

## Original Research Article

# Incidence of biliary complications in living donor liver transplantation

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### ABSTRACT

**Background:** Liver transplantation is a widely accepted treatment for end stage liver diseases and selected cases of hepatocellular carcinoma, if it is limited to the liver. Biliary complications such as biliary strictures and bile leaks after the liver transplantation remain the major cause for morbidity and mortality. This study was aimed to estimate the incidence of biliary complications in live donor liver transplantation (LDLT) patients and the rate of radiological intervention in its management.

**Methods:** Case records of LDLT patients during the past two years were retrospectively studied to estimate the incidence of biliary complications. Biliary complications were diagnosed based on clinical features like pain, fever, jaundice or increased bile from biliary drains. The patients were imaged using ultrasonogram, computed tomogram, magnetic resonance imaging or Endoscopic retrograde cholangiopancreatography (ERCP) for any biliary strictures and leaks, choledocholithiasis or sphincter of oddi dysfunction. The rate of ERCP and Percutaneous Trans Biliary Drainage (PTBD) interventions in these patients was recorded.

**Results:** Fifty cases of post LDLT patients (both prospective and retrospective) were analysed in the study. The incidence of biliary stricture was 12% (6/50) and among the 6 patients with biliary stricture, 4 had bile leak. Among the total cases, the incidence of biliary leak was 8%. Eighty three percent of the biliary complications were managed by ERCP, whilst 17% by PTBD.

**Conclusions:** The incidence of biliary stricture was 12% and biliary leak was 8%. The biliary complications were managed by ERCP in 83% and percutaneous approach in 17% of cases.

**Keywords:** Bilioma, Biliary stricture, Biliary complications, Hepatocellular carcinoma, Liver transplantation, Living donor liver transplantation

### INTRODUCTION

Liver transplantation is a widely accepted treatment for end stage diseases of the liver and selected cases of hepatocellular carcinoma, when it is limited to the liver. Biliary complications after the liver transplantation remain a major cause of morbidity and mortality.<sup>1,2</sup> The incidence of biliary complications is found to be highest in the first few months after the transplantation.<sup>3</sup> Bile leaks usually occur in the immediate post-operative

period, while biliary strictures occur many weeks after the transplant.<sup>4</sup> These complications result from a variety of contributing factors including the reconstruction technique used for biliary slintage, type of liver transplant procedure, organ preservation.<sup>2</sup> Biliary strictures are divided into anastomotic strictures (AS) and non-anastomotic strictures (NAS). AS tend to be single, shorter in length, and usually present at the site of anastomosis. NAS can be further classified into macroangiopathic, microangiopathic and immunogenic

causes, chronic rejection, hepatic arterial thrombosis and other recipient and donor characteristics.<sup>5</sup>

Biliary leakage is the second most common complication after the transplantation. There are three different entities in biliary leakage, A) leakage from anastomotic site, B) leakage from cut surface of the partial graft and C) leakage after T tube removal. The complications are identified by clinical assessment, various modalities of imaging techniques.<sup>6</sup> The complications are managed by Endoscopic retrograde cholangiopancreatography (ERCP) or Percutaneous Trans Biliary Drainage (PTBD).<sup>6</sup> In living donor liver transplantation (LDLT), management of the biliary complications is important for patient survival. The rate of biliary complications was found to be varying among previous studies.<sup>1-4</sup> Studies conducted on the biliary complications in liver transplantations are very scant in this region. Therefore, this study was aimed to estimate the incidence of biliary complications in LDLT patients and its management by ERCP and PTBD.

**METHODS**

**Study design, sample size and patients selection**

Both retrospective and prospective study was designed among the patients underwent LDLT at department of Gastroenterology, Amrita Institute of Medical Sciences, Kochi, Kerala, India during the period from September 2010 to September 2014. The patients, irrespective of age, indications of transplant and sex, who had undergone LDLT were included in the study and the cases were followed up to two and half years to detect any biliary complication and biliary leak. Retrospective cases of post LDLT cases up to two years. (September 2010 to September 2012) were also included in the study. Patients with cadaveric liver transplant were excluded. The study procedure was approved by the Institutional ethical committee and written consent was obtained from the patients. Based on the results of existing literature and with 95% confidence and 20% error minimum sample size was found to be 360.<sup>7</sup>

