the success of biliary drainage in patients with surgical obstructive jaundice. It plays an important role in deciding whether to undertake a percutaneous or endoscopic drainage and in patients undergoing PTBD; it helps in allowing adequate planning of the procedure.

The choice of the optimal technique in patients with malignant obstructive jaundice is based on several factors including site of obstruction (e.g. proximal or distal), the expected survival, the purpose of drainage, the postprocedural therapeutic strategies and the level of expertise of the centre (Tapping et al., 2011).

Obstructive jaundice is not a definitive diagnosis. Early investigation to elucidate the precise etiology is of great importance because pathological changes (e.g., secondary biliary cirrhosis) can occur if the obstruction is unrelieved. A vast array of invasive and non-invasive diagnostic tests are available to diagnose and establish the etiology of surgical obstructive jaundice (Briggs & Peterson *et al*, 2007). Invasive tests may cause cholangitis and imaging techniques like computed tomography (CT) scan, PTC, ERCP and MRCP are expensive and are not readily available in most centers in developing countries, and ultrasonography remains the only diagnostic test available (Chalya, Kanumba, & Mchembe, *et al* 2011).

Patients with tumors causing biliary tract obstruction are often asymptomatic until disease is significantly advanced. Symptoms of obstructive jaundice can significantly impair quality-of-life unless intervention to decompress the biliary tract, either curative or palliative, is performed.

Most of the cases of malignant obstructive jaundice are already advanced and unresectable by the time they are diagnosed, hence carry dismal prognosis with palliation being the only option left. Obstruction needs to be drained even in such cases for alleviation of pain, cholangitis, and pruritus or in certain cases to initiate chemotherapy or intrabiliary brachytherapy. Over the years, palliative care has evolved with the introduction of newer methods and improvisation of existing techniques. Recent palliative measures not only prolong longevity of the patients but also improve the quality of life, hence increasing the acceptance to such procedures (Teixeira *et al*., 2013).

The outcome of treatment of malignant obstructive jaundice may be poor especially in developing countries where advanced diagnostic imaging and therapeutic facilities are not readily available in most centers. The mortality and morbidity of malignant obstructive jaundice are dependent on the cause of the obstruction, and the assessment of any factors associated with it which influence the morbidity and mortality. It has been reported that obstructive jaundice continues to be associated with significant morbidity and mortality despite recent advances both in preoperative diagnosis and postoperative care. Understanding complications responsible for increased morbidity and mortality in these patients will better guide appropriate management and lead to improved survival according to (Chalya *et al*., 2011) a study done in north western Tanzania . Further more a study by (stoker *el al* 2003) looked at early complications which were defined as complications occurring within 30 days of the procedure, of which cholangitis was the most common at 9%.

Methods of biliary drainage include: bypass, minimally invasive imaging guided procedures; Percutaneous Transhepatic Biliary Drainage (PTBD) and Endoscopic retrograde cholangiopancreatography (ERCP).

Both ERCP and PTBD are well-established and effective means of biliary drainage for palliation in unresectable cases. With increased technical success rate and expertise in these minimally invasive procedure, recent time has witnessed an exemplary surge in the demand for such procedure over surgical bypass. Selecting an option over other; however, is a multidisciplinary opinion, which not only involves expertise of operator and the site of obstruction but also takes into consideration other factors such as expected survival and the level of post-procedural care provided to the patients. ERCP is usually performed in cases of distal CBD block (beyond hilum), while PTBD is preferred in proximal biliary obstruction (Covey & Brown, 2008).

Radical tumor resection is the primary means of treating a malignancy causing obstructive jaundice. But many patients (approximately 80%) lose radical surgery opportunity because of these features of tumors including insidious onset, low early diagnosis rate, etc. So far, endoscopic retrograde cholangiopancreatography (ERCP) has become the best treatment choice for malignant obstructive jaundice. But even if operated by experienced endoscopists, there are still 3% to 10% failure rate in the management of these patients with malignant obstructive jaundice (Shu *et al*., 2012) Percutaneous transhepatic biliary drainage (PTBD) or endoscopic ultrasonography guided biliary drainage (EUS-BD) has become the preferred treatment for malignant obstructive jaundice when ERCP failed. Several studies (Dhir *et al*., 2014; Ogura *et al*., 2016; Xu *et al*., 2015) have demonstrated that these procedures are effective and safe for palliative biliary drainage in patients with malignant obstructive jaundice. However, there have been few published studies on PTBD procedure locally, and the associated complications (Lee *et al*., 2016).

2.2 Patient clinical and laboratory parameters before and after percutaneous transhepatic biliary drainage.

In Croatia, it was found that the mean value of serum concentrations of total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase and gamma glutamiltransferase 24 hours before the biliary decompression by ERCP were significantly above the upper referential value, and 24 hours after the ERCP it dropped to normal with their being statistically significant difference (Gudelj Gracanin et al., 2013).

In a study in Pakistan on aetiology of malignant obstructive jaundice, liver functions biochemical investigations was done which showed high serum bilirubin and alkaline phosphatase level (Siddique *et al*., 2008). In another study in Pakistan, the values of bilirubin and alkaline phosphatase were found to be higher In the malignant cases (Cheema, Ahmad, & Gondal, 2001).

In a study in India, a total of 50 cases of histologically proven malignant obstructive jaundice were evaluated. The most common presentation of the patients was with yellowish discolouration of sclera and urine seen in 44 patients followed by pruritus seen in 38 patients. Dilated Common Bile Duct with/without pancreatic duct dilatation was the most common finding on sonography followed by a mass seen in the head of the pancreas. Moderately differentiated adenocarcinoma was the most common finding on histopathology followed by well-differentiated adenocarcinoma (Shetty *et al*., 2016). In another study in India, raised bilirubin, alkaline phosphatase and decreased albumin were more pronounced in malignancy (Kumar *et al*., 2016).

In a study done by (Knap *et al*., 2016), they were able to show that PTBD normalized the levels of plasma bilirubin and alleviate the symptoms of jaundice by looking at the levels of plasma bilirubin pre and post procedure. They also reported a significant improvement in the quality of life of the patients in the period following successful completion of the procedure. Apart from looking at the level of plasma bilirubin they also looked at the gamma GT and ALP levels. This method of data collection also agreed with a similar study that was done in Alexandria University in Egypt by (El-Haddad, Kassem, Shehata, & Afifi, 2016) where the data collection tools involved looking at Clinical data which were symptoms of jaundice, cholangitis and right hypochondrial pains while looking at similar lab parameters.

In their study evaluating clinical and technical outcomes after percutaneous biliary drainage, Zhang et al. described a successful technical outcome as correct placement of the biliary drain with subsequent active drainage of bile. They described a successful clinical outcome as a reduction of >20% in the serum bilirubin levels done seven days after the procedure (G. Y. Zhang et al., 2014). Kumar et al., in evaluating liver function recovery after biliary drainage percutaneously, found that although bilirubin levels were shown to decrease after the procedure, certain other factors influenced the rate of decrease. These factors included the duration of biliary obstruction, the degree of hepatic parenchymal disease or tumour extent, the initial serum bilirubin levels and the presence of biliary sepsis. These factors were found to delay the rate of reduction of bilirubin levels, thought to be due to their association with ongoing hepatocyte impairment (S. Kumar et al., 2020).

No study has been done regarding this country's PTBD clinical and technical outcomes. PTBD, worldwide, has been shown to be invaluable in the treatment of non-resectable causes of obstructive jaundice. The cost of the procedure and the lack of adequate numbers of trained IR in Kenya have been prohibitive in getting these services to deserving patients. The same situation is seen in similar developing countries like Ghana (Sarkodie, Botwe, & Brakohiapa, 2020).

This study aims to show technical and clinical success rates from PTBD with the objective of influencing policy decisions regarding mainstreaming PTBD procedures in the management of obstructive jaundice, to improve quality of life and support or permit palliative or definitive surgical or oncological management.

Technical outcomes are described as measures of technical success while performing a procedure and can be influenced by the skill of the interventional radiologist, patient factors and the anatomical and technical difficulties in carrying out the procedure.

The correct placement of the catheter into the biliary system, and drainage of bile, shall be an indication of technical success in this study. The inability to cannulate the biliary system or place the drain in the correct position will be termed a technical failure. Any complications arising from the attempt to cannulate the biliary ducts will be documented.

Clinical outcomes are described as measures of changes of the patients' symptomatology, improving or worsening health condition, quality of life and presence of complications after a procedure. In this study, we shall evaluate the percentage reduction in bilirubin levels in the intermediate short term and the document the changes in symptomatology.

2.4 Complications related to the Percutaneous Transhepatic Biliary Drainage (PTBD)

Obstructive jaundice secondary to malignancy represents a relatively frequent clinical condition in patients affected by primary or secondary hepato-biliopancreatic malignancies and it is considered a negative prognostic factor with important sequelae for quality of life and survival, regardless of the extent of the disease (Khan et al., 2019). In a retrospective study including patients with gallbladder cancer and who underwent surgical resection with curative intent, patients who presented with obstructive jaundice secondary to malignancy showed poorer outcomes than patients without jaundice (Young et al., 2012). Since the onset of jaundice is often insidious and silent, only about 20% of

patients with obstructive jaundice due to a malignancy can receive radical surgery because of the extent of the disease; for patients without surgical indications or for patients with unresectable malignant obstruction, percutaneous and endoscopic palliative procedures can relieve symptoms and improve quality of life (Vogel et al., 2015).

The rate of complications in PTBD is relatively low, between 4 and 12%. Rees et al. showed a strong correlation between the annual number of PTBD placements per centre and complication rates, with more experienced centres having the lowest reported complication rates (Rees et al., 2020). (Liu et al.,2018) showed that subsegmental entry was associated with a lower complication rate compared to a most possible peripheral entry level .

Complications occur more frequently when bile ducts are not dilated. The most common complication is haemobilia, which occurs in up to 10% of all cases. Bleeding complications and biliovascular fistulas occur in up to 2.5% and 1.5% of cases. Infectious complications include sepsis, cholangitis and cholecystitis. Pneumothorax and peritonitis are rare complications. In long-term drainage, drains can become obstructed which may cause discomfort, leakage or cholangitis. If venous or arterial bleeding occurs, the optimal treatment strategy depends on the extent of bleeding and the sources of the bleeding. Potential treatment consists of upsizing the catheter, checking positions of the side holes of the drain and flushing of the drain over several days. Transfemoral angiography may be necessary to locate the bleeding and treat with embolisation (e.g. coils or glue).

During PTBD, presence of significant free fluid in perihepatic space hampers the access into the biliary system as well as increases the risk of bleeding or bile leak into the peritoneal space (Gown and Laasch, 2015). Deranged coagulation profile increases the risk of hemorrhagic complications (Patel et al., 2012). A significant number of patients with severe cholangitis and/or those with biliary-enteric anastomoses may have minimal biliary ductal dilatation, altered sensorium, ascites, or coagulopathy. In the presence of these situations, patients may be denied potentially lifesaving procedure. The present study evaluates the technical and clinical success as well as safety of PTBD in these patients at higher risk for adverse events.

In a systematic review that looked at the technical success rate and safety of percutaneous transhepatic biliary drainage (PTBD) versus endoscopic biliary drainage (EBD) in obstructive jaundice secondary to a malignancy, patients receiving PTBD showed a lower risk of pancreatitis (OR=0.14) and cholangitis (OR=0.52) when compared to EBD while PTBD was associated with higher risk of bleeding (OR=1.78). (Rizzo et al., 2020).

In a study assessing the complications and risks associated with PTBD, Hemobilia [transient (lasting < 12 h) in 5 (8.7%) patients and persistent in 1 (1.7%) patient], vasovagal reaction (n = 1, 1.7%), and biliary peritonitis (n = 3, 5.2%) were observed in the post-procedural period. The patients who had persistent hemobilia responded to catheter upgradation. Two (3.5%) patients who developed biliary peritonitis had moderate ascites in the pre-procedure period. Biliary peritonitis required prolonged hospitalization and percutaneous catheter drainage (Gupta et al., 2020).

At the endpoint of the study at 3-months, majority of the patients (56.2%) continued to be on external drainage due to failure of a single session of internalization (n = 18, 31.5%). One-month mortality was recorded in 10 (17.5%) patients. Four (7%) deaths in this period occurred in patients who underwent bedside PTBD. At 3-month follow-up, mortality was recorded in 37 (64.9%) patients. Out of the overall mortality, 78.4% (n = 44) of deaths occurred in patients with underlying malignancy. There was no statistically significant difference in the technical success and complication rate between patients with non-dilated and dilated biliary systems (Gupta et al., 2020).

Complications occur more commonly in patients with minimally dilated or un-dilated bile ducts due to the complexity or difficulty of cannulating the ducts. They can be summarized as being due to the access, catheter, or stent, or due to vascular and non-vascular complications (Venkatanarasimha et al., 2017).:

Stent related complications include fracture, migration, obstruction, disjunction, and balloon ruptured by stent struts. Access related complications including pain, pleural space transgression, Inadvertent arterial access, bile duct perforation, ascites, inadvertent extrahepatic bile duct access and subcapsular hematoma. Non-vascular complications including cholangitis, acute pancreatitis, bile leakage, abscess or biloma. Bleeding or vascular complications including bilioportal vein fistula, pseudoaneurysm, catheter erosion into inferior vena cava and bilioarterial fistula. Catheter related complications include buckling, dislodgement, obstruction, and fracture (Venkatanarasimha et al., 2017).

