Hepatolithiasis and Surgical Approach - Experience of Hepatectomies in a Rural Medical College in North-East India

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ABSTRACT

BACKGROUND

Hepatolithiasis or intrahepatic stones irrespective of gall bladder stones or common bile duct stones are common in East Asian countries but rare in Western countries. Although Gall bladder stones are common in India, there is scarcity of literatures reporting hepatolithiasis from the Indian subcontinent. This study aimed to evaluate the clinical result of our first-hand experience of hepatectomies along with other standard surgical options for this low prevalence disease in a North East Indian institute catering to a rural population.

METHODS

11 patients with diagnosis of hepatolithiasis operated from the period June, 2014 to June 2019 were included in this study. Pre-operative radiological and biochemical, operative & postoperative variables were assessed. Patients were followed in a planned program.

RESULTS

Hepatic involvement were noted as Left lobe in 7 (64 %) cases, only right lobe in one case (9 %) and bilateral in three cases (27 %). Five cases (45.5 %) were associated with extrahepatic biliary pathology; concomitant intrahepatic and extrahepatic stones were seen in four cases (36 %). Anatomical left hepatectomies (3), left lateral sectionectomies (2) choledochotomy and T-tube drainage (6 primarily or one additional) were carried out. Functional outcomes were satisfactory in all patients. Postoperative morbidity was mostly due to wound infection and there was no mortality.

CONCLUSIONS

Preoperative optimization of patients, relative absence of risk factors and knowledge of biliary anatomy planned with modern imaging tools makes hepatectomy a safe definitive surgical option for localised hepatolithiasis. Hepaticojejunostomy may be contemplated selectively for bilateral hepatolithiasis. Long term follow up is necessary as recurrence is associated with this disease.

KEYWORDS

Hepatolithiasis, Hepatectomy, Sectionectomy, Hepaticojejunostomy, Choledochotomy and T-Tube Drainage

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BACKGROUND

Hepatolithiasis is defined as presence of gallstones in the bile ducts proximal to the confluence of the right and left hepatic ducts, irrespective of the co-existence of gallstones in the common bile duct (CBD) and / or gall bladder.[1] Hepatolithiasis is a rare disease in Western countries with a prevalence of 0.6 - 1.3 % in the past but is endemic in East Asia and its prevalence there can range as high as 30 – 50 %.[1,2,3] The aetiology of hepatolithiasis is diverse but yet to be fully understood. Genetic, dietary and environmental factors are thought to contribute to the disease.[3] Low fat and low protein dietary habit along with lower socioeconomic conditions and malnutrition & parasitic infestation (of biliary ascariasis, Clonorchis sinensis) are associated with a high incidence of intrahepatic stones.[4,5,6,7] In Western countries, hepatolithiasis is generally seen secondary to gall bladder stones, choledochal cysts or malignant biliary tumours primarily associated with sclerosing cholangitis, benign biliary strictures and Caroli's disease.[6,8] Hepatolithiasis is an uncommon entity in South India.[9] However, hepatolithiasis appears to be common in Northern India as reported in a retrospective study where ascariasis is endemic.[4]

Several management strategies for hepatolithiasis ranging from non-surgical to surgical modalities are proposed which are influenced by concomitant existence of extrahepatic stones, presence of strictures and cholangiocarcinoma.[10] The goal of treatment is the complete removal of intrahepatic and extrahepatic stones as well as duct strictures and to promote adequate drainage of the remaining segments of the biliary tree thus preventing recurrent cholangitis and subsequent atrophy of liver or progression to cholangiocarcinoma.[11] A novel classification called Dong's Classification can be used to determine possible surgical approach to treat hepatolithiasis.[3] Liver resection is considered a potentially curative treatment for unilateral hepatolithiasis.[3,11] For bilateral hepatolithiasis, the ideal treatment is not established yet; bilioenteric anastomosis or a percutaneous approach associated with or without liver resection have been employed.[11,12]

Aim: This study was undertaken at Fakhruddin Ali Ahmed Medical College to document the clinical result of our firsthand experience of hepatectomies along with other standard surgical options for this low prevalence disease in rural population of NE India.