**Procedure**

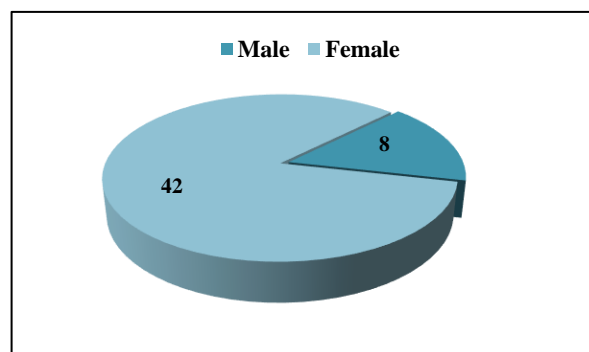
The incidence of biliary tract complication in patients undergoing LDLT was assessed. Biliary complications were diagnosed based on the clinical features like pain, fever, jaundice or increased bile from biliary drains. The patients were imaged using ultrasonogram (USG), computed tomogram (CT), magnetic resonance imaging or ERCP for any biliary strictures and leaks, choledocholithiasis or sphincter of oddi dysfunction. The rate of ERCP and PTBD interventions in these patients was recorded.

**Statistical analysis**

The data were expressed as percentage/number of cases.

**RESULTS**

According to the statistical calculation, 360 cases were needed for the study with 95% confidence and 20% error minimum. However, we could get only 50 cases (20 prospective and 30 retrospective cases) during the four years period (2010-14) of the study. The average age of patients’ was 30 years with female dominance. More number (29/50) of patients was found in the age group of 40-60 years, whereas the number of patients from the age group of 0-20 years was the least, 20/50 (40%). Number of patients in the 21-40 years of age was 11/50 (22%). Female patients were found to be 42/50 (84%), while the male patients were 8/50 (16%) (Figure 1).



**Figure 1: Distribution of gender.**

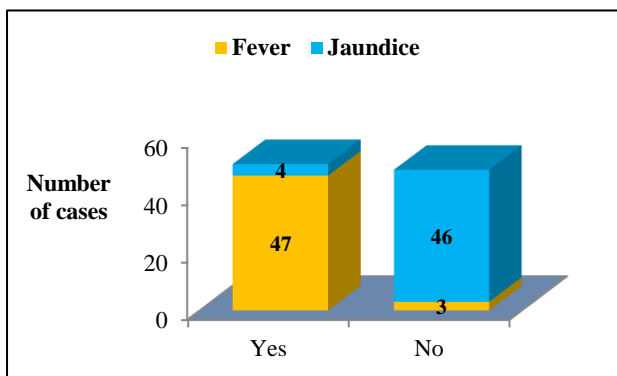
The male to female ratio was found to be 4:21. The indications for the liver transplantation were depicted in Table 1.

**Table 1: Indications for liver transplantations.**

Indications	Number of cases (%)
Cryptogenic cirrhosis	30 (60)
Ethanol related	5 (10)
Zinc phosphide	2 (4)
Wilson’s disease	2 (4)
Extrahepatic biliary atresia	2 (4)
Hepatitis B	2 (4)
Hepatocellular carcinoma	2 (4)
Fulminant hepatic failure	2 (4)
Hepatitis A	1 (2)
Caroli’s disease	1 (2)
Drug induced	1 (2)

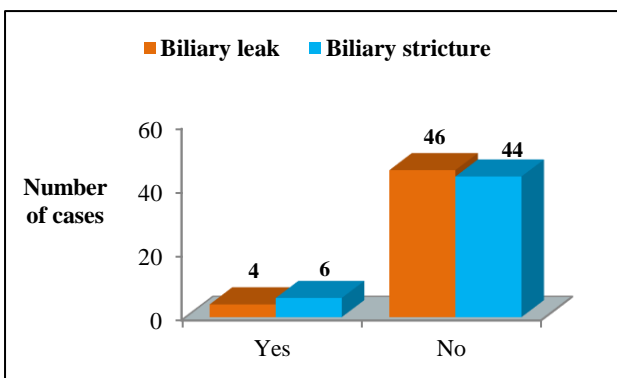
The cryptogenic cirrhosis was found as the major indication 30/50 (60 %) for transplantation. Among the total 50 patients, 5 cases (10%) were ethanol related. Caroli’s disease and drug induced cases were only 1/50 each (2%). The virus associated total cases were 3/50 (6%). Among this, hepatitis A was associated in only 2%, whilst the hepatitis B was the aetiology involved in 2/50 cases (4%). Hepatocellular carcinoma (2/50) and fulminant hepatic failure cases were also 2/50 each (4%).

The major clinical finding presented among the liver transplanted patients with biliary complications was fever. It was found in 47/50 patients (94%) and was found to be the major presentation. The Jaundice was found only in 4/50 cases (8%) (Figure 2).