Pain

Pain at the access site is the commonly reported complication associated with PTBD intervention and might occur during the PTBD procedure as a result of the distension of the capsule of the liver or due to dilation of stricture and during catheter or dilator manipulation (Venkatanarasimha et al., 2017). While intravenous sedation is the common approach to intraprocedural pain management, general anesthesia has been recommended by some interventionist whenever available to maximize the control of pain and enable large caliber biliary catheters placement (Sutter and Ryu, 2015). For the preprocedural pain prevention, nerve blocks have also been recommended (Culp et al., 2006). Whenever the catheter is inadvertently put inferior to the rib, access site pain associated with periosteal irritation or nerve irritation becomes common especially with the punctures are made to the right side hence impinging on the intercostal nerve. While pain is mainly managed using paravertebral nerve blocks or anaesthesia, patients who have intractable pain might need the replacement of the percutaneous biliary drainage catheter with a new percutaneous access site or indwelling biliary stents (Venkatanarasimha et al., 2017).

Pleural Transgression

During drainage catheter placement, inadvertent pleural transgression can occur leading to clinically significant pneumothorax, bilious effusion and hemothorax. This occurs in 0.5% to 2% of the PTBD cases (Winick et al., 2001). Besides, the trans pleural catheter placement is a bacterial seeding predisposing factor, especially along the tract, which can lead to chronic fistulation or empyema. In case of pleural transgression, transhepatic access site is recommended with the removal of the catheter placed initially within weeks to provide time for tract maturation and

eliminate possibilities of complications (Maher et al., 2002). Despite this, the management of these complications can be difficult and high hepatic punctures should be avoided by individuals carrying out this procedure in order to prevent the occurrence of pleural transgression (Venkatanarasimha et al., 2017).

Subcapsular Hematoma

These are rare in occurrence and are commonly associated with venous bleeding. Subcapsular hematoma can be reduced through the minimization of the frequency of needle puncture through the liver capsule (Venkatanarasimha et al., 2017).

Inadvertent Vascular Access

The inadvertent punctures of venous radicle or peripheral arterial especially with the 22- or 21-gauge need are common but not clinically important. However, large caliber puncture of the segmental or central hepatic artery has the potential of causing serious bleeding (Saad et al., 2008).

Nonvascular Complications

The non-vascular complications associated with biliary drainage include cholangitis, peri catheter bile leakage into the skin or peritoneum, biloma, fistula formation, pancreatitis and abscess.

Bile leakage

This is a prevalence complication which is manifested as exudation of fluid around the site of catheter insertion or as pain in the upper right quadrant. The bile leakage into the peritoneum is likely to result in peritonitis and this is mainly as a result of the catheters central portions being blocked due to debris. This necessitates the

replacement of the earlier catheter with another one that is of a larger size. Bile leakage might also result if the proximal hole is located beyond the blockage and the catheter slips forward or if the catheters holes on the proximal side is closer to the edge of the hepatic ducts. In this situation, re-adjustment, change or follow up cholangiography are recommended.

Acute Pancreatitis

The occurrence of acute pancreatitis is more common after biliary drainage. Its prevalence has been found to range between 4% to 6% (Al-Bahrani et al., 2006). The external and/or internal biliary drainage catheter placement, distal biliary manipulation, and ampulla vater stent placement are associated with greater risk for acute pancreatitis hence important for interventionist to explain the risk to the patients before PTBD. Alerting patients for them to stay alert for the likelihood of pancreatitis in case they experience severe abdominal pain after the intervention is a recommended measure to ensure timely diagnosis and intervention (Venkatanarasimha et al., 2016).

Biloma and Hepatic Abscess

Biloma formation can result due to biliary catheter obstruction that is persistent in nature. This may progress to the formation of an abscess. Patients with biloma and hepatic abscess may present with elevated body temperature, which is recurrent in nature and might not improve even after antibiotic treatment. Gas fluid collection is usually show on catheter cholangiogram which communicates with the tree of the biliary. In some instances, inadequate length may be noted in the side holes located proximal to the biliary obstruction location (Venkatanarasimha et al., 2016).

Vascular Complications

Bleeding s one of the most common complications occurring in 2% to 3% of the patients undergoing PTBD (Saad et al., 2008). Due to nontreated or undiagnosed bleeding, it has proven fatal hence need for all interventionist to have a high suspicion index for it and offer management using interventional radiology techniques. There is varied manifestation of bleeding clinically, varying with the cause. For the case of major vessel injuries, the bleeding mainly manifest 3 to 7 days post the original PTBD (Fidelman et al., 2008).

Peri tubal bleeding can occur with oozing of blood from the perihepatic, skin, occurring ad hemothorax, subcapsular hematoma or hemoperitoneum, or condition of gastrointestinal bleeding like melena or haemobilia. The common signs of bleeding are drainage of the frank blood into the external drainage bag, at rates more than 200-250Ml for each hour, skin site red blood cells squirting, and hemodynamic instability. The course of treatment is determined based on the hemodynamic stability of the patient and this can be an indication of the injured blood vessel type (Venkatanarasimha et al., 2016).

Arterial Injury

In a review covering 13 years, including 1,386 PTBD cases, the prevalence of arterial injuries was found to be 2.2% (Fidelman et al., 2008). The most common arterial injury risk factor found in the review included access with a no longer utilized needle of 18-guage, and insertion of more than 3 catheters for PTBD. In patients who are hemodynamically stable, the cause of the bleeding can be revealed using CT angiography including information on bilio-arterial fistula, pseudoaneurysm, and intercostal arterial injuries. The manifestation of the arterial injury might occur

months or weeks after PTBD, during the change of the catheter, as this leads to the catheter tamponade release. The insertion and capping of the catheter should be done immediately for the management of this situation. Arterial injury cases are also concrete indications for urgent embolization and angiography. During angiography, in case it becomes difficult to identify extravasation of the contrast material or arterial injury when the catheter for PTBD is in place, withdrawal of the catheter should be done and obtaining of angiogram done while the wire is in situ to identify the transgressed artery. When the identification of the injury is done, replacement of the catheter can be done over the wire to offer a tamponade. The coil can be used to embolize and super selectively cannulate the injured artery. In case the coil embolization is utilized, the back and front pseudoaneurysm openings should be closed to avoid reperfusion from the intrahepatic arterial collateral vessels which might lead to bleeding. (Venkatanarasimha et al., 2016).

Bilioportal Fistula

Venous injury can be indicated by continuous oozing of blood, dark in colour from the site of peri tubal together with haemobilia. In such circumstances, removal of the catheter should be done to show extra dark venous blood an indicator of biliovenous fistula possibility (Lynskey et al., 2007). The bilioportal fistula is common due to the portal triad anatomy where bile duct and hepatic artery lies side by side anterior to the radicle of the portal vein.

In case the injury is located on a small portal venous radicle on the peripheral, the problem can be solved by re-insertion of a catheter, larger in size using the same tract with the positioning of the side holes done deeper into the biliary tree. This is due to the fact that larger tube will result in a tamponage of the bleeding offering the tract

opportunity to heal. However, in case of transgression of the central venous radicle, which is larger, tract embolization using the coil on any side of the transgressed vein during the withdrawal of the sheath can allow for the tract tamponage hence helping keep the potency of the portal venous radicle (Chanyaputhipong et al., 2014). Consideration for the insertion of stent graft can also be done (Lorenz et al., 2010).

Catheter Erosion into the Inferior Vena Cava

This complication is not common. However, it might result in vessels adjacent to the biliary catheter resulting in haemobilia or catheter blockage (Venkatanarasimha et al., 2016).

Catheter-related Complications

Catheter fracture

Catheter fracture can lead to catheter fragments remining inside the biliary tree. Such fragments might not be detected especially when the pieces are small or when the personnel do not if the catheter retrieved is intact. utilizing the sign-out checklist after the procedure is recommended to determine if the catheter and guide wires are intact. Some intervention radiologists are in support of leaving the fragments inside as long as obstruction does not occur due to them while others support the removal of the remaining fragments due to fear of likelihood of infections occurring or likelihood of future obstruction (Maher et al., 2002).

Obstruction and Blockage

In both acute and chronic settings, catheter blockage Is a common complication. Occlusion of the catheter is likely to result in cases of thickened debris or materials or products of blood in the bile. Patient education on the need for frequently flushing the

catheter with saline solution that is sterile is recommended. The challenging bit I s the exchange or unblocking of the catheter, especially where the catheter has been in vivo for more time. Probing the catheter or unblocking the catheter by injecting sterile warm and saline solution through it is recommended for removing the occluding material (Maher et al., 2002).

Dislodgement and Malpositioning

Malposition of the catheter can result due to movements during respiratory, leading to them moving away from the biliary tree. This is usually a problem in the more flexible, small caliber drainage catheters that are purely external. During 7 to 10 days post initial placement of the catheter, a granulating parenchymal tract is established from the biliary tree to the capsule of the liver. Re-insertion of the completed dislodged catheter can be done using the same tract. This can be done after gaining access via hydrophilic guidewire and a diagnostic catheter using guidance of the fluoroscopy (Venkatanarasimha et al., 2016).

Buckling

Buckling results due to tight fixing of the catheter to the entry site of the skin. In such scenario, pulling out of the catheter from the liver occurs due to movements during breathing resulting in looping between abdominal wall and liver. This can result in catheter obstruction or kinking. Reposition of the catheter can be done via a guide wire under the guidance of fluoroscopy

The PTBD procedure has been linked with complication of varied prevalence, 3% to 10% and mortality rates inked to the procedure ranging from 0.1% to 0.8% (Weber et al., 2009).

(ii) Complications and instruments

Increased expertise and better instrumentation observed technical success of PTBD to be approximately 90–95% with fewer complications. These complications can be further reduced by keeping the biliary manipulation to minimum and good antibiotic coverage (Burke *et al*., 2003). This can be done with the use of new and more improved hardware for the procedure.

These complications include pain, pericatheter leak, Cholangitis, sepsis biliary peritonitis, haemorrhage, pancreatitis and Pleural effusion, pneumothorax. Catheter dislodgement is more common in external than internal drainage catheters due to better anchorage in the latter (Xu *et al*., 2015).

Pericatheter leak (bile leak along catheter) is a frequently observed complication. It can be due to side holes of catheter lying outside the biliary system, catheter kink/block, or ascites. Management in such cases consists of catheter repositioning or upgradation depending on the findings of check cholangiogram (Xu *et al*., 2015).

Cholangitis and biliary sepsis are inevitable complications which can occur despite adequate antibiotic coverage. Although exact etiology is unknown, it can occur due to multitude of factors such as retrograde reflux of intestinal flora during the procedure, ex vitro infection tracking along the drainage catheter, or may be of hematogenous origin. Prophylactically, broad spectrum intravenous antibiotics covering Gram-negative bacteria should be instituted. In addition, during the procedure, manipulations should be kept to minimum coupled with limited use of iodinated contrast during procedural cholangiography. Symptomatic management should be done in such cases by continuing the antibiotics and maintaining the fluid balance (Xu *et al*., 2015).

According to Covey and Brown, hemorrhage/hemobilia after PTBD is usually transient and is less commonly seen with more peripheral biliary radicle puncture. As hepatic artery and portal vein also accompany the dilated biliary radicle, side holes of the drainage catheter may get positioned in these vascular structures, which can be corrected by catheter repositioning (Covey & Brown *et al*., 2008).

According to Padillo and colleagues, sudden onset or hemobilia occurring 1–2 weeks after the procedure is usually due to arterial injury (active extravasation or pseudoaneurysm), especially if it is pulsatile and there is pericatheter hemorrhage. Angiography needs to be done in such cases followed by embolization of bleeding artery (Padillo *et al*., 2001).

In a study on Percutaneous Transhepatic Biliary Drainage in the management of malignant obstructive jaundice, common complications of PTBD were found to be biliary bleeding, abdominal or hepatic subcapsular hemorrhage and bile leakage (Huang P, Zhang, Zhang, Lv, & Lou *et al*., 2017).

According to a study in Germany, out of 385 of PTBD patients, 243 (63%) had malignant and 142 (37%) had benign bile duct strictures. At least 1 drainage-related complication was observed in 40% of the patients. With respect to the total number of drains, prosthesis complications occurred in 23%. Occlusion, dislocation, and cholangitis were the most common complications observed during PTBD therapy. Risk factors for cholangitis and occlusion were malignant disease, prior occurrence of complications, and bilateral drainage. Proximal stenosis of the biliary system was close to significant (Nennstiel *et al*., 2015).