METHODS

We included 11 patients who underwent standard surgical procedures for intrahepatic stones and coexistent extrahepatic stones / pathology from the period June, 2014 to June 2019. Relevant information regarding their personal particulars, past history, symptoms and the outcomes of the surgical procedures were recorded for each patient. In each patient the disease extent was assessed with abdominal USG (Ultra-Sound Sonography) and CECT (Contrast Enhanced Computerized Tomography) or MRCP (Magnetic Resonance Cholangiopancreatography) depending on the location of intrahepatic duct & CBD calculi and parenchymal atrophy; and correlated to Dong's classification system to decide surgical procedures appropriately. Pre-operative biochemical investigations and tumour markers (α-fetoprotein, CA19-9) were measured in all cases. Hepatectomies were performed using anatomic techniques according to Couinaud's segmentation and Brisbane 2000 terminology were used to denote various types of resections. Indications for anatomical hepatectomies were radiological evidence of multiple calculi in intrahepatic ductal system with atrophy of affected segments not amenable to treat with ERCP (Endoscopic Retrograde Cholangio-Pancreatography) or PTC (Percutaneous Transhepatic Cholangiography) and / or the possible presence of cholangiocarcinoma / cystic mass. In all cases a drain was placed routinely. All the patients were kept at ICU for initial 48 hrs. and intravenous broad-spectrum antibiotic prophylaxis were used. Twelve outcome variables recorded for each patients includes operative time (min), intraoperative blood transfusion (mL), postoperative hospital stay (day), post-anaesthetic recovery, starting oral feed (day), type of analgesia and impact, post-operative FFP (Fresh Frozen Plasma) transfusion (number of unit), complication, LFT (Liver Function Test) on postoperative day 1 or 2 and 5, postoperative intervention (if any), residual stone and histopathological review. Patients were subjected to a planned follow up program (at 1, 3, 6, and yearly after discharge) and liver morphological findings were obtained by ultrasonography and / or MRCP at least once.

ERCP and PTC facilities are not available in our institution.

RESULTS

11 patients of hepatolithiasis were treated during this period. All the eleven cases were from remote rural areas with limited access to health care. The median age of cases was 52 (23 - 62) years with male to female ratio 6:5 and overall 64 % cases of hepatolithiasis were seen among people of 51 to 70 years. Hepatic involvement was noted in left lobe only in 7 (64 %) cases, only right lobe in one case (9 %) and bilateral in three cases (27 %). Six cases (54.5 %) were associated with extrahepatic biliary pathology; concomitant intrahepatic and extrahepatic stones were seen in four cases (36 %) with median age 50 years, post-cholecystectomy was associated in one case and a dead CBD worm was found in one case who presented with acute pancreatitis. One case had intrahepatic biliary cystoadenoma. Age distribution and associated diseases are shown in table 1 and table 2.

Age Group (in Years)	Male	Female	Total (%)
Below 30	1	0	1 (9.09)
31 - 40	0	1	1 (9.09)
41 - 50	0	2	2 (18.18)
51 - 60	5	1	6 (54.54)
61 - 70	1	0	1 (9.09)

Table 1. Age Distribution

Choledocholithiasis	4
Post-Cholecystectomy	1
Acute Biliary Pancreatitis	1
Intrahepatic Biliary Cystoadenoma	1

Table 2. Associated Disease

Pain abdomen alone was presenting symptom in one case only (23 year and no co morbidity) and LFT values were normal. Pain abdomen and episodes of transient self-limiting jaundice was seen in 2 patients with parenchymal atrophy and 2 patients without parenchymal atrophy. Clinical cholangitis was seen in 3 cases with atrophy and 3 patients without parenchymal atrophy. Among the 6 cases of clinical cholangitis 5 had CBD pathology. All these 10 patients had varying degree of liver function derangements; in addition one of them who presented with acute pancreatitis had serum amylase level of 1213 U / L and TC 27.3 X 10^3 / mm^3. No cases had thrombocytopenia. Results of α-fetoprotein, CA19-9 were within normal limit in each patient. Mean duration of symptoms was 3.13 years.

Anatomical left hepatectomies were performed in 3 cases of left sided type Ia hepatolithiasis with atrophy and left lateral sectionectomies were performed in 2 cases of left sided type Ia hepatolithiasis with atrophy; choledochotomy and T tube drainages was performed in one case as additional procedure. Choledochotomy, stone extraction and T-tube drainage was performed in 6 cases : 3 cases where stones were located throughout the intrahepatic bile ducts of both lobes without atrophy and stones in common bile duct (type IIa + Ea), 1 right sided and 2 left sided type Ia cases of hepatolithiasis without atrophy [Table 3].

