To Assess the Frequency of Different Clinical Presentations in Patients with Living Donor Liver Transplant Anastomotic Biliary Stricture

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ABSTRACT

Introduction: Liver cirrhosis is one the leading cause of death in Pakistan. Liver Transplant is the only curative treatment option in decompensated liver cirrhosis. Deceased donor organs are seldom available in Pakistan, so organs from living donors are used. Until now only one deceased donor liver transplant has been performed in Pakistan. Living Donor Liver Transplant (LDLT) is associated with many complications; most common among all is anastomotic biliary stricture (AS). Patients with AS presents with different symptoms such as itching, jaundice, dark urine etc. Aims and Objectives: The aim of this study was to evaluate frequency of different presentations in patients with LDLT AS. 60 patients with LDLT AS were enrolled in this cross-sectional study and data was recorded on proforma and analyzed using SPSS 22 to evaluate the frequency of different presenting symptoms. Place and Duration of Study: Department of Gastroenterology, Shaikh Zayed Hospital Lahore from February 2017 to July 2017. Material and Methods: 60 patients who fulfilled the inclusion and exclusion criteria were enrolled. After confirmation of anastomotic stricture by radiological means (Ultrasound and MRCP), patients’ clinical data was recorded and analyzed. Results: Results showed that pruritus alone was present in 55% (33/60) of the enrolled patients. Pruritus along with jaundice was present in 5% (3/60). Dark urine along with jaundice was present in 6.66% (4/60) while clay colored stools along with jaundice were present in 3.33% (2/60) patients. 5% (3/60) patients presented with cholangitis. 1.66% (1/60%) had only elevated liver enzymes i.e. ALT, AST, ALP and GGT and combination of more than two symptoms were present in 23.33% (14/60) of the enrolled patients. MRCP was found to be superior to ultrasound in detecting post LDLT AS: 40% v/s 100% (p<0.05). Conclusion: We concluded that patients with post LDLT AS presents with subtle symptoms and high index of suspicion should be maintained for early diagnosis and prompt management to save graft.

Key words: Living Donor, Liver Transplant, Anastomotic Biliary Stricture

INTRODUCTION

Liver cirrhosis is one of the commonest causes of morbidity and mortality all over the world. It is also prevalent in south Asia, especially in Pakistan. Data on exact prevalence of cirrhosis in world population is scarce but estimates are around 1%1. Long term alcohol intake, viral hepatitis B and C, Non-Alcoholic Fatty Liver Disease (NAFLD) and other metabolic causes can lead to cirrhosis. In Pakistan, viral hepatitis B & C are responsible for majority of cases of cirrhosis2. Data on exact incidence of viral hepatitis in Pakistan is scarce but estimates range from 5-10%3-4. With progression of liver disease, decompensation occurs. The only definitive treatment option in decompensated cirrhosis is liver transplantation5.

The first successful Living Donor Liver Transplant was performed in 1989 in a child and in an adult in 19946-7. Living Donor liver transplant is the only option in countries like Pakistan as deceased donor livers are scarce due to lack of education on organ donation. Living donor liver transplant is associated with relatively more
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complications due to technical complexities. Due to improvements in surgical techniques and technology, 1-year survival in liver transplant patients has reached 85-90%\(^8\). Because of improved survival, now more patients are presenting with complications. Hepatic artery thrombosis, bile leak, acute cellular rejection, chronic ductopenic rejection, opportunistic infections and anastomotic strictures are few of the complications. In living donor liver transplant patients, anastomotic biliary strictures are more common. Anastomotic biliary strictures are single, short segment and occur at the site of duct to duct anastomosis. Bile ducts are more prone to ischemic injury as these ducts are supplied by only hepatic artery in contrast to hepatic parenchyma which is supplied by both hepatic artery and portal vein. Tissue ischemia can lead to necrosis of biliary epithelium which ultimately results in fibrosis leading to stricture formation. Patients with stricture at anastomotic site usually present in first year after liver transplant. The reported incidence of biliary stricture after living donor liver transplant is 28-32%\(^9\). Patients usually presents with pruritus, jaundice, clay colored stools, dark urine, fever (cholangitis), pain in the right hypochondrial region, deranged liver enzymes or any combination of these symptoms. The diagnosis is usually confirmed by deranged liver enzymes and abnormalities on Radiological testing. Data about presenting symptoms in post LDLT AS is scarce and it is the first study conducted in Pakistan on this topic. In this study, we evaluated the frequency of different presenting symptoms in patients with post LDLT anastomotic stricture and aimed to identify the most common features.

MATERIAL AND METHODS

This was a cross sectional study conducted at Gastroenterology department, Shaikh Zayed Hospital Lahore from February 2017 to July 2017. Living donor liver transplant patients were defined as patients with liver transplant in which donor organ was taken from living donor i.e. right lobe of the donor liver was used as graft. Anastomotic biliary stricture was defined as stricture at anastomotic site of donor and recipient bile duct which was confirmed on ultrasound, MRCP and ERCP. All Patients with LDLT AS of either sex, aged 18 Years and above were included. Patients with malignant biliary strictures were excluded from the study.

Data Collection Procedure:
In this cross-sectional study, 60 patients who had undergone living donor liver transplant and met the inclusion and exclusion criteria were enrolled. Complete history was taken. All baseline investigations were sent. Ultrasound abdomen was done initially by expert radiologist followed by Magnetic resonance Cholangio-Pancreaticography (MRCP) and later on cholangiogram by ERCP to confirm and manage AS. Written informed consent was obtained from patients before induction in the study. All the data was recorded on a specially designed proforma.