Weber assessed complications associated with PTBD in Germany. Overall, there were 39/419 patients (9.31%) with procedure related complications including bleeding

(2.86%), acute cholangitis (1.67%), sepsis (1.43%), acute pancreatitis (0.48%), biloma (0.48%), intrahepatic haematoma (0.48%), biliovenous fistula (0.48%), biliopleural fistula (0.48%), pneumothorax (0.24%), peritonitis (0.24%), and perforation (0.24%). In patients with dilated and non-dilated intrahepatic bile ducts, total percentage of procedure related complication rates was 6.94% versus 14.5%, respectively. Procedure related deaths within this observation period were observed in 3 patients (0.7%). The cause of death was cholangiosepsis in all 3 patients. Major bleeding was observed in 5 patients (Weber *et al*., 2009).

(Teplick *et al*., 1991) performed transhepatic cholangiography in 107 patients who had non-dilated intrahepatic bile ducts. In 23/107 patients (21%) complications including two deaths (1.87%) occured.

(Funaki *et al*.,1999) evaluated the technical success and complications of percutaneous transhepatic biliary drainage in 130 patients with non-dilated intrahepatic bile ducts. Percutaneous biliary drainage was successful in 117/130 patients (90%). The overall complication rate was 9%, and no procedure-related death occurred. Technical success and complication rates in patients with dilated intrahepatic bile ducts were not analyzed.

Yee and colleagues investigated procedure-related complications and deaths in 206 patients with benign or malignant biliary diseases who underwent percutaneous transhepatic biliary drainage. The prevalence of procedure-related major complications and deaths were 5.34% and 1.94%, respectively. The authors reported substantially fewer complications in benign biliary diseases than those with malignant biliary diseases (Yee & Ho *et al*., 1987).

Review of of the tools used

The SIR (society of interventional radiology) developed the tools using the following methodology. Standards documents of relevance and timelines are conceptualized by the membersof the Standardsof Practice Committee. A recognized expert is identified to serve as the principal author for the standard. Additional authors are assigned dependent upon the magnitude of the project. An in-depth literature search is performed using electronic medical literature databases. Then a critical review of peer-reviewed articles is performed with regards to the study methodology, results, and conclusions. The qualitative weight of these articles is assembled into an evidence table, which is used to write the document such that it contains evidence-based data with respect to content, success and complication rates, and thresholds. When the evidence of literature is weak, conflicting, or contradictory, consensus for the parameter is reached by a minimum of 12 committee members using a Modified Delphi Consensus Method. Consensus is defined as 80% Delphi participant agreement on a value or parameter. Reported complication-specific rates in some cases reflect the aggregate of major and minor complications. Thresholds are derived from critical evaluation of the literature, evaluation of empirical data from Standards of Practice Committee members' practices and, when available, the SIR HIIQ® System national database. The draft document is critically reviewed by members of the Standards of Practice Committee via conference call and/or face-to-face meetings. Once the Committee finalizes the draft it is circulated to the SIR membership for further input/criticism during a 30-day comment period. These comments are reviewed and discussed by the Committee and appropriate revisions made to create the finished standards document. Prior to its publication the document is approved by the SIR Executive Council. The membership of the SIR Standards of Practice

Committee represents experts in a broad spectrum of interventional procedures from both the private and academic sectors of medicine. Generally Standards of Practice Committee members dedicate the vast majority of their professional time to performing interventional procedures; as such they represent a valid broad expert constituency of the subject matter under consideration for standards production. Technical documents specifying the exact consensus and literature review methodologies as well as the institutional affiliations and professional credentials of the authors of each document are available upon request from the SIR headquarters office. Complications are categorized using the definitions listed in Appendix II section C. The standards division understands that assignment of a particular event or case as a complication or failure can be subjective. The division is working on a system to allow more uniform categorization of such events. A series of vignettes has been created describing a range of interventional cases. Principles have been developed to assign events into categories. The cases described in the vignettes were assigned into categories of complication and failure using a consensus process similar to that used to create the quality improvement guidelines. The intent is to create consensus on the principles to be used and to create a library of "events" that will allow more uniform categorization of complications and failures.

Evaluation of pruritus

Although various methods have been described to evaluate pruritus, validation of these instruments in chronic pruritus is still pending. The Intemational Forum for the Study of Itch (IFSI) established a special interest group (SIG) for the evaluation and harmonization of measurement tools. The aim was to investigate the reliability and validity (criterion, concurrent and construct validity) and the internal consistency (Cronbach's alpha) of three pruritus intensity scales; namely, the visual analogue scale

(VAS), numerical rating scale (NRS) and verbal rating scale (VRS) in patients with pruritus. Statistical analysis showed a high reliability and concurrent validity ($r > 0.8$; $p < 0.01$) for all tools. Mean values of all scales showed a high correlation. In conclusion, high reliability and concurrent validity was fonnd for VAS, NRS and VRS. On re-test, higher correlation and less missing values were observed

2.3 Summary of review and research gap

From the reviews, it was noted that there is limited information on outcomes and complications of PTBD in Sub-saharan Africa. There is also paucity of such information in Kenya as we could not find any local study on the same.

CHAPTER THREE: METHODOLOGY

3.1 Study Site

The study was conducted at the Moi Teaching and Referral hospital, Radiology and Imaging department, in the Interventional Radiology section.

The hospital is in Eldoret town, the headquarters of Uasin Gishu county. It is 310km North West of the Kenyan capital Nairobi. It is the second National referral hospital which also serves as a teaching hospital for Moi University school of Medicine (MUSOM), School of Nursing, School of Public Health, and the School of Dentistry and Kenya Medial Training Centre, (KMTC). MTRH is an internship Centre for medical, nursing, and clinical officers.

Its catchment includes the western part of Kenya, parts of Eastern Uganda and South Sudan, roughly about 24 million people. The hospital has a bed capacity of 991 patients, with several departments which include surgery, pediatrics, medicine, obstetrics and gynecology, radiology and imaging, accident and emergency department, among others (www.mtrh.or.ke/24/09/2020).

There are several sub specialities including oncology services, intensive care unit services, kidney transplant services, alcohol and drug abuse rehabilitation services, spine and neurosurgical operations, cardiology and cardiothoracic services including open heart surgeries, corneal transplants, arthroscopic knee and shoulder surgeries and many more.

3.2 Study Design

This was a prospective study done over one year from July 2019-July 2020 following approval by IREC.

3.3 Study Population

It included all patients sent to the Interventional Radiology unit with biliary obstruction for PTBD placement. This patients were from the Medical and Surgical wards and the outpatient department.

3.4 Eligibility Criteria

3.4.1 Inclusion criteria

i. All patients with obstructive jaundice requiring intervention. Specifically those patients in the medical and surgical wards that have been designated by their primary doctors for percutaneous biliary drainage.

ii. Patients that have been referred from other centers to get PTBD placement at MTRH.

3.4.2 Exclusion criteria

i. All patients with previous PTBD drains who had come for reinsertion of the drain due to complications that arose.

3.5 Sampling technique

Census sampling was used. For the one-year study period, a total of 66 patients were included in the study. The previous year a total of 48 patients underwent the procedure.

3.6 Study procedure

The clinical teams working at the medical and surgical wards were sensitized on the study. All the patients with obstructive jaundice requiring PTBD were sent to the interventional radiology unit for PTBD placement from the medical and surgical wards. Written consent was sought from patients who met the inclusion criteria.

Percutaneous Transhepatic Biliary Drainage was done by the consultant interventional radiologist assisted by the researcher. Follow up was done routinely for all patients at MTRH after two weeks to assess acute complications and changes in laboratory and clinical parameters.

3.7 Data collection and management

Data abstraction form was used to extract data on demographic information, history of the patient, clinical examinations and laboratory results.

The clinical feature investigated was pruritus.

For pruritus intensity the verbal rating scale (VRS) was used. It's a tool with a high reliability and correlation index and therefore valuable clinical data can be obtained as per (Adam Reich *et al*., 2011). This scale is a 4 point Likert scale in which patients are asked to categorize their pruritus (eg, 0="no itch," 1="low itch," 2="moderate itch," 3="severe itch"). These tool is commonly used to measure pruritus at the moment of the assessment.

Complications were evaluated using the Society of Interventional Radiology (SIR) Clinical Practice Guidelines tool for complications by outcome. It classifies early complications as complications which occur within 30 days and late complications as those occurring upto 6 months post procedure. In our case early complications were evaluated after 2 weeks which fell in the category of within 30 days as per the SIR guidelines to allow it to coincide with the normal clinic review time in MTRH.

The laboratory investigation results were extracted to assess the bilirubin levels, alkaline phosphatase, ALT and AST levels. The pre PTBD laboratory results were obtained on the day of the procedure, while the post PTBD laboratory results were

obtained 2 weeks after the procedure when the patient came for the regular clinic review.

PTBD procedure was carried out as follows.

3.7.1 Patient Preparation

Before Percutaneous Transhepatic biliary drainage was done; the coagulation profile was checked. The parameters that were checked were prothrombin time (PT) and international normalized ratio (INR).

The recommended values for Prothrombin Time was less than four seconds while that of INR less than 1.5. Patients with higher values are more likely to bleed both during and after the procedure. For cases where the coagulation factors were deranged, vitamin K was given prior to the procedure and checked again to see if they were within the required range for the procedure to be done.

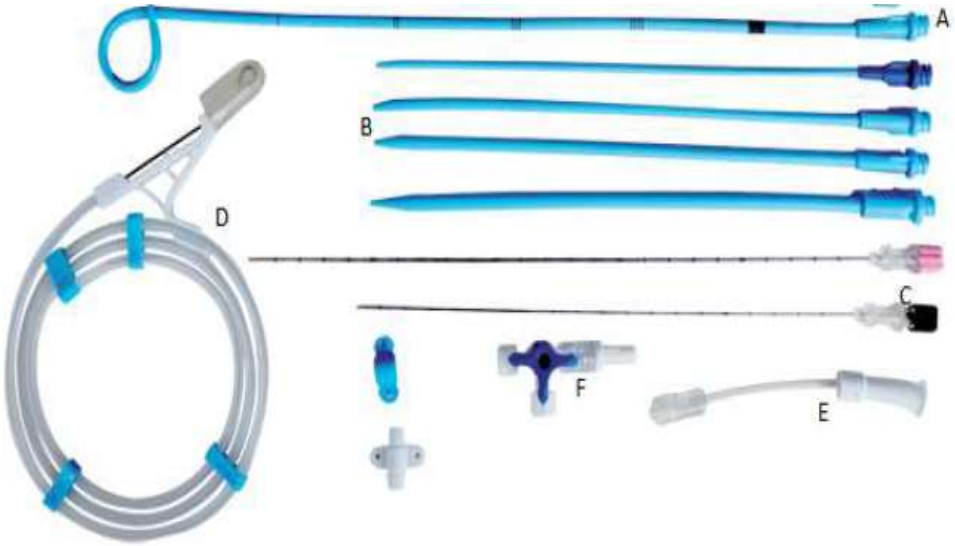
A dose of prophylactic intravenous antibiotics and fluids were given to provide prophylactic cover for infection prior to the procedure. The procedure was performed after at least six hours of fasting. In cases where there was ascites which is a relative contraindication it was drained before PTBD was performed.

During the procedure, local anesthesia (2% lignocaine) was infiltrated into the skin over the site of drain insertion to provide pain relief and for cases where the patient was uncooperative light conscious sedation with ketamine was used under the supervision of a qualified anaesthetist.

3.7.2 Equipment and Technique

1. Chiba needle 21G and an initial puncture needle 18G
2. Pigtail catheter + stylet
3. Mindray ultrasound machine – Model name /number M7
4. Serial plastic dilators
5. Guide wires
6. lignocaine
7. surgical blade

    1. lignocaine



A-PIG TAIL DRAINAGE CATHETER

B-FASCIAL DILATORS

C-INITIAL PUNCTURE NEEDLE-2 PART

D-J TIPED GUIDE WIRE TEFLON COATED

E-URINE BAG CONNECTOR

F-2 WAY STOP COCK

3.7.3 Procedure

Before starting the procedure the researcher went through the patients notes to confirm that the patient is indeed the right patient and that the consent forms have been signed and pre medications given. This is the prophylactic antibiotics to cover for infections, buscopan to reduce biliary spasms and morphine for analgesia.

The procedure was done with the patient in supine position after preliminary screening with ultrasonography. Depending on whether the right, left or both ductal system needed drainage a plan was made on how to make the approach to ensure maximum drainage was achieved. The skin over the area was cleaned and draped and 2% lignocaine injection was infiltrated over the site of drain insertion. The 18G Chiba needle was then used to puncture the skin and using ultrasonography as guidance it was advanced to a point approximately 1-3 cm away from the secondary biliary confluence. Once there was backflow of bile, a 0.032/0.035 inch soft "J" tip guidewire was passed through the needle, which was then exchanged for a 5Fr or 6Fr dilator followed by removing the Chiba access needle. Serial dilation was then done before placement of the 16Fr or 18Fr pigtail catheter with multiple holes for drainage. The catheter was then anchored to the skin with nylon sutures and using a connector. It was joined to a drainage bag.

Patients with the PTBD drain in situ were followed up for two weeks, there after discharged from the interventional radiology clinic. For the patients with diagnosed malignant causes that were unresectable they continued with chemotherapy and radiotherapy. Those with benign causes of obstruction like gall stones who had the procedure as a bridge to definitive management where followed up in the surgical clinic.

The patients were assessed post PTBD, and the findings on the laboratory tests and complications were recorded in a pre tested data form.