Case No.	Location	EBD Calculus /Dilatation	Parenchymal Atrophy	Type	Treatment*
1	L lobe duct (segment IV)	no	Present	Ia	Left Hepatectomy
2	L lobe duct (segment II, III, IV)	Post - cholecystectomy	Present	Ia	Left Hepatectomy
3	L lobe duct (segment II, III, IV)	Multiple calculi	Present	Ia + Ea	L Hepatectomy + Choledochotomy + T - tube drainage
4, 5	L lobe duct (segment II, III)	no	Present	Ia	Left lateral sectionectomy
6	R lobe duct (segment V, VIII)	no	Absent	Ia	Choledochotomy +T-tube drainage
7	L Hepatic Duct	no,	Absent	Ia	Choledochotomy +T-tube drainage
8	L hepatic duct & Segment IV Duct	Dead worm in CBD, dilatation	Absent	Ia	Choledochotomy + T-tube drainage
9,10, 11	Both lobe (diffuse)	Multiple calculi, dilatation	Absent	IIa + Ea	Choledochotomy + T-tube drainage

Table 3. Case Wise Distribution into Dong's Classification and Treatment

LH: Left Hepatectomy, CBD: Common Bile Duct L: Left R: Right, EBD: Extra Hepatic Bile Duct

The mean operative time, mean intra-operative transfusion and mean hospital stay for hepatic resections (n = 5) were 344 min, 390 mL and 17 days (range 12 – 31 days) respectively. While mean operative time and mean hospital stay for others (n = 6) were 200 min and 11.33 days (range 9 - 14 days) respectively; they did not require intra-operative blood transfusion. Post anaesthetic recovery was uneventful in all cases.

Minor deflection in liver enzymes and PT (Prothrombin Time) but INR (International Normalized Ratio) less than 1.5 was noted in eight cases including post-hepatectomies and three post-choledochotomies and 2-unit FFP transfusion was done in all eight cases. All hepatectomies received epidural analgesia through epidural catheter placed before induction of general anaesthesia. No additional intramuscular analgesic required. Patient's mobilisation was done after catheter was removed on 3rd day without any major issue. Wound infections were seen in 3 cases; two in post-hepatectomies and one in post-choledochotomy case. Pleural effusion and subhepatic and subphrenic collection was seen in 1 case with post-hepatectomy with choledochotomy due to T tube removal on 14th postoperative day and managed by combined USG guided aspiration and ERCP stenting. No mortality was seen. Follow up period range from 6 - 36 months; no recurrence was observed.

Histopathological Report

The histopathological findings of hepatectomies included hepatic fibrosis, strictures and dilatations of intrahepatic bile ductles with denuded epithelium and ductal lithiasis. Surrounding hepatic parenchyma showed areas of degeneration and necrosis with chronic inflammatory cell infiltration, mostly around portal triads. In one case, the specimen on macroscopic examination showed a multiloculated cavity with smooth lining and filled with clear and greenish bile like material in addition to calculi in central and dilated ducts and surrounding atrophy and occasional calcification in septa. Final histopathology report was cystoadenoma. Presence of cholangiocarcinoma was not reported in any case.

DISCUSSION

In our present study, predominantly left lobe is affected which is consistent with findings in other series;[3,4,5,9,11] the above fact has been explained by the fact of poor evacuation of bile and stasis due to left hepatic duct meeting the common hepatic duct at nearly an acute angle.[5] Xi Ran et al mentioned four chief factors cholestasis, infection, anatomic anomalies of bile duct, and bile metabolic defect in the development of hepatolithiasis. The majority of the cases of hepatolithiasis are calcium bilirubinate stones in East Asia whereas in the west is usually composed of cholesterol stone; however a decrease prevalence of bilirubin stones in Japan may be related to multiple factors including eradication of parasites and westernization of diet.[13] They also found that the occurrence rate for intrahepatic stones was similar for the patients with bilirubin stones solely in the common bile ducts suggesting a pathogenetic similarity and observed increasing prevalence with age. In our present study most of the patients were seen in 51 - 60 age group and concomitant intrahepatic and extrahepatic stones were seen in four cases (36 %) with median age 50 years. The majority of cases of biliary ascariasis in India are seen in endemic regions and present with biliary pain, acute

cholangitis, acute cholecystitis and acute pancreatitis. Duration of symptoms may vary over few years. Migration of the worms into the bile duct is often noticed after cholecystectomy, sphincterotomy, choledocho-duodenostomy or sphincteroplasty. If a worm is dead within the billiary tree, it acts as a nidus for stone formation.[4,5,6,7,8] In a series of 47 cases of biliary ascariasis from NE (North East) India, hepatolithiasis was recorded in 3 patients (6.3 %).[6] In another series of 110 cases of left hepatolithiasis from an institute in highly endemic region of India, biliary ascariasis (live or dead) contributed towards 7.3 % of the total aetiologies of hepatolithiasis.[4] Although co-existence of parasitic infestations with hepatolithiasis appears to be incidental finding rather than causative one as viewed by few authors,[11] similar findings in endemic areas as in our case may play a role in aetiopathogenesis of hepatolithiasis.

