

# A Retro-Pro prospective Study of Histopathological Findings in Isolated Left Sided Hepatic Resections in Cases of Isolated Left Sided Hepatolithiasis

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## ABSTRACT

**Objective:** To study detailed preoperative anatomy of left hepatobiliary system in cases of isolated left sided hepatolithiasis, appropriate surgical management and histopathology findings in isolated left hepatic resection specimens.

**Material and Methods:** This retro-prospective study was conducted at Sher-i-Kashmir Institute of Medical Science, Srinagar between May 2003 and December 2011. A total number of 80 cases were included in the study. All cases of isolated left sided hepatolithiasis were preoperatively evaluated for detailed anatomical assessment of left hepatobiliary system. Based on anatomical assessment appropriate surgical management; left hemi-hepatectomy or left lateral sectionectomy was done. Histopathological examination of isolated left hepatic resection specimen in left hepatolithiasis was carried out for grading of fibrosis/glandular changes/inflammation/other changes of chronic proliferative cholangitis and detection of any malignant changes.

**Results:** The results of present study show that Left lateral section of the liver (segment 2 & 3) is most commonly involved in isolated left hepatolithiasis (70.0%) and Type 1 LHD Anatomy is the principal variant seen in 72 cases (90%). Total left hepatic resections carried out were 80. Left lateral sectionectomy was done in 56 subjects, left hemi hepatectomy was done in 23 patients and left hemihepatectomy with caudate lobe resection was done in 1 subject. In the present study detailed histopathological examination revealed; Severe portal fibrosis (43.7%) is the most common type of portal fibrosis, Severe periportal fibrosis (42.5%) is the most common type of periportal fibrosis, Moderate portal inflammation (73.75%) is the most common type of portal inflammation seen,

Moderate periportal inflammation seen in 70.0% of patients is the most common type of periportal inflammation. Moderate ductal proliferation seen in 35.0% is the most common type of ductal proliferation seen; Cholestasis is seen in 83.75% and hepatic necrosis in 46.25%. Cholangiocarcinoma is seen in 2 cases (2.5%). Bacterial culture of the cases showed Escherchia coli in 41.25%cases, klebsiella in 21.25%, proteus in 12.5%, pseudomonas aerugenosa in 8.7% and multiple organisms in 16.2%of the cases.

**Conclusion:** Isolated left sided hepatic resection is an appropriate management for isolated left sided hepatolithiasis as it removes all intrahepatic stones along with the pathological bile ducts thus eliminating the chances of recurrent intrahepatic stones and the most unfavorable complication of disease i.e intra-hepatic Cholangiocarcinoma (IHCC).

**Key Words:** Hepatolithiasis, Hepatic Resections, Cholangiocarcinoma, Left Hepatic Duct Anatomy.

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## INTRODUCTION

Hepatolithiasis or intra-hepatic calculi by definition refers to concretions existing in intra-hepatic duct, proximal to the confluence of right or left hepatic ducts<sup>1</sup> irrespective of coexistence of choledocholithiasis and/or cholecystolithiasis.<sup>2</sup>

Hepatolithiasis most commonly affect the left hepatobiliary system because left hepatic duct has a more acute angle than the right hepatic duct.<sup>3</sup> The disease is characterized by its intractable nature and frequent recurrences, requiring multiple operative

intervention, in distinct contrast to gall bladder cholesterol or black pigment stones. Moreover, the most unfavorable complication of the disease is an intra-hepatic Cholangiocarcinoma (IHCC), incidence of 2.36% to 10%.<sup>4</sup>

## MATERIAL AND METHODS

This retro-prospective study was conducted at Sher-i-Kashmir Institute of Medical Science, Srinagar between May 2003 and December 2011. A total number of 80 cases were included in the study. All cases of isolated left sided hepatolithiasis were preoperatively evaluated for detailed anatomical assessment of left hepatobiliary system with investigations like ultrasonography, MRCP, CT Scan and if needed ERCP.

Three types of variations observed in left hepatic duct anatomy were described by using nomenclature given by Cho A and et al.<sup>5</sup>

- Type 1 variant. Segment II and III ducts unite just above or laterally to umbilical portion; segment IV duct then joins medially to umbilical portion.
- Type 2 variant. Segment III and IV ducts unite medially to umbilical portion; segment II duct then joins close to the hepatic hilum.
- Type 3 variant. Three ducts from segments II-IV immediately unite medially to Umbilical portion.

Based on anatomical assessment appropriate surgical management; left hemi-hepatectomy or left lateral sectionectomy was done. Exclusion criteria for isolated left hepatic resection in left hepatolithiasis was the right anterior or the right posterior sectoral bile duct draining into the left hepatic duct. Brisbane nomenclature was used for anatomic hepatic resections.