In general, the following information was recorded; patients' bio-data, the severity of clinical sysmptoms pre and post PTBD, laboratory findings before and after the procedure and post PTBD acute complications which were assessed in the two weeks post procedure.

3.8 Data analysis

The data was entered into MS Excel and analyzed using IBM Statistical Package for Social Sciences (SPSS) version 23.0. Continuous data such as age, creatinine levels, AST, and ALT were analyzed using measures of central tendency; means, median, and their respective measures of dispersion i.e (standard deviation, and interquartile range). Categorical variables were analyzed using frequencies tables and proportions. A comparison between continuous variables was made using the paired-sample t-test and a p-value of < 0.005 was considered statistically significant. This was for data that was normally distributed. The data where the variables were not normally distributed a Wilcoxon signed rank test was used.

3.9 Data Presentation

The results are presented in the form of tables, figures, graphs, prose form, and radiological images

3.10 Ethical Considerations

The study proposal was reviewed by the Moi University/ MTRH Institutional Research and Ethics Committee (IREC), and ethical approval granted. Permission was sought from the management of MTRH for the study to be carried out at the facility. Written informed consent was sought directly from the patients undergoing the procedure.

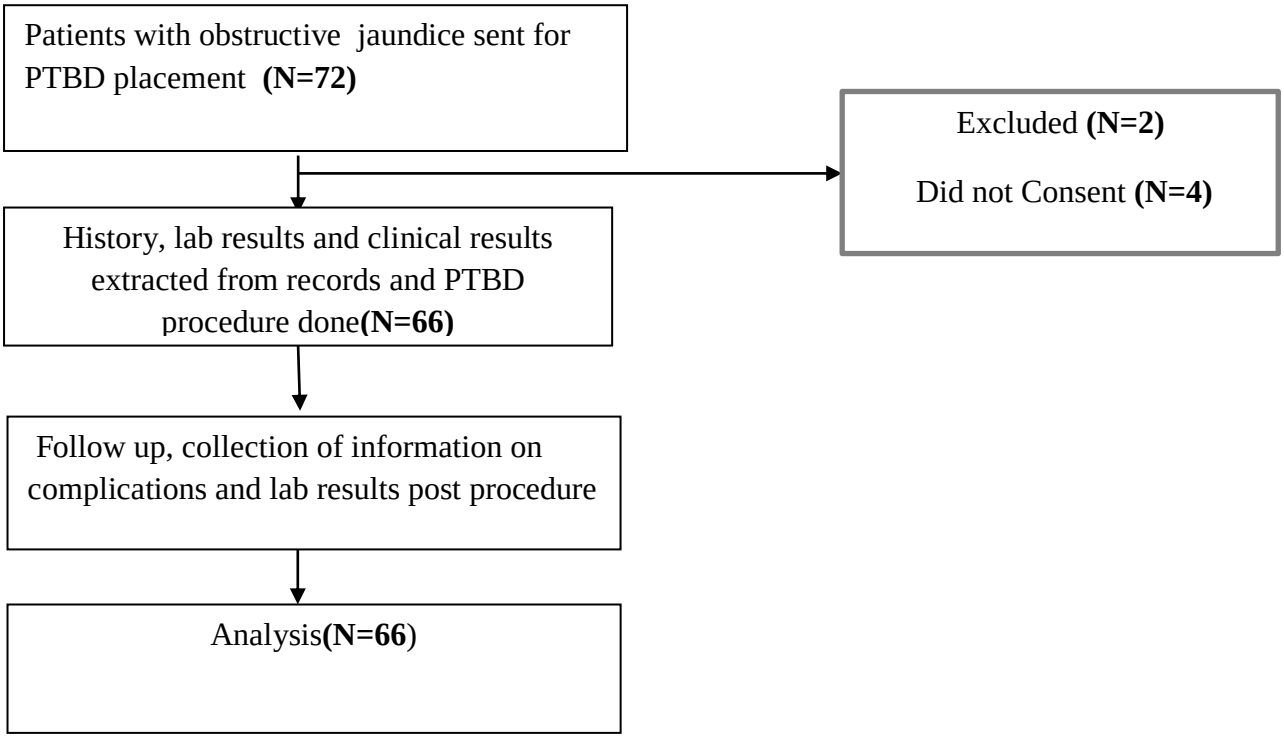
Consent: Written informed consent was sought from patients above 18 years undergoing the procedure. For those below 18 years of age, consent was sought from their parents or guardians or legally acceptable representatives. Participation in the study was voluntary, and the participants were free to withdraw at any time.

Confidentiality: The patients' information obtained from their medical records was kept confidential and stored in a lockable cabinet. The data was entered into a password-protected computer, and serial numbers were used instead of the respondents' names to protect their identity.

Benefits: There were no direct monetary benefits in the participation of the study; however, the findings of the study have the potential of informing the understanding of the complication of PTBD and main etiologies of obstructive malignancy jaundice hence informing improvement of the procedure and the management of such patients.

Risks: There were no significant risks because of participating in the study except the time spent participating in this study. Other risks were the fear of personal data leaks. This was solved by handling and maintaining the confidentiality of the information provided.

3.11 The study schema



CHAPTER FOUR: RESULTS

4.1 Demographic information

The mean age of the 66 participants was 62.65±12.15 (sd) years. The youngest was 33 years while the oldest was 83 years.

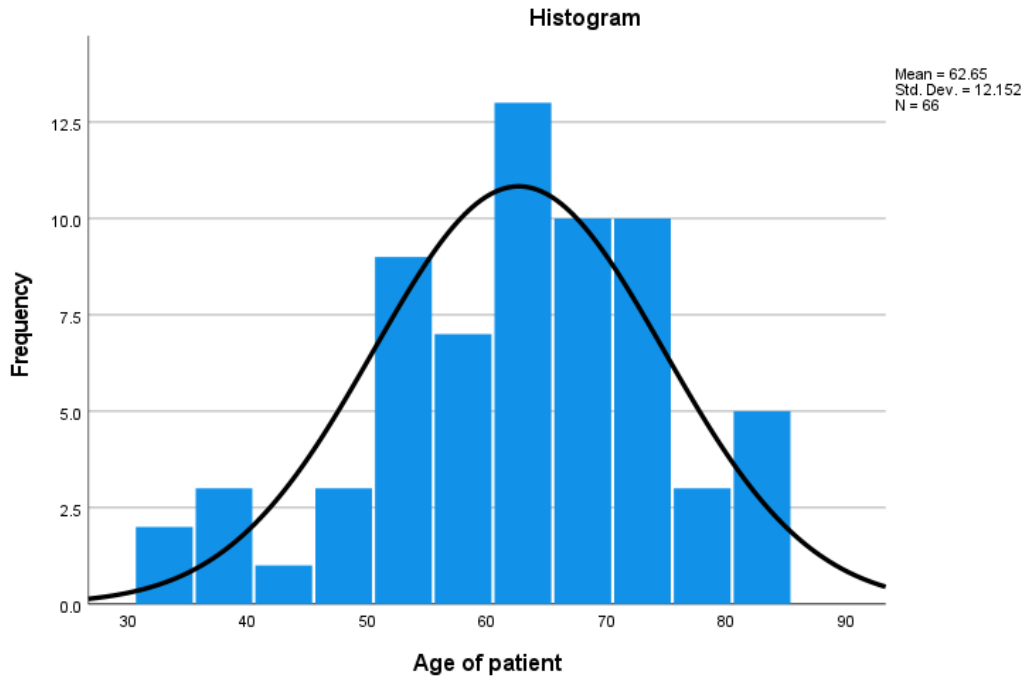


Figure 2: Age distribution

Of the participants, 35 (53.0%) were male while the rest (31; 47.0%) were female.

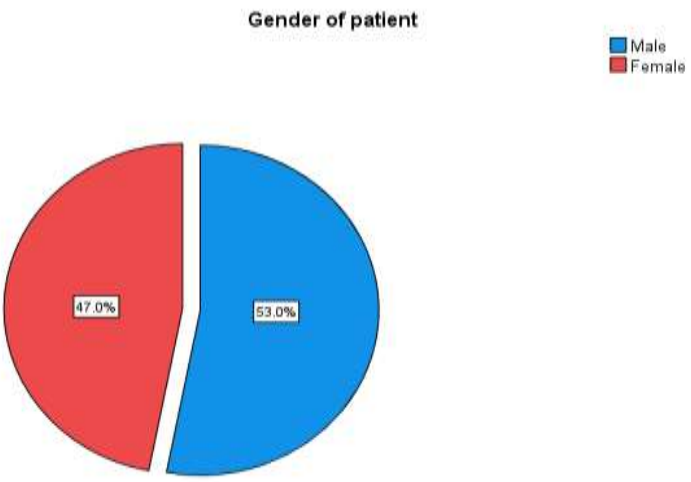


Figure 3: Gender of the patients

4.3 Clinical and laboratory parameters before and after percutaneous transhepatic biliary drainage

Most of the patients, 59 (89.4%) had pruritus before PTBD placement, while 7 (10.6%), did not have it.

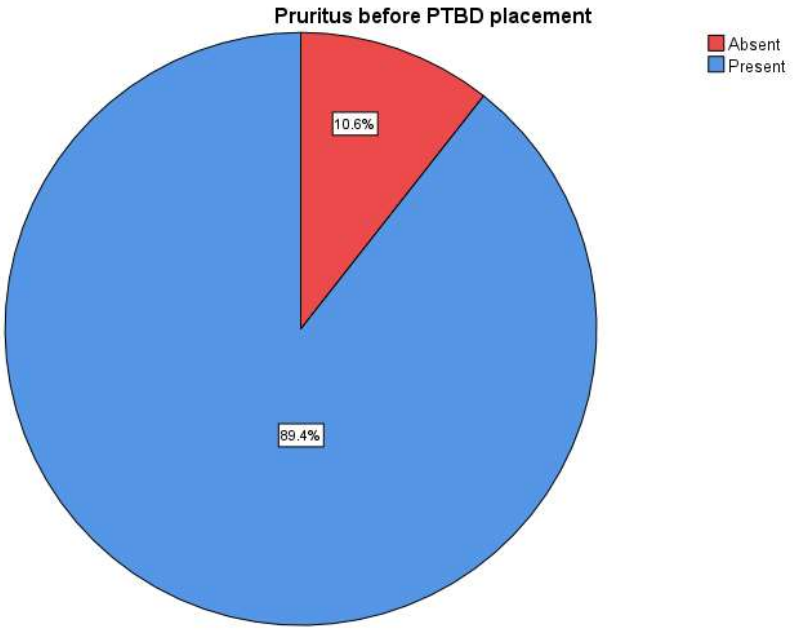


Figure 3: Pruritus before PTBD placement

Among the 59 who had pruritus before PTBD placement, 36 (61.0%) improved significantly, 12 (20.3|%) did not have any improvement, 8 (12.1%) had moderate improvement, and 3 (5.1%) had slight improvement.

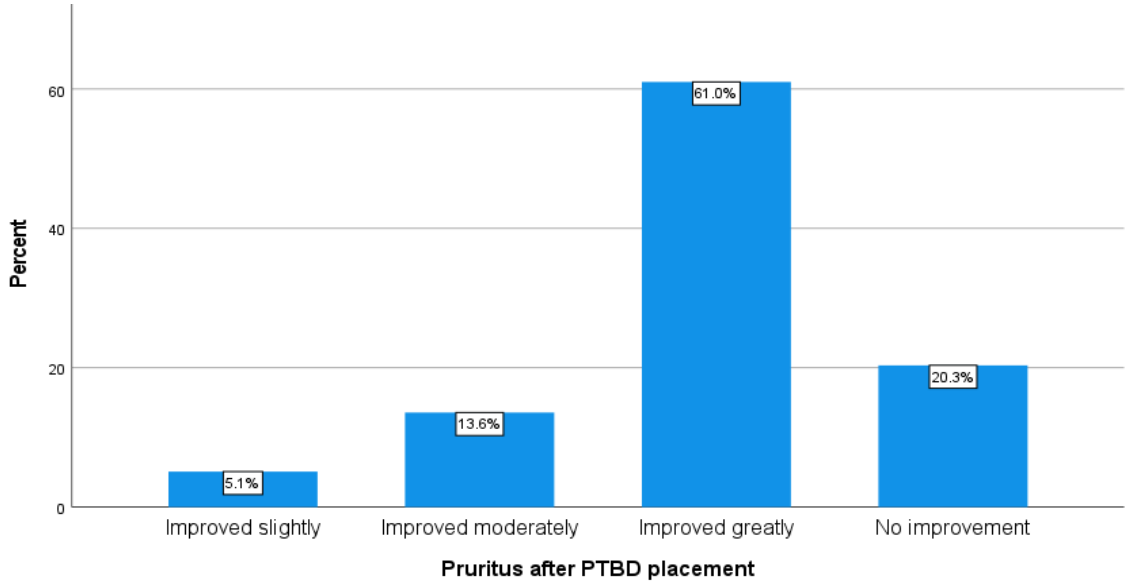


Figure 4: Pruritus after PTBD placement

Laboratory findings

The normal ranges for the laboratory parameters are as follows:-

AST	5-40 µ/L
ALT	5-40 µ/L
Total Bilirubin	5-17 µmol/L
Gamma GT	10-48 µ/L
ALP	35-130 µ/L

The mean AST before PTBD was 154.16 ±101.21 µ/L and 128.76 ±92.58 µ/L after PTBD. The mean ALT was also reduced from 158.57 ±184.58 before PTBD to 124.32 ±174.80 µ/L after the procedure. Similar trend was seen with mean bilirubin which reduced from 364.62± 145.45 µ/L to 273.68 ±128.41 µ/L, Gamma GT which reduced from 468.71 ±277.52 µ/L before the procedure to 357.71± 231.38 µ/L after the procedure and mean ALP which was 635.90± 478.97 µ/L before procedure to 454.62 ±324.75 µ/L after the procedure.