Acute cholangitis was major presenting symptoms in 86.2 % cases in a series of 123 patients undergoing hepatectomy for hepatolithiasis and presence of bacteria in bile of hepatolithiasis is 100 %.[14] According to literatures, only 50 - 70 % cases of acute cholangitis manifest Charcot's triad.[15] Although fever was not a component of clinical Charcot's triad in four out of ten cases, the laboratory and imaging findings supported that ten cases had cholangitis. Nine cases responded well to initial conservative treatment and operated after optimization; they can be considered grade I cholangitis. The biochemical data (LFT and TC) did not showed remarkable improvement with conservative treatment in one patient with dead worm in CBD and had to undergo surgery in same condition but satisfactory post-operative recovery was noted and can be considered grade II cholangitis.[15] Bacterial infection of bile and varying level of biliary obstruction and strictures may have caused cholangitis.

Hepatolithiasis is a disease thought to be uncommonly encountered in Indian scenario. However, with the introduction of CT scan and MRI into the rural health system, we got the opportunity to understand this disease in terms of true demographic characteristics and to record our firsthand experience of clinical management of this disease. Both Abdominal USG and CT were used primarily for diagnosis of hepatolithiasis and evaluation of the biliary system with degree of hepatic atrophies. CT is useful for detection of strictures and dilatation of ducts, intrahepatic tumours, cholangiocarcinoma and calcification.[16] MRCP can provide realistic biliary tree mapping, distal CBD status and also detect stones.[17] In our present study none of them had CT demonstrable cirrhosis / steatohepatitis. Hepatic atrophy of the left lobe was present in 5 cases along with intrahepatic stones; in one case that had USG and CT demonstrable intrahepatic calculi and atrophy, biliary cystoadenoma was considered a differential diagnosis. However, no case had radiological evidence of cholangiocarcinoma.

Preoperative radiological diagnosis of cystoadenoma is challenging. Intrahepatic biliary cystoadenoma is a rare tumour of liver with fewer than 100 reported cases worldwide.[18] Although there has been controversy regarding the distinction between hepatic mucinous cystic neoplasm and biliary intraductal papillary neoplasm which is more commonly seen in Asian countries partly because of a higher incidence of hepatolithiasis or Clonorchis infection, few authors consider them as two distinct entities and observed that cystadenomas are multilocular, benign and have a female preponderance.[19,20] However, intrahepatic multiloculated biliary cystoadenoma with intracystic calculi is reported once.[21] Shize Lei observed that the communication of cystadenoma to large intrahepatic bile duct, its bile-like content, and the type of lining of the cyst favours its congenital origin. Because of rarity of this condition much is not known about this tumour, but malignant propensity has also have been reported.[22] Lewis and associates on their basis of experiences concluded that complete surgical resection is the treatment of choice.[23] In our present series, the female case with cystoadenoma and intracystic calculi, was treated with anatomic left hepatectomy and without any local recurrence.

Management of hepatolithiasis can be either surgical or endoscopic or through PTC depending on the extent of the disease. Although ERCP or PTC may prove to be effective in temporarily managing cholestasis and stone extraction, they do not allow definitive removal of sclerotic intrahepatic bile ducts. Thus these techniques may predispose to subsequent recurrence of cholangitis and septic complications and require repetitive interventions.[11] Thus surgical resection remains the definitive treatment for complete removal of intrahepatic stones and strictures and cholangiocarcinoma and should be indicated for all cases.[3,11] However some authors observed that operative interventions are not acceptable in instances like patients with high risk co-morbidities or stones distributed in multiple segments bilaterally.[24,25] Sectionectomy is an effective treatment in type I (localized stone disease: unilobar or bilobar) and type IIb (diffuse stone disease with segmental atrophy and / stricture) hepatolithiasis. Liver transplant is usually indicated in type IIc (diffuse stone disease with secondary biliary cirrhosis) hepatolithiasis. Type IIa (diffuse stone disease without segmental atrophy and / stricture and IIb patient should undergo stone removal along with Roux en Y hepaticojejunostomy as they are associated with high risk of stone recurrence.[3,26,27] If a CBD stricture or extrahepatic stones are present in combination with intrahepatic stones, then resection of atrophic segment and hepaticojejunostomy is recommended;[3,28] in contrast, few authors recommended resection of hepatic segments with CBD exploration and T tube drainage and advocate use of hepaticojejunostomy selectively.[26] We did not performed hepaticojejunostomies in our all three type IIa cases of hepatolithiasis (along with extrahepatic stones and dilatation) but opted for choledochotomy, stones extraction and T tube drainage. Several authors concluded that treatment outcome of hepaticojejunostomies are not satisfactory in terms of high rate of residual stones, cholangitis and recurrence; also prevents postoperative choledochoscopic intervention. In fact Roux en Y hepaticojejunostomy does not efficiently drain peripherally located intrahepatic stones as popularly thought. Choledochotomy and T tube drainage preserves the chance of postoperative interventions for residual stones. There was no statistical difference between HJ group and choledochotomy and T tube drainage group in terms of residual stone rate. So HJ should be treatment of choice only