Statistical Analysis:
Collected data was analysed by using the Statistical Package for Social Sciences (SPSS) version 22. The demographic variables included identification data and demographic characteristics. Quantitative data was described by mean, median, standard deviation and qualitative data was described using frequency and percentages. \(P\)-value \(\leq 0.05\) was taken as significant.

RESULTS

Our study was conducted on LDLT patients who developed anastomotic biliary stricture. All of our enrolled patients had received right lobe of the donor liver as a graft. Mean age of patients enrolled in our study was 47.2 +/-10.01 years. Out of these 78.33%(47/60) were male and 21.67%(13/60) were female patients. Cause of liver transplant was hepatitis C related cirrhosis liver in 80%(48/60) patients, hepatitis B related cirrhosis in 13.33%(8/60) patients, alcoholic cirrhosis in 3.33%(2/60)patients and other causes in 3.33%(2/60) patients. 70%(42/60) Patients enrolled in our study had a single biliary anastomosis while 30%(18/60) patients had two anastomosis. Ductoplasty was done in 41.66%(25/60) patients. Mean interval between liver transplant and diagnosis of AS was 5.3 +/-1.34 months. Pruritus alone was the most frequent presenting symptom which was present in 55%(33/60) of the enrolled patients. Pruritus along with jaundice was present in 5%(3/60). 6.66%(4/60) of the enrolled patients presented with dark urine along with jaundice. Clay colored stools along with jaundice were present in
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3.33% (2/60) patients. 5% (3/60) patient had fever secondary to cholangitis resulting because of obstruction secondary to AS. 1.66% (1/60) had only elevated liver enzymes and combination of more than two symptoms was present in 23.33% (14/60) of the enrolled patient population. Ultrasound abdomen and MRCP was used to diagnose biliary stricture and later confirmed on cholangiography by using ERCP. Ultrasound with liver and biliary protocol only confirms anastomotic biliary stricture or ductal dilatation in 40% of enrolled patients while MRCP showed anastomotic biliary stricture in 100% of patients which was later on confirmed on cholangiography done by using ERCP.

DISCUSSION

Liver cirrhosis is the leading cause of morbidity and mortality in Pakistan. About one fourth (27%) of hospital admissions in Pakistan are related to liver disease whereas cardiovascular causes accounts for 16.2%. It is in contrast to international studies showing cardiovascular diseases as the leading cause of hospital admission. Viral Hepatitis i.e. Hepatitis C and Hepatitis B is the culprit in overwhelming majority of cirrhotic patients. Pakistan has the second highest burden of HCV in the world. With millions of cirrhotic patients, the number of decompensated patients is also increasing. The only definite treatment option for decompensated cirrhosis is liver transplant. Organ donation is not a trend in Pakistan. The only option left for Pakistani patients with liver cirrhosis is living donor liver transplant. The first successful living donor liver transplant in Pakistan was done in 2011 at Shaikh Zayed Hospital, Lahore, Pakistan. Since then more than 600 Living donors Liver transplant have been performed in Pakistan. Living donor liver transplant is associated with some complications. Anastomotic biliary stricture is one of the common complications. In this study, we evaluated the different presentations of AS. Prompt management is the key to save graft. For proper management, early diagnosis is the cornerstone. To diagnose patients early, we need to know the different presentations. In iatrogenic and malignant biliary strictures, patients typically presents with deep jaundice, itching and clay colored stools. In contrast to this, patients with Post LDLT AS presenting symptoms are usually subtle and sometimes needs to be differentiated from acute cellular rejection and opportunistic infections. Liver biopsy is essential to rule out rejection and other tests are carried out for infections if suspected. As patients presents with non-specific symptoms, a high index of suspicion should be maintained. Symptoms in patients with biliary anastomotic stricture are usually due to obstruction and in few patients due to cholangitis. Mild itching in majority of recipients is usually the only presenting symptom. Minimal derangement of liver enzymes predominantly alkaline phosphatase and gamma glutamyl transferase is another clue to start thinking about stricture formation. Only a few patients present with full blown picture of obstructive jaundice. Biliary strictures usually present early after LDLT. The mean time from LDLT transplant to development of biliary stricture is 5-8 months. 70-87% of biliary strictures develop within one year of transplant. Development of biliary stricture after one year slows down and plateaus at 3 years. In our study, mean interval between liver transplant and diagnosis of biliary stricture was 5.3+/-1.34 months which are in accordance with the previous studies. 70% patients in our study who developed biliary strictures had a single biliary anastomosis while 30% had two anastomoses. So, single biliary anastomosis is not better than two or more anastomoses to prevent development of biliary strictures which is also backed by previous studies. Ultrasound only showed narrowing at anastomotic site of bile duct or ductal dilatation in only 40% of patients who had a definite stricture on cholangiogram obtained by ERCP. Ductal dilatation is not a consistent finding in patients with biliary obstruction in transplanted liver. It is because of less pliable biliary ducts after transplant due to biliary fibrosis with diminished ability to dilate. Without proximal ductal dilatation, it is difficult to pick biliary obstruction using ultrasound. All patients enrolled in our study who had a stricture on MRCP were found to have a definite stricture on cholangiogram obtained during ERCP. So, MRCP should be the preferred choice for patients suspected to have a post LDLT stricture. Although cholangiogram is considered to be the gold standard, MRCP is also a reliable non-invasive imaging modality. MRCP can be used with confidence to diagnose post LDLT anastomotic biliary stricture as ERCP is associated with complications and should only be reserved for therapeutic purposes. Data about presenting symptoms in post LDLT AS is
scarce and it is the first study conducted in Pakistan on this topic.

CONCLUSION:

Patients with post LDLT biliary stricture present with subtle symptoms and high index of suspicion is the key for early diagnosis and prompt management. MRCP is a good modality for diagnosing anastomotic biliary stricture. Early diagnosis and prompt management can prevent graft loss.

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