Table *1*: Laboratory parameters

Laboratory characteristics	Mean (sd)	95% CI	Median (IQR)
AST before PTBD placement in µ/L	154.16 ±101.21	129.28-179.04	129.95 (56.15-230.23)
AST after PTBD placement µ/L	128.76 ±92.58	106.00-151.52	101.40 (53.55-171.28)
ALT before PTBD placement µ/L	158.57 ±184.58	113.19-203.94	79.90 (55.23-216.28)
ALT after PTBD placement µ/L	124.32 ±174.80	81.35-167.30	67.35 (45.85-146.20)
Total bilirubin before PTBD placement in µmol/L	364.62± 145.45	328.87-400.38	367.80 (250.03-473.60)
Total bilirubin after PTBD placement µmol/L	273.68 ±128.41	242.12-305.25	222.10 (184.00-368.45)
Gamma GT before PTBD placement µ/L	468.71 ±277.52	400.49-536.93	516.95 (202.30-641.45)
Gamma GT after PTBD placement µ/L	357.71± 231.38	300.83-414.59	360.35 (145.80- 497.45)
ALP before PTBD placement µ/L	635.90± 478.97	518.15-753.64	594.80 (351.50 -721.63)
ALP after PTBD placement µ/L	454.62 ±324.75	374.79-534.46	400.95 (213.50-521.65)

Paired sample t test was carried out to determine the mean differences in laboratory parameters before and after the procedure. There was statistically significant mean differences between AST before and after PTBD; 25.40±29.45, t (65)=7.01, P value<0.001, ALT before and after PTBD; 34.24±50.73, t(65)=5.48, P value<0.001, total Bilirubin before and after PTBD 90.94±95.99, t(65)= 7.70, P value<0.001, Gamma GT before and after PTBD; t(65)=5.34, P value<0.001and ALP before and after PTBD placement; t(65)=5.25, P value<0.001.

Table 2: Paired sample t-test for laboratory parameters before and after PTBD

	Paired Differences				T	df	Sig. (2-tailed)
			95% CI of the Difference				
Paired sample T-test	Mean	SD	Lower	Upper			
AST before PTBD placement in μ/L - AST after PTBD placement μ/L	25.40	29.45	18.16	32.64	7.01	65	.000
ALT before PTBD placement μ/L - ALT after PTBD placement μ/L	34.24	50.73	21.77	46.71	5.48	65	.000
Total Bilirubin before PTBD placement in μmol/L - Total Bilirubin after PTBD placement μmol/L	90.94	95.99	67.35	114.54	7.70	65	.000
GAMMA GT before PTBD placement μ/L - GAMMA GT after PTBD placement μ/L	110.99	168.83	69.49	152.50	5.34	65	.000
ALP before PTBD placement μ/L - ALP after PTBD placement μ/L	181.27	280.512	112.31	250.23	5.25	65	.000

When the non-parametric Wilcoxon Signed Ranks Test was used there was significant reduction in laboratory test parameters after PTBD placement from the pre procedure results (P value< 0.001). The median AST before and after PTBD placement 129.95 IQR (56.15-230.23) and 101.40, IQR (53.55-171.28), respectively (Z = -5.82, p = 0.001). The median ALT before PTBD placement was 79.90 IQR (55.23-216.28) and 67.35 (45.85-146.20) after PTBD placement (Z = -5.44, p = 0.001).

The median total bilirubin before PTBD placement was 367.80 IQR (250.03-473.60), which reduced to 222.10 IQR (184.00-368.45) after PTBD placement (Z = -5.56, p = 0.001).

Similar scenario was observed with gamma GT levels which reduced from a median of 516.95 IQR (202.30-641.45) to 360.35 IQR (145.80- 497.45) after PTBD placement (Z = -4.60, p = 0.001) and ALP levels which reduced from 594.80,

IQR(351.50 -721.63) to 400.95, IQR(213.50-521.65) after the placement of PTBD (Z = -6.28, p = 0.001).

Table 3: Wilcoxon Signed Ranks Test for the differences in parameters before and after PTBD placement

Ranks		N	Mean Rank	Sum of Ranks
AST after PTBD placement μ/L - AST before PTBD placement in μ/L	Negative Ranks	57	35.38	2016.50
	Positive Ranks	9	21.61	194.50
ALT after PTBD placement μ/L - ALT before PTBD placement μ/L	Negative Ranks	55	35.59	1957.50
	Positive Ranks	11	23.05	253.50
Total bilirubin after PTBD placement μmol/L - total bilirubin before PTBD placement in μmol/L	Negative Ranks	50	39.52	1976.00
	Positive Ranks	16	14.69	235.00
Gamma GT after PTBD placement μ/L - gamma GT before PTBD placement μ/L	Negative Ranks	48	38.02	1825.00
	Positive Ranks	18	21.44	386.00
ALP after PTBD placement μ/L - ALP before PTBD placement μ/L	Negative Ranks	63	33.14	2088.00
	Positive Ranks	3	41.00	123.00

Table 4: Wilcoxon Signed Ranks Test

Wilcoxon Signed Ranks Test	AST after PTBD placement μ/L - AST before PTBD placement in μ/L	ALT after PTBD placement μ/L - ALT before PTBD placement μ/L	Total bilirubin after PTBD placement μmol/l - total bilirubin before PTBD placement in μmol/L	Gamma GT after PTBD placement μ/L - Gamma GT before PTBD placement μ/L	ALP after PTBD placement μ/L - ALP before PTBD placement μ/L
Z	-5.820[b]	-5.443[b]	-5.561[b]	-4.596[b]	-6.276[b]
Asymp. Sig. (2-tailed)	.000	.000	.000	.000	.000

The complications related to the PTBD procedure

A total of 28 (42.4%) patients had minor complications level A (no therapy required) & level B (minimal therapy, includes admission for overnight observation). In

comparison, 35 (53.0%) patients had major complications level C & D (resulting in hospitalization longer than an overnight or increased level of care). No patient had Major complications level E (permanent change)

and Major complication level F (death).

Table5: Complications after PTBD

Complication	Frequency (n)	Percent (%)
Complications level A and B	28	42.4
Major complications level C & D	35	55
Major complications level E	0	0
Major complication level F	0	0

Of the 28 minor complications that occurred and fell under level A and B, 12 (42.9%) were pain, 9 (32.1%) fever post-procedure, and 7 (25.0%) leaking around the catheter, which required intervention.

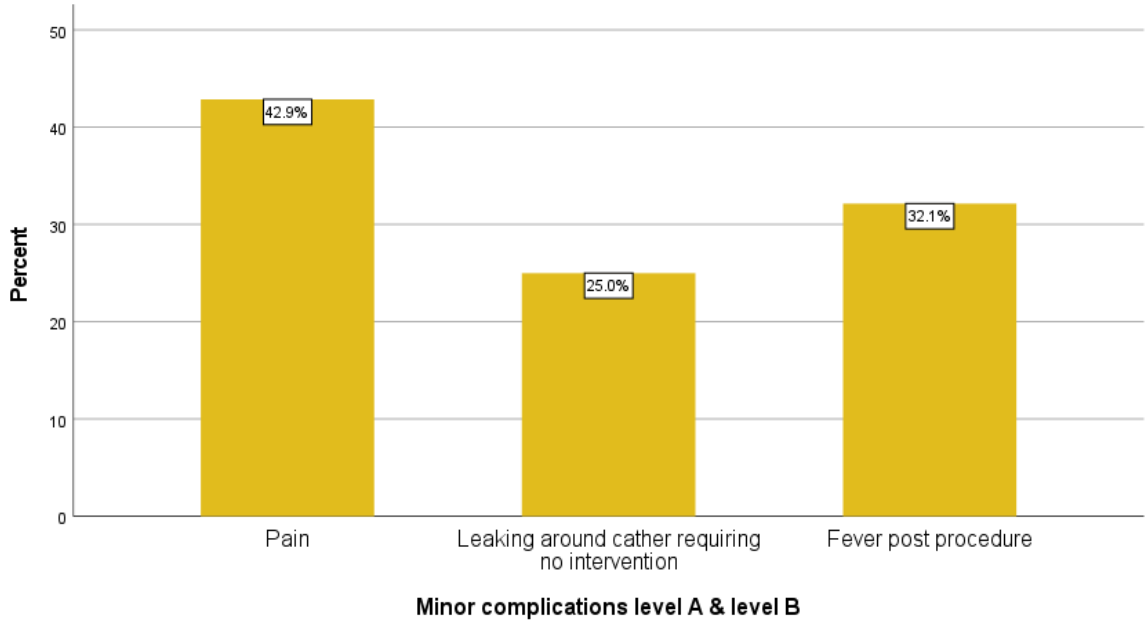


Figure 5:Minor complications

Of the 35 major complications that occurred which fell under level C and D, 10 (28.6%) consisted of dislodged drain, 9 (25.7%) pain, 8 (22.9%) occlusion or non-functional drain, 3 (8.6%) infectious complications, 3 (8.6%) bleeding complications and 2 (5.7%) peri-catheter leakage requiring catheter change.

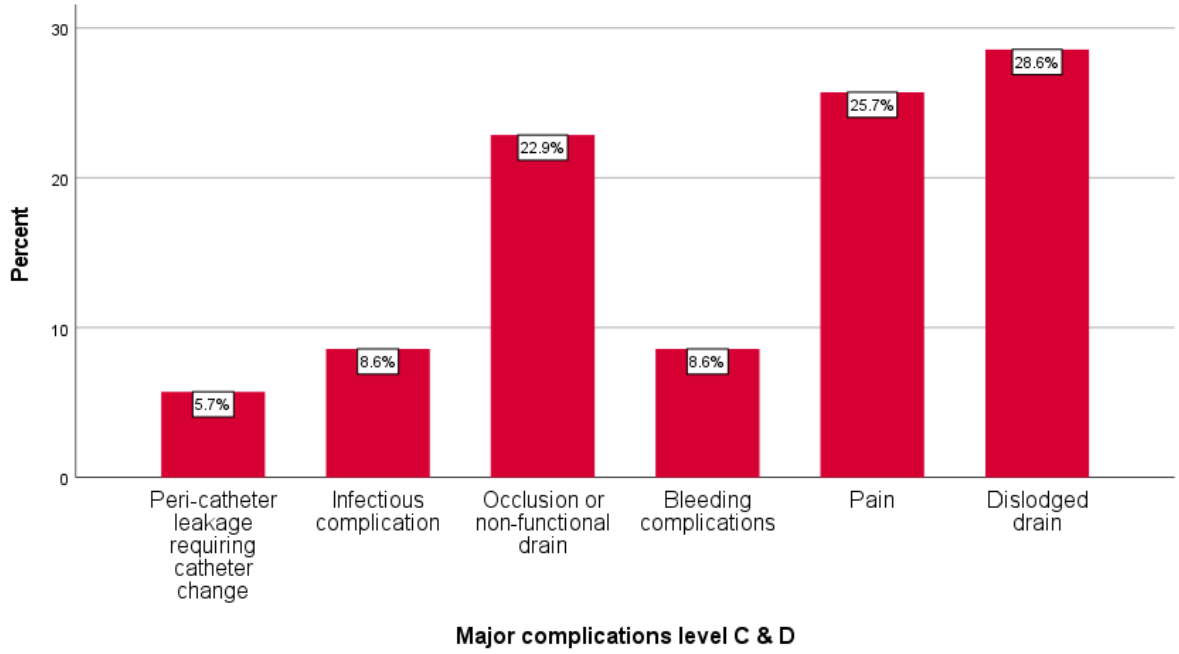


Figure 6 :Major complications

CHAPTER FIVE: DISCUSSION

This study sought to evaluate the pre and post PTBD clinical and laboratory outcomes, as well as look at the complications related to PTBD among patients with obstructive jaundice within a 2-week period at MTRH. From the study, there was a statistically significant reduction in aspartate aminotransferase (AST), alanine phosphatase (ALP), total bilirubin, and Gamma Glutamyl transferase (GGT) after PTBD with (A p value< 0.005). More than half (53.0%) of the patients had major complications while 42.4% had minor complications after the PTBD procedure.

This is among the few studies examining the outcomes and complications of patients undergoing PTBD in the Kenyan setting. The PTBD procedure is considered the gold standard treatment for patients where ERCP is not possible or has been unsuccessful (Cozzi et al., 2006).