in situation where bile duct stricture or congenital cystic dilatations of bile duct exist along with bilateral hepatolithiasis.[28] In another study immediate stone clearance rate after hepatectomy was 92.7 % and final stone clearance rate using subsequent T-tube route or ERCP was 96 %.[14]

Patients undergoing hepatectomies for hepatolithiasis operative morbidity rate was 13.3 %, 25.5 %, 32 % in three different series but mostly comprising of wound infection, biliary leakage, pleural effusion, pneumonia, stress ulcer, abdominal bleeding and post-hepatectomy liver failure.[3,29,30] Presence of cholangitis and dissections in post inflammatory adhesions surrounding the diseased lobe and porta requiring prolong dissection time and increase blood loss may be considered for postoperative septic condition in the form of wound infection and pleural effusion in present series. Patients who underwent hepatectomies had no major postoperative bile leakages, residual stones or recurrence of stones during follow-up. This observation may be attributed due to selection of anatomical hepatectomies. Several authors have concluded that anatomical liver resection have established benefit over non-anatomical resection in terms of reducing the postoperative bile leakage, residual stones and recurrent stones.[31,32] Also worth to mention that higher rate of biliary leakage after hepatectomies had been observed in patient of hepatolithiasis with Caroli's disease.[32] We did not use harmonic scalpel in any case but using Kelly clasis also has the advantage of not causing any lateral damage to liver parenchyma which becomes important to save the trunk of middle hepatic vein in particular. Hepatic hilar clamping as first demonstrated by Pringle is well accepted by the hepatobiliary surgeons and practically very useful for the occasional liver surgeons in small institutions for the purpose of both anatomical and non-anatomical hepatic resections combined with Kelly classic or finger fracture method in the absence of harmonic scalpel or CUSA. As adjunct to transection, to minimize blood loss use of low CVP (Central Venous Pressure) was not practised in our cases. Also, a Cochrane review of low CVP failed to demonstrate any significant clinical benefit.[33] Our preliminary experience of epidural analgesia in hepatic resection is excellent in terms of pain relief and early return of bowel sounds. No associated epidural haematoma observed.[34]

Although mild hepatic insufficiency characterised by transient hyperbilirubinemia and raised liver enzymes existed on postoperative period in hepatectomy patients, it did not alter the expected postoperative outcome in our cases. Patients were prescribed with ursodeoxycholic acid once they could tolerate oral semisolids. All cases of hepatectomies got FFP routinely in postoperative period. Presence of increase age, long operative time with high blood loss owing to severe inflammatory adhesion at porta may have played role in the development of postoperative transient rise in LFT; but whether the prophylactic use of FFP or relative absence of known factors of post hepatectomy liver failure like obesity, DM (Diabetes Mellitus), underlying cirrhosis, major resection with low FLR (Future Liver Remnant), brings down LFT to normal is not clear.

CONCLUSIONS

Anatomical hepatectomies are safe and effective procedures for localised hepatolithiasis. Avoiding additional hepaticojejunostomy to anatomical hepatectomies, or selective use of hepaticojejunostomy and CBD exploration for bilateral hepatolithiasis may contribute towards positive outcome in terms of reducing morbidity or mortality. Further we believe that the real clinical practice may be different in different countries depending upon the expertise, experience and availability of sophisticated infrastructures. However well planned preoperative and perioperative approach based on overall condition including general status, comorbidities, liver function, estimate of FLR, and presence of biliary sepsis should be essentially outlined for individual patients to reduce postoperative complications and achieve optimal outcome.

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