**Figure 2: Distribution of clinical presentation.**

The biliary complications are depicted in Figure 3. The complications such as biliary leak was found in only 4/50 cases (8%), whereas the biliary stricture was found in 6/50 cases (12%). The bilioma was detected by both USG and CT. The incident was found only in 2/50 cases (4%). The mean time of presentation of biliary complications after the transplantation was found to be 2.6 months. The biliary complication was managed by ERCP in 83% of cases. Percutaneous approach was selected for the remaining 17% of the cases.



**Figure 3: Distribution of biliary complications.**

**DISCUSSION**

Results of the study reveal that the biliary complications such as leak, and stricture were observed in only 8 and 12% of cases, respectively. Biliary complications were evaluated by the modalities like USG, CT, MRCP and ERCP.<sup>8</sup> USG is the initial imaging modality of choice for the detection of biliary dilatation. Ultrasound is highly sensitive for the detection of biliary obstruction (accuracy >90%) and the level of obstruction. However, the accuracy of ultrasound for the detection of the underlying cause varies widely (38-66%).<sup>9</sup> Ultrasound shows intrahepatic biliary radical dilatation in cases of biliary

stricture and anechoic sub-diaphragmatic collection in cases of bile leak and bilioma. Bile duct rupture and extravasation of the bile within the liver or the abdominal cavity result in a bilioma. In this study, only 2 cases were diagnosed as bilioma by USG or CT.

Multidetector computed tomography (MRCP) helps in the detection of biliary dilatation, the underlying cause of biliary obstruction, and complications such as cholangitis and cholangitic abscess. MRCP has 93-100% sensitivity in detection of biliary strictures and is increasingly used to avoid the risks of ERCP or PTBD. Furthermore, MRCP offers the advantage of non-invasive imaging allows evaluation of the biliary system beyond a tight stricture, and also allows the assessment of the hepatic parenchyma and other intra-abdominal viscera. But ERCP and PTBD play a potential therapeutic role in the management of biliary complications in post liver transplant. ERCP has been the gold standard investigation for the evaluation of biliary obstruction. The major advantage of ERCP involves obtaining a tissue diagnosis to differentiate benign from malignant causes. The main cause of macroangiopathic NAS is hepatic artery thrombosis. In this study, we encountered only AS.

Previous study by Akamatsu et al, found that the incidence of biliary stricture among the 14359 liver transplant cases was 19%.<sup>10</sup> The incidence of stricture in our study was significantly less. A study with larger numbers is needed to validate this result. Akamatsu et al, found that the incidence of biliary leak is 9.5%.<sup>10</sup> The incidence of biliary leak in this study is also less. The discrepancy may be due to the relatively small number of patients.

Bile duct variations are common and intraoperative cholangiogram is done to find any bile duct variations before transplantation. The most common anatomic variant involves the right posterior duct joining the right anterior or left hepatic duct. In this study, there was no correlation between biliary complication and biliary anatomical variation. Li et al, found no correlation between biliary complications and biliary anatomical variations.<sup>11</sup> Prior knowledge of the variation obtained with MRCP helps to plan any modification of surgical technique and, thereby, avoid complications. The incidence of biliary complications is highest in the first few months after transplantation. In this study, the mean time of presentation of biliary complications was 2.6 months. Ayoub et al, found that the mean time of presentation of biliary complication is 3.3 to 5.9 months.<sup>12</sup>

ERCP is the first line modality for the management of postoperative biliary complications. In this study, 83% of the biliary complications were managed by ERCP and 17% by PTBD. Chingchan et al, in their study found that the success rate of ERCP in treating biliary stricture is about 75% of cases.<sup>13</sup> Short biliary anastomotic strictures are usually amenable to dilatation by ERCP followed by

temporary stenting. It is more difficult if stricture is long and extends into the graft and segregate into right anterior and posterior hepatic ducts. PTBD becomes very useful under these circumstances and is usually successful. The procedure is especially challenging when collapsed intrahepatic ducts have to be cannulated in the presence of biliary leak. A significant proportion of patients develop biliary complication following LDLT. Biliary complications require multi-modality imaging for diagnosis and follow-up in all patients and interventional management is required in a small subset of patients.

## CONCLUSION

The incidence of biliary stricture in the live donor liver transplant patients is 12% and biliary leak is 8%. The mean time of presentation of biliary complications is 2.6 months. ERCP was used in 83% of cases for managing biliary complications and in 17% of cases percutaneous approach was used. There was no correlation between biliary anatomical variation and biliary complications.

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