Patient characteristics

The mean age of the participants was 65 years, an indicator that the biliary obstruction resulting in PTBD was more common among the elderly in the Kenyan population. However, these patients were younger than the UK population undergoing a similar procedure where the median age of 72years was reported (Rees et al., 2020). More than half (53%) were males. However, it seems like the gender difference was not significant.

5.1 Patient clinical and laboratory parameters

Generally, abnormally high levels of bilirubin and ALP are common in patients with biliary obstruction, as was the case in a study conducted in India (P. N. Kumar, Lakshmi, & Karthik, 2016). There was a significant reduction in total bilirubin and direct bilirubin levels post-intervention compared to pre-PTBD intervention. This is

consistent with what has been found in previous studies. In a study in Croatia, the mean total bilirubin aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, and alkaline phosphatase significantly reduced post-procedure (Gudelj Gracanin, Kujundzic, Petrovecki, & Rahelic, 2013), an indicator of its high clinical success rates. Such was the case in a study in Poland that reported a reduction in these laboratory parameters after the PTBD procedure; as was the case with (Fedak, Uchto, & Urbanik, 2013; Oberholzer et al., 2002; Robson et al., 2010). This is an indicator of PTBD's ability to alleviate jaundice symptoms based on the bilirubin levels' significant reduction post-procedure (Knap et al., 2016).

In this study, the clinical success rate was 81.6%. This was comparable to what has been found in previous studies. A study by Becker et al (Becker, Glättli, Maibach, & Baer, 1993) and Dinkel et al., (Dinkel & Triller, 2001) reported a clinical success rate of 77%. A clinical success rate of 88% was found in the study by Inal and colleagues (Inal, Akgül, Aksungur, Demiryürek, & Yağmur, 2003), and 91% in the studies by Roeren et al. (Roeren, Tonn, Richter, Brambs, & Kauffmann, 1996) and Lee et al., (Lee et al., 1992), 96% in the study by Indar and colleagues (Indar et al., 2003) and 98% in the study by Kaskarelis and colleagues (Kaskarelis et al., 1999). This indicates the consistent high PTBD clinical success rate, making it an effective procedure.

Pruritus was at (89%) in this study which compared well with a study done by (shetty *et al*., 2016) where it was (76%). However it contrasted with a study by (chalya *et al*., 2011) where pruritus was (43.1%).

Consistent with the trend observed in our study, a Study in Croatia found that the mean value of serum concentrations of total bilirubin, alkaline phosphatase, aspartate

aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase before the biliary decompression procedure were significantly above the upper referential value, and after the procedure they dropped significantly. (Gudelj Gracanin *et al*., 2013).

Complications

This study had several post-procedure complications, including pain, post procedure fever, infections, bleeding complications, peri-catheter leakage and leakage around the catheter, drain dislodgement, and occlusion However, the true extent of the complications can well be established through randomized studies which have the potential of providing a true indication of the procedures complications when compared to other interventions used for such conditions.

Unlike in this study, where there were complication in more than a quarter of the patients, in the study done in the United Kingdom by (Rees et al., 2020) , only 5.9% of the patients who underwent PTBD had complications one week post-procedure, while only 20% had complications three months post-procedure.

In this study, pain was the most common complication which is similar to the study done by (Rees et al., 2020).

Related to this study, where infections accounted for 8.9% of the complications, was the study in United Kingdom where the infections prevalence was approximately 8% and they including cholangitis at 3.9%, sepsis at 3.9% and unspecified site bacterial infection at 0.8% (Rees et al., 2020).

In the United Kingdom study, 2.9% had stent displacement or blockage within a mean of 6.3 months (Rees et al., 2020). This contrasted the findings in this study, where a higher proportion of post-procedure catheter dislodgement (25.7%) happened within

the 2 week intervening period. Explained by the patients being followed up for two weeks post-procedure; hence not possible to determine long-term complications such as and including catheter dislodgment.

Similar to this study where a significant prevalence of complications was noted post-PTBD, previous studies in other settings have reported high proportions of complications within this one-month period. In the study by Turan and colleagues, the one-month complication rate was 62.8%, with infectious complications occurring in 40.6% of the cases and non-infectious complications occurring in 34.7% of the cases (Turan et al., 2021). Other previous studies reported infectious complication rates of up to 17% (Asadi et al., 2016; Hamlin, Friedman, Stein, & Bray, 1986; Rees et al., 2020; Tapping, Byass, & Cast, 2011). A previous Dutch study showed that infectious complications were common in patients with malignant biliary obstruction, often drainage-related and occur more often after PTBD (Coelen et al., 2018).

While in this study, no case of mortality was reported 30 days post-procedure, in the study by Turan and colleagues, mortality was 17.2% one-month post-procedure, with more than half of the mortality cases being due to the underlying malignancy and not related to the procedure while 8.2% of the mortality were thought to be directly related to the procedure, occurring during the management of the procedure-related complications like sepsis or bacteraemia (Turan et al., 2021).

A high complication rate of 40% was also reported in a study conducted at a single centre in Germany. Broken down, the mortality rate was 23% for benign disorders and 70% for malignant obstructions as reported by (Nennstiel et al., 2015), which was high compared to this study which had no reported mortality. However, the reported

mortality in the German centre study was associated with a long follow-up period unlike the 2 weeks in this study.

In a related study by (Knap et al. 2015), mortality was (7.53%). Besides, several other studies reported higher all-cause mortality rates 30 days to post PTBD, ranging from 10-23.1% (Asadi et al., 2016; Khan, Hussain, Bari, & Fiaz, 2019; Rees et al., 2020; Sha, Dong, & Niu, 2019).

The median survival rate of patients who have undergone PTBD was 2.9 months after the procedure (Teixeira et al., 2013), with high mortality found in previous studies (Iwasaki et al., 1996; Robson et al., 2010; Saluja et al., 2008; Sut, Kennedy, McNamee, Collins, & Clements, 2010).

However, as was the case in this study, we have other studies where no or low mortality was reported, as was the case in the study by Weber *et al*.(Weber et al., 2009), where 3 (0.7%) patients died after the PTBD procedure and in Yee *et al*. (Yee & Ho, 1987) where 1.9% mortality was reported.

Generally, all-cause mortality and complications in this study were comparable to previous studies where nearly or more than 50% of the patients had complications post-PTBD and few or none in terms of mortality (Coelen et al., 2018; Turan et al., 2021).

Malignant biliary obstruction is the most common cause of biliary obstruction, and as such complications are expected. (Knap et al., 2016), the leading cause of mortality was the primary tumour progression and not the complications arising from from the procedure. The study by (Knap et al., 2016) went on to study the survival rates ate 3

and 6 months which in this study by comparison was out of scope because of the shorter follow-up period.

(8.6%) of the patients with major complications and (32.1%) of those with minor complications presented with fevers. Fever is a common indicator of sepsis. However, in several previous studies, sepsis and infection were a common complication post procedure (Teixeira *et al*., 2013; Xu *et al*., 2015). In accordance with the findings of (Smith, Ryan, & Niklason, 2004) it highlights that sepsis may still occurs despite antibiotics prophylaxis. The likely causes include intestinal flora reflux during PTBD and drainage catheter ex vitro infection.

However on sepsis (Knap *et al*., 2016) contrasts the findings, where they found only (1.08%) of the study subjects had sepsis post procedure while in this study it was (8.6%) and (32.1%) respectively.

This could be attributed to post procedural care by our patients and maybe differences in the types of antibiotic treatments used.

Risk factors for occlusion were a malignant disease, the prior occurrence of complications, and bilateral drainage and proximal stenosis of the biliary system (Nennstiel *et al*., 2015).

Leakages problem can result from ascites, catheter kinks, or side holes of catheter lying outside the biliary system. Catheter upgradation or repositioning can manage this challenge as per the cholangiogram check results (Xu *et al*., 2015).

The bleeding complication was less common in this study, with only 3 cases among the 35 patients with major complications. Overall these findings are in accordance with what was reported by (Covey & Brown, 2008) for hemorrhage complications to

be less common in patients who have undergone PTBD, with exception being in cases with peripheral biliary radicle puncture.

Contrary to these findings, biliary bleeding and hemorrhage were found to be common complications of PTBD by (P. Huang *et al*., 2017).

A possible explanation to such cases is that portal vein branches and hepatic artery branches which accompany biliary radicles that are dilated, have an increased chance of injury by the drainage catheter during the procedure.

No case of hemobilia was found in our study. This was in agreement with (Abraham, Barkun, & Barkun, 2002; Covey & Brown, 2008; Fedak *et al*., 2013; Robson *et al*., 2010) who found it to be the least common complication in their study. By contrast (Knap *et al*., 2016) found it to be common.

A possible explanation could be in the technique of PTBD placement which highly user dependent. Differences between interventional radiologists in terms of experience could be a factor.

We did not have any case of mortality in this study. This is in contrast to other studies where death was reported as was the case in the study by (Weber *et al*.) where 3 (0.7%) patients died after the PTBD procedure and in (Yee *et al*. 1987) where 1.9% mortality was reported or (Knap *et al*. 2015) where mortality was (7.53%).

This difference is likely to be due to the short follow-up period in this study compared to those that reported mortality cases which ranged from 6 months to 1 year.

PTBD has been associated with a high mortality rate previously (Robson *et al*., 2020). The median survival rate of patients who have undergone PTBD was reported to be 2.9 months after the procedure (Teixeira *et al*., 2013), with corresponding figures

being reported in other previous studies (Iwasaki *et al*., 1996; Saluja *et al*., 2008; Sut, Kennedy, McNamee, Collins, & Clements, 2010). In the study by (Knap *et al*., 2016), the leading cause of mortality was the primary tumor progression.

However, with increased expertise and better instrumentation, a PTBD success rate of approximately 95% with fewer complications has been reported. The likelihood of complication occurrence can be reduced further by minimizing biliary manipulation and ensuring optimal antibiotic coverage (Burke *et al*., 2003).

5.2 Limitations

Some of the participants of the study would drop off and fail to return after the first clinic visit following the procedure.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

i. PTBD improves both the patient clinical and laboratory outcomes.

ii. No life threatening complications were encountered in this study.

6.2 Recommendations

There is improvement in patient clinical and laboratory outcomes and no life threatening complications were encountered thus the intervention is safe and it should be encouraged by doctors for their patients.

PTBD like other interventional radiological procedures are fairly new in our set up and further studies should be done to understand more on how it impacts the quality of life for the patients who undergo this procedure.

There is a need for extended follow-up on the patients who have undergone PTBD to understand the full extent of the procedure's long term complications, including mortality.

REFERENCES

Abraham, N. S., Barkun, J. S., & Barkun, A. N. (2002). Palliation of malignant biliary obstruction: a prospective trial examining impact on quality of life. *Gastrointestinal endoscopy, 56*(6), 835-841.

Ba, Y., Yue, P., Leung, J. W., Wang, H., Lin, Y., Bai, B., Zhu, X., Zhang, L., Zhu, K., Wang, W., Meng, W., Zhou, W., Liu, Y., Li, X. (2020). Percutaneous transhepatic biliary drainage may be the preferred preoperative drainage method in hilar cholangiocarcinoma. Endoscopy International Open, 8, E203-E210. https://dx.doi.org/10.1055/a-0990-9114

Behera, R. K., Srivastava, D. N., Kumar, P., Pal, S., Ranjan, N., Garg, P., Sahni, P., Madhusudhan, K. S. (2021). Right-sided versus left-sided percutaneous transhepatic biliary drainage in the management of malignant biliary obstruction: a randomized controlled study. Abdominal Radiology, 46, 768-775. https://dx.doi.org/10.1007/s00261-020-02651-y

Bonshock R, McLaughlin S, Duncan C. et al. Complication rates of percutaneous biliary drainage in the presence of ascites. J Vasc Interv Radiol 2017; 28: S54

Briggs, C., & Peterson, M. (2007). Investigation and management of obstructive jaundice. *Surgery (Oxford), 25*(2), 74-80.

Burke, D. R., Lewis, C. A., Cardella, J. F., Citron, S. J., Drooz, A. T., Haskal, Z. J., . . . Oglevie, S. B. (2003). Quality improvement guidelines for percutaneous transhepatic cholangiography and biliary drainage. *Journal of vascular and interventional radiology: JVIR, 14*(9 Pt 2), S243.

Chalya, P. L., Kanumba, E. S., & Mchembe, M. (2011). Etiological spectrum and treatment outcome of Obstructive jaundice at a University teaching Hospital in northwestern Tanzania: A diagnostic and therapeutic challenges. *BMC research notes, 4*(1), 147.

Chandrashekhara, S., Gamanagatti, S., Singh, A., & Bhatnagar, S. (2016). Current status of percutaneous transhepatic biliary drainage in palliation of malignant obstructive jaundice: a review. *Indian journal of palliative care, 22*(4), 378.

Cheema, K., Ahmad, F., & Gondal, S. (2001). Evaluation of etiological incidence and diagnostic modalities in obstructive jaundice. *Pak Postgrad Med J, 12*(4), 160-164.

Covey, A. M., & Brown, K. T. (2008). Percutaneous transhepatic biliary drainage. *Techniques in vascular and interventional radiology, 11*(1), 14-20.

Dhir, V., Artifon, E. L., Gupta, K., Vila, J. J., Maselli, R., Frazao, M., & Maydeo, A. (2014). Multicenter study on endoscopic ultrasound- guided expandable biliary metal stent placement: choice of access route, direction of stent insertion, and drainage route. *Digestive Endoscopy, 26*(3), 430-435.

El-Haddad, H. M., Kassem, M. I., Shehata, G. M., & Afifi, A. H. (2016). Predictors of success of treatment of distal two thirds common bile duct strictures: A retrospective Cohort study over two years. *International Journal of Surgery, 28*, 106-111.

Fedak, A., Uchto, W., & Urbanik, A. (2013). Transcutaneal drainage intrahepatic biliary ducts as a method of paliative treatment of inoperative liver hilum tumours. *Przeglad lekarski, 70*(5), 275-280.

Funaki, B., Zaleski, G., Straus, C., Leef, J., Funaki, A., Lorenz, J., . . . Rosenblum, J. (1999). Percutaneous biliary drainage in patients with nondilated intrahepatic bile ducts. *AJR. American journal of roentgenology, 173*(6), 1541-1544.

Gudelj Gracanin, A., Kujundzic, M., Petrovecki, M., & Rahelic, D. (2013). Etiology and epidemiology of obstructive jaundice in Continental Croatia. *Collegium antropologicum, 37*(1), 131-133.

Gupta P, Kalra N, Kumar A, Kochhar R, Gupta V, Khandelwal N. Balloon dilatation of a benign biliary stricture through a T-tube tract. Indian J Radiol Imaging 2015; 25 (01) 21-24

Gupta P, Maralakunte M, Rathee S. et al. Percutaneous transhepatic biliary drainage in patients at high risk for adverse events: experience from a tertiary care referral centre. Abdom Radiol 2019; [epub ahead of print] DOI: 10.1007/s000261-091-02344-1.

Gupta, P., Bansal, V., Kalra, N., Samanta, J., Mandavdhare, H., Sharma, V., Dutta, U., Kochhar, R., Sandhu, M. S. (2021). Should patients with unresectable gallbladder cancer with hilar involvement undergo unilateral or bilateral percutaneous biliary drainage in the setting of cholangitis? Clinical & Experimental Hepatology, 7, 7-12.

Gupta, P., Gupta, J., & Kumar-M, P. (2020). Imaging in obstructive jaundice: what a radiologist needs to know before doing a percutaneous transhepatic biliary drainage. *Journal of Clinical Interventional Radiology ISVIR, 4*(01), 31-37.

Gwon DI, Laasch HU. Radiological approach to benign biliary strictures. Gastrointest Interv 2015;4:9-14. 4.

Henry, A. C., Smits, F. J., van Lienden, K., van den Heuvel, D. A. F., Hofman, L., Busch, O. R., van Delden, O. M., Zijlstra, I. A., Schreuder, S. M., Lamers, A. B., van Leersum, M., van Strijen, M. J. L., Vos, J. A., Te Riele, W. W., Molenaar, I. Q., Besselink, M. G., van Santvoort, H. C. (2021). Biliopancreatic and biliary leak after pancreatoduodenectomy treated by percutaneous transhepatic biliary drainage. HPB, https://dx.doi.org/10.1016/j.hpb.2021.08.941

Hu, Q. L., Liu, J. B., Ellis, R. J., Liu, J. Y., Yang, A. D., D'Angelica, M. I., Ko, C. Y., Merkow, R. P. (2020). Association of preoperative biliary drainage technique with postoperative outcomes among patients with resectable hepatobiliary malignancy. HPB, 22, 249-257.

Huang, J., Bao, X., & Lu, X. (1993). The common causes and differential diagnosis of malignant jaundice. *Zhonghua nei ke za zhi, 32*(6), 400-404.

Huang, P., Zhang, H., Zhang, X.-F., Lv, W., & Lou, S. (2017). Comparison of endoscopic ultrasonography guided biliary drainage and percutaneous transhepatic biliary drainage in the management of malignant obstructive jaundice after failed ERCP. *Surgical Laparoscopy Endoscopy & Percutaneous Techniques, 27*(6), e127-e131.

Iwasaki, M., Furuse, J., Yoshino, M., Konishi, M., Kawano, N., Kinoshita, T., & Ryu, M. (1996). Percutaneous transhepatic biliary drainage for the treatment of obstructive jaundice caused by metastases from nonbiliary and nonpancreatic cancers. *Japanese journal of clinical oncology, 26*(6), 465-468.

Iwashita, T., Uemura, S., Mita, N., Iwasa, Y., Ichikawa, H., Mukai, T., Yasuda, I., Shimizu, M. (2020). Endoscopic ultrasound guided-antegrade biliary stenting vs percutaneous transhepatic biliary stenting for unresectable distal malignant biliary obstruction in patients with surgically altered anatomy. Journal of Hepato-biliary-pancreatic Sciences, 27, 968-976.

Katabathina VS, Dasyam AK, Dasyam N, Hosseinzadeh K. Adult bile duct strictures: role of MR imaging and MR cholangiopancreatography in characterization. Radiographics 2014; 34 (03) 565-586

Khan SA, Tavolari S and Brandi G: Cholangiocarcinoma: Epidemiology and risk factors. Liver Int 39: 19-31, 2019. PMID: 30851228. DOI: 10.1111/liv.14095

Knap, D., Orlecka, N., Judka, R., Juza, A., Drabek, M., Honkowicz, M., . . . Baron, J. (2016). Biliary duct obstruction treatment with aid of percutaneous transhepatic biliary drainage. *Alexandria Journal of Medicine, 52*(2), 185–191.

Kongkam, P., Orprayoon, T., Boonmee, C., Sodarat, P., Seabmuangsai, O., Wachiramatharuch, C., Auan-Klin, Y., Pham, K. C., Tasneem, A. A., Kerr, S. J., Romano, R., Jangsirikul, S., Ridtitid, W., Angsuwatcharakon, P., Ratanachu-Ek, T., Rerknimitr, R. (2021). Ercp plus endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage for malignant hilar biliary obstruction: a multicenter observational open-label study. Endoscopy, 53, 55-62.

Kumar, P. N., Lakshmi, R. M., & Karthik, G. S. R. S. (2016). A CLINICAL STUDY ON OBSTRUCTIVE JAUNDICE. *JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS, 5*(101), 7444-7447.

Kumar, S., Masood, S., Srivastava, U., Madhavan, S. M., Chauhan, S., Pandey, A. (2020). Factors predicting recovery of liver function after percutaneous drainage in malignant biliary obstruction: the role of hospital-acquired biliary sepsis. Clinical & Experimental Hepatology, 6, 295-303.

Kumar, S., Singh, P., Kumar, V., Kumar, M., Mahto, M. (2021). Survival benefit of percutaneous transhepatic biliary drainage for malignant biliary tract obstruction-a prospective study comparing external and internal drainage techniques. Abdominal Radiology,

Lee, T. H., Choi, J.-H., Park, D. H., Song, T. J., Kim, D. U., Paik, W. H., . . . Lee, S. K. (2016). Similar efficacies of endoscopic ultrasound–guided transmural and percutaneous drainage for malignant distal biliary obstruction. *Clinical Gastroenterology and Hepatology*, *14*(7), 1011-1019. e1013.

Li, J., Yu, T., Zhang, L., Yang, M., Gao, S., Pu, N., Li, C., Wang, C., Gong, G., Cheng, J., Wang, L., Li, G., Wang, X., Chen, Y. (2021). An iodine-125 seed strand combined with a metal stent versus a metal stent alone for obstructive jaundice caused by pancreatic ductal adenocarcinoma. Brachytherapy, 20, 446-453.

Li, S., Li, B., Li, L., Yang, X., Xu, F., Wang, W. (2020). The efficacy of the combination of percutaneous transhepatic biliary drainage and 125i stranded seeds for malignant bile duct obstruction treatment. Journal of Contemporary Brachytherapy, 12, 225-232.

Liu YS, Lin CY, Chuang MT, Tsai YS, Wang CK, Ou MC. Success and complications of percutaneous transhepatic biliary drainage are influenced by liver entry segment and level of catheter placement. Abdom Radiol (NY). 2018;43(3):713–22

Matsunaga, Y., Higuchi, R., Yazawa, T., Uemura, S., Izumo, W., Ota, T., Furukawa, T., Yamamoto, M. (2021). Negative prognostic outcomes of percutaneous transhepatic biliary drainage in distal cholangiocarcinoma: a retrospective analysis using propensity score matching. International Journal of Clinical Oncology, 26, 1492-1499.

Minami, Y., & Kudo, M. (2012). Hepatocellular carcinoma with obstructive jaundice: endoscopic and percutaneous biliary drainage. *Digestive diseases*, *30*(6), 592-597.

Moghimi, M., Marashi, S. A., Salehian, M. T., & Sheikhvatan, M. (2008). Obstructive jaundice in Iran: factors affecting early outcome. *Hepatobiliary & Pancreatic Diseases International*, *7*(5), 515-519.

Nennstiel, S., Weber, A., Frick, G., Haller, B., Meining, A., Schmid, R. M., & Neu, B. (2015). Drainage-related complications in percutaneous transhepatic biliary drainage. *Journal of clinical gastroenterology*, *49*(9), 764-770.

Niemela, J., Syrjala, H., Ohtonen, P., Saarnio, J., Kallio, R. (2021). Chemotherapy improves survival after percutaneous biliary drainage in patients with pancreatic or biliary tract cancer with biliary obstruction. Anticancer Research, 41, 2979-2984.

Oberholzer, K., Pitton, M., Mildenberger, P., Lechner, C., Düber, C., & Thelen, M. (2002). The current value of percutaneous transhepatic biliary drainage. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin, 174*(9), 1081-1088.

Ogura, T., Chiba, Y., Masuda, D., Kitano, M., Sano, T., Saori, O., . . . Takeuchi, T. (2016). Comparison of the clinical impact of endoscopic ultrasound-guided choledochoduodenostomy and hepaticogastrostomy for bile duct obstruction with duodenal obstruction. *Endoscopy, 48*(02), 156-163.

Padhy B, Murmu D, Samal D, Jha S. Clinical study of surgical jaundice: an institutional experience. Int Surg J 2018; 5: 138-142

Padillo, F. J., Andicoberry, B., Naranjo, A., Miño, G., Pera, C., & Sitges-Serra, A. (2001). Anorexia and the effect of internal biliary drainage on food intake in patients with obstructive jaundice. *Journal of the American College of Surgeons, 192*(5), 584-590.

Patel IJ, Davidson JC, Nikolic B, Salazar GM, et al. Standards of Practice Committee, with Cardiovascular and Interventional Radiological Society of Europe (CIRSE) Endorsement. Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-guided Interventions. J Vasc Interv Radiol 2012;23:727-36

Patel NA, Parekh H, Vasavada DP, Mehta SG, Porecha MM, Shah J. A pictorial essay-imaging in surgical jaundice. Indian J Radiol Imaging 2006; 16 (01) 75-82

Patel V, McLaughlin SW, Shlansky-Goldberg R. et al. Complication rates of percutaneous biliary drainage in the presence of ascites. Abdom Radiol (NY) 2019; 44 (05) 1901-1906

Rees J, Mytton J, Evison F, Mangat KS, Patel P, Trudgill N. The outcomes of biliary drainage by percutaneous transhepatic cholangiography for the palliation of malignant biliary obstruction in England between 2001 and 2014: a retrospective cohort study. BMJ Open. 2020;10(1):e033576.

Rees, J., Mytton, J., Evison, F., Mangat, K. S., Patel, P., Trudgill, N. (2020). The outcomes of biliary drainage by percutaneous transhepatic cholangiography for the palliation of malignant biliary obstruction in england between 2001 and 2014: a retrospective cohort study. BMJ Open, 10, e033576. https://dx.doi.org/10.1136/bmjopen-2019-033576

Rizzo, A., Ricci, A. D., Frega, G., Palloni, A., De Lorenzo, S., Abbati, F., ... & Brandi, G. (2020). How to choose between percutaneous transhepatic and endoscopic biliary drainage in malignant obstructive jaundice: An updated systematic review and meta-analysis. *in vivo, 34*(4), 1701-1714.

Robson, P., Heffernan, N., Gonen, M., Thornton, R., Brody, L., Holmes, R., . . . Getrajdman, G. (2010). Prospective study of outcomes after percutaneous biliary drainage for malignant biliary obstruction. *Annals of surgical oncology, 17*(9), 2303-2311.

Roche, S. P., & Kobos, R. (2004). Jaundice in the adult patient. *American family physician, 69*(2), 299-304.

Saddique, M., & Iqbal, S. A. (2007). Management of Obstructive Jaundice: Experience in a tertiary care surgical unit. *Pakistan J Surg*, *23*(1), 23-25.

Sahinli, H., Ozet, A. (2020). Prognostic and predictive factors in cancer patients with obstructive jaundice treated by percutaneous transhepatic biliary drainage: a single-center experience. Journal of Cancer Research & Therapeutics, 16, S99-S103.

Saluja, S. S., Gulati, M., Garg, P. K., Pal, H., Pal, S., Sahni, P., & Chattopadhyay, T. K. (2008). Endoscopic or percutaneous biliary drainage for gallbladder cancer: a randomized trial and quality of life assessment. *Clinical Gastroenterology and Hepatology*, *6*(8), 944-950. e943.

Selvasekaran R, Nagalakshmi G, Anandan H. Clinical spectrum of presentation of obstructive jaundice in inflammation, stone disease and malignancy. Int J Sci Stud 2017; 5: 10-14

Serrano Hermosilla, C., Prieto Calvo, M., Gastaca Mateo, M., Perfecto Valero, A., Valdivieso Lopez, A. (2020). Parietal recurrence of hiliar cholangiocarcinoma: is percutaneous transhepatic biliary drainage the best choice in patients with hiliarcholangiocarcinoma?98,368370.https://dx.doi.org/10.1016/j.ciresp.2019.08.008

She, W. H., Cheung, T. T., Ma, K. W., Yin Tsang, S. H., Dai, W. C., Yan Chan, A. C., Lo, C. M. (2021). Impact of preoperative biliary drainage on postoperative outcomes in hilar cholangiocarcinoma. *Asian Journal of Surgery*, https://dx.doi.org/10.1016/j.asjsur.2021.07.075

Shetty, T. S., Ghetla, S. R., Shaikh, S. T., Pilania, V., Gupta, A., & Mundada, R. (2016). Malignant obstructive jaundice: A study of investigative parameters and its outcome. *JEBMH, 69*(3), 3752-3759.

Siddique, K., Ali, Q., Mirza, S., Jamil, A., Ehsan, A., Latif, S., & Malik, A. Z. (2008). Evaluation of the aetiological spectrum of obstructive jaundice. *J Ayub Med Coll Abbottabad, 20*(4), 62-66.

Singh, A. P., Inavolu, P., Asif, S., Reddy, D. N., Lakhtakia, S. (2021). Eus-guided choledochoduodenostomy as a rescue after failed ercp and percutaneous transhepatic biliary drainage in the management of postoperative benign biliary stricture. VideoGIE : An Official Video Journal of the American Society for Gastrointestinal Endoscopy, 6, 90-92.

Skoczylas K, Pawełas A. Ultrasound imaging of the liver and bile ducts - expectations of a clinician. J Ultrason 2015; 15 (62) 292-306

Smith, T. P., Ryan, J. M., & Niklason, L. E. (2004). Sepsis in the interventional radiology patient. *Journal of vascular and interventional radiology, 15*(4), 317-325.

Subramani, V. N., Avudaiappan, M., Yadav, T. D., Kumar, H., Sharma, V., Mandavdhare, H., Gorsi, U., Singh, H. (2021). Outcome following percutaneous transhepatic biliary drainage (ptbd) in carcinoma gallbladder: a prospective observational study. Journal of Gastrointestinal Cancer, https://dx.doi.org/10.1007/s12029-021-00655-5#

Subramani, V. N., Avudaiappan, M., Yadav, T. D., Kumar, H., Sharma, V., Mandavdhare, H., Gorsi, U., Singh, H. (2021). Outcome following percutaneous transhepatic biliary drainage (ptbd) in carcinoma gallbladder: a prospective observational study. Journal of Gastrointestinal Cancer

Sut, M., Kennedy, R., McNamee, J., Collins, A., & Clements, B. (2010). Long-term results of percutaneous transhepatic cholangiographic drainage for palliation of malignant biliary obstruction. *Journal of palliative medicine, 13*(11), 1311-1313.

Teixeira, M. C., Mak, M. P., Marques, D. F., Capareli, F., Carnevale, F. C., Moreira, A. M., . . . Hoff, P. M. (2013). Percutaneous transhepatic biliary drainage in patients with advanced solid malignancies: prognostic factors and clinical outcomes. *Journal of gastrointestinal cancer, 44*(4), 398-403.

Teplick, S. K., Flick, P., & Brandon, J. C. (1991). Transhepatic cholangiography in patients with suspected biliary disease and nondilated intrahepatic bile ducts. *Gastrointestinal radiology, 16*(1), 193-197.

Vogel A, Kullmann F, Kunzmann V, Al-Batran SE, Oettle H, Plentz R, Siveke J, Springfield C and Riess H: Patients with advanced pancreatic cancer and hyperbilirubinaemia: review and german expert opinion on treatment with nabpaclitaxel plus gemcitabine. Oncol Res Treat 38(11): 596-603, 2015. PMID: 26599274.

Wang, H. B., Peng, F., Wang, M., Qin, R. Y., Zhu, F. (2021). Impact of percutaneous transhepatic biliary drainage on clinical outcomes of patients with malignant obstructive jaundice undergoing laparoscopic pancreaticoduodenectomy. Current Medical Science, 41, 375-380.

Weber, A., Gaa, J., Rosca, B., Born, P., Neu, B., Schmid, R. M., & Prinz, C. (2009). Complications of percutaneous transhepatic biliary drainage in patients with dilated and nondilated intrahepatic bile ducts. *European journal of radiology, 72*(3), 412-417.

Xu, C., Huang, X.-E., Wang, S.-X., Lv, P.-H., Sun, L., & Wang, F.-A. (2015). Comparison of infection between internal-external and external percutaneous transhepatic biliary drainage in treating patients with malignant obstructive jaundice. *Asian Pac J Cancer Prev, 16*(6), 2543-2546.

Yadav A, Condoti NK, Mukund A. et al. Percutaneous transhepatic biliary interventions. J Clin Interv Radiol ISVIR 2018; 2: 27-37

Yang XW, Yang J, Li L, Man XB, Zhang BH, Shen F and Wu MC: Analysis of the relationships between clinicopathologic factors and survival in gallbladder cancer following surgical resection with curative intent. PLoS One 7(12): e51513, 2012. PMID:

APPENDICES

Appendix I: Consent Form

English version

Information

This informed consent form is for patients with suspected obstructive jaundice.

What is medical research?

Medical research is when doctors collect information to get new knowledge or add to the existing pool of knowledge about a disease or illness. This helps doctors find better ways of treating illnesses for best outcomes.

What is this research study about?

This is a research study on how we can use percutaneous tubes to drain bile and improve liver functions as well as the signs and symptoms of obstructive jaundice. This will allow for other interventions such as radiotherapy, chemotherapy and surgery -where indicated- to be done and improve outcome in the long run.

Who is doing this research?

My name is Dr Kiptoo Kipyator Sammin and I'm a medical doctor. I'm currently studying for my second degree (Masters in Medicine) in Radiology & Imaging at Moi University.

What will happen to me in this study?

I will invite you to be a part of this study. If you agree to participate in this study, I will collect information about your laboratory tests, your histology tests, clinical signs and symptoms and a record of any problems that may arise after the procedure is done.

There are no risks or benefits of participating in this study and you will be given the same medical care as the rest of the patients who are not in the study. You can choose

whether or not you would like to participate in the study. In case you refuse to be a part of the study you will not be forced to participate.

In case of any questions, feel free to ask, I will be happy to assist.

Certificate of assent

Do you understand this research study and are willing to take part in it?

Yes: …….. No: ……..

Has the researcher answered all your questions?

Yes: ……... No: ……..

Do you understand that you can pull out of the study at any time?

Yes: ……. No: …….

I agree to take part in the study……

OR

I do not wish to take part in the study.

Signed ……

Date ……

Kiswahili version

Fomu hii ya idhini ni ya watu wazima wenye umri wa miaka kumi na minane au zaidi ambao wanashukiwa kuwa na ugonjwa wa saratani ya maini inayosababisha mishipa ya kupitisha nyongo kufungana kwa njia ya kuzibwa.

Utafiti wa matibabu ni nini?

Utafiti wa matibabu ni pale ambapo madaktari hutafuta maarifa zaidi ili kupata ujuzi mpya kuhusu magonjwa. Hii husaidia madaktari kupata njia bora za kutibu magonjwa.

Utafiti huu unahusu nini?

Utafiti huu unahusisha wote walioshukiwa kuwa na saratani ambayo inasababisha mishipa ya kupitisha nyongo zi zibike. Itachukua takwimu kutoka majibu ya vipimo ya maabara pamoja na hali jinsi unavyo jihisi. Nitaangalia pia shida zitakazo tokana na matibabu kwa njia hii ya kuwekewa pipu ili kuwe na njia mbadala wa kupitisha hio bile.

Nani anafanya utafiti huu?

Jina langu ni Dkt. Kiptoo Kipyator Sammin na mimi ni daktari aliyehitimu. Kwa sasa ninaongeza ujuzi ili nitunukiwe shahada yangu ya pili (Masters in Medicine) katika somo la kupiga picha na matibabu kwa njia ya kutumia picha katika Chuo Kikuu cha Moi.

Nini kitatokea kwangu katika utafiti huu?

Utaalikwa kushiriki katika utafiti huu. Iwapo utakubali majibu yako ya maabara ita orodheshwa na kurekodiwa ili itumike katika utafiti huu. Hakuna hatari zozote au faida za kushiriki katika utafiti huu na utapewa huduma sawa ya matibabu kama wale

ambao hawatashiriki kwenye utafiti. Pia ni muhimu nikueleze kwamba kushiriki katitika utafiti huu sio lazima na unaruhusiwa kujiondoa wakati wowote ambao ungependa.

Ikiwa kuna maswali yoyote, jisikie huru kuuliza, nitafurahia kusaidia.

Hati ya kukubali

Je unaelewa utafiti huu na uko tayari kushiriki?

Ndio: ..... La: .....

Je, mtafiti alijibu maswali yako yote?

Ndio: ..... La: .....

Je unaelewa kwamba unaweza kujiondoa kwa utafiti huu wakati wowote?

Ndio: ……. La: ……

Nakubali kushiriki katika utafiti huu …….

AU

Sijakubali kushiriki katika utafiti huu na sipeani idhini .....

Tarehe: ……

Appendix II: Data Collection Form

Instructions

1. All sections to be filled accordingly.

2. Writings should be clear and legible.

3. To be filled in by the principal investigator or assistant once the patient has given consent to be part of the study.

IP/OP No: …….

Serial No: ……..

Date: ……..

PART 1: DEMOGRAPHIC DATA

1. DOB/ Age ……....

2. Gender ……

3. Residence ……..

4. Contact No: ……...

PART 2: FINDINGS

SECTION A: Clinical features findings

Fill in appropriately to indicate severity

1:- improved slightly

2:- improved moderately

3:- improved greatly

4:- no improvement

Clinical features

	Before PTBD placement	After PTBD placement
Pruritus		
Deep yellow eyes		
Dark urine		
Coma		

Lab parameters

	Before PTBD placement	After PTBD placement
AST		
ALT		
TOTAL BILIRUBIN		
GAMMA GT		
ALP		

SECTION C: COMPLICATIONS.

Procedural Complications	Number of patients experiencing given complication	Percentage of total patients
No Reported Complications		
Minor Complications Level A (no therapy required) & Level B (minimal therapy, includes admission for overnight observation)		
Pain		
Leaking around catheter requiring no intervention		
Fever post procedure		
Other: minor abscess , elevated creatinine , biliary tree thrombus , rigors, hypotension		
Total minor complications:		
Major Complication Level C & D (resulting in hospitalization longer than overnight or increased level of care)		
Peri-catheter Leakage requiring catheter change		

Infectious complication		
occlusion or non-functional drain		
Bleeding complications		
Pain		
Dislodged drain		
Chronic renal insufficiency due to dehydration from drainage catheter		
Major Complication Level E (permanent change)		
Persistent Unresolved Leaking		
Persistent unresolved fevers with sepsis		
Major Complication Level F (death)		
Arterial Bleed		
Septic Shock		
Total Major Complications:		

Appendix III:Work plan

Activity	**2018- 2019**		**2019**	**2019- 2020**			**2020**
	Sept	Oct – Feb	Feb-March	April-April	May	June	July
Concept Formulation							
Proposal writing							
Ethical approval							
Actual data collection							
Data analysis							
Report writing							
Presentation of the final report							

Appendix IV:IREC Approval

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

28th June, 2019

Dr. Kiptoo Kipyator Sammin,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Causes, Clinical Features and Radiological Management of Malignant Obstructive Jaundice at Moi Teaching and Referral Hospital, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

MOI TEACHING AND REFERRAL HOSPITAL
CEO
APPROVED
01 JUL 2019
P. O. Box 3 - 30100, ELDORET

01/07/2019

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - Senior Director, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM

Appendix V:Hospital approval (MTRH)

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2019/40
Approval Number: 0003357

27th June, 2019

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
27 JUN 2019
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dr. Kiptoo Kipyator Sammin,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Kiptoo,

CAUSES, CLINICAL FEATURES AND RADIOLOGICAL MANAGEMENT OF MALIGNANT OBSTRUCTIVE JAUNDICE AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA

This is to inform you that ***MU/MTRH-IREC*** has reviewed and approved your above research proposal. Your application approval number is ***FAN:0003357.*** The approval period is ***27th June, 2019 – 26th June, 2020.***

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MU/MTRH-IREC.***
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MU/MTRH-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MU/MTRH-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MU/MTRH-IREC.***

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH; Principal - CHS; Dean - SOP; Dean - SON; Dean - SOM; Dean - SOD