### The indications for hepatectomy in our series were:

- Hepatolithiasis lateralized in the unilateral lobe i.e left lobe of liver
- The hepatic bile duct containing stone is markedly constricted or dilated
- Combination with intrahepatic bile duct carcinoma
- Hepatolithiasis accompanied by hepatic lesions including hepatic abscess and atrophy.

Histopathological examination of isolated left hepatic resection specimen in left hepatolithiasis was carried out for grading of fibrosis/glandular changes/inflammation/other changes of chronic proliferative cholangitis and detection of any malignant changes.

## RESULTS

A total of 80 cases were studied in this series. Out of which, 51 cases were females and 29 cases were males. Male to female ratio was 1: 1.76. Their age at presentation was in range of 19-60 years with mean age at presentation being 38.08 years in males and 37.75 years in females. MRCP was done in 66 (82.5%) and CT scan done in 14 (17.5%) patients. Ultrasonography and biochemical profile of every patient was done. Pre-operatively ERCP was done in 44 cases for diagnostic purpose; out of these therapeutic interventions were done in 12 which included papillotomy in 4, CBD clearance in 7, biliary stenting in 3 and endoscopic nasobiliary drainage in 2. Assessment of left duct anatomy by means of MRCP and ERCP revealed type 1 anatomy in 90.0%, type 2 anatomy in 6.25% and type 3 anatomy in 3.75%. In 56 (70.0%) subjects stones were located in segment 2 & 3, in 23(28.75%) in segment 2-4 and in 1 (1.25%) patient in segment

1-4 of the affected liver. Total left hepatic resections carried out were 80. Left lateral sectionectomy was done in 56 subjects, left hemi hepatectomy was done in 23 patients and left hemihepatectomy with caudate lobe resection was done in 1 subject. Bacterial culture of 80 bile samples showed 100% positive results, Escherchia coli (41.25%), klebsiella (21.25%), proteus(12.5%), pseudomonas aerugenosa (8.7%) and multiple organisms 16.2%

**Table 1: Left hepatic resections done in patients n=80**

	n	%
<b>Left lateral sectionectomy</b>	56	70.00
<b>Left hemi- hepatectomy</b>	23	28.75
<b>Left hemi- hepatectomy + caudate lobe resection</b>	1	1.25

**Table 2: Histopathological results in surgery subjects (n=80)**

	n	%
<b>Left hepatic duct Stricture</b>	60	75.0
<b>Worm Fragments in left IHBR</b>	7	8.7
<b>Cholestasis</b>	67	83.7
<b>Portal Inflammation</b>		
<b>Mild</b>	20	25
<b>Moderate</b>	59	73.5
<b>Severe</b>	1	1.25
<b>Periportal Inflammation</b>		
<b>Mild</b>	23	28.7
<b>Moderate</b>	56	70.0
<b>Severe</b>	1	1.25
<b>Portal Fibrosis</b>		
<b>Mild</b>	19	23.7
<b>Moderate</b>	26	32.5
<b>Severe</b>	35	43.7
<b>Periportal Fibrosis</b>		
<b>Mild</b>	17	21.2
<b>Moderate</b>	29	36.2
<b>Severe</b>	34	42.5
<b>Ductal proliferation</b>		
<b>Mild</b>	18	22.5
<b>Moderate</b>	28	35.0
<b>Severe</b>	26	32.5
<b>Hepatic Necrosis</b>	37	46.2
<b>Cholangiocarcinoma</b>	2	2.5

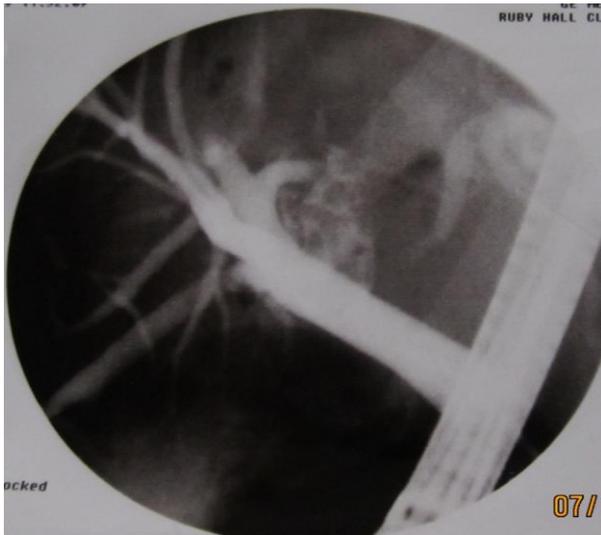
## DISCUSSION

A majority of IHS is associated with recurrent pyogenic cholangitis (RPC)<sup>6</sup> seen primarily in regions with prevalent parasitic infestations, especially Clonorchis sinensis and Ascaris Lumbricoids.<sup>7</sup> Biliary ascariasis is a common cause of biliary and pancreatic disease in an endemic area like ours as studied by Khuroo and Zargar.<sup>8</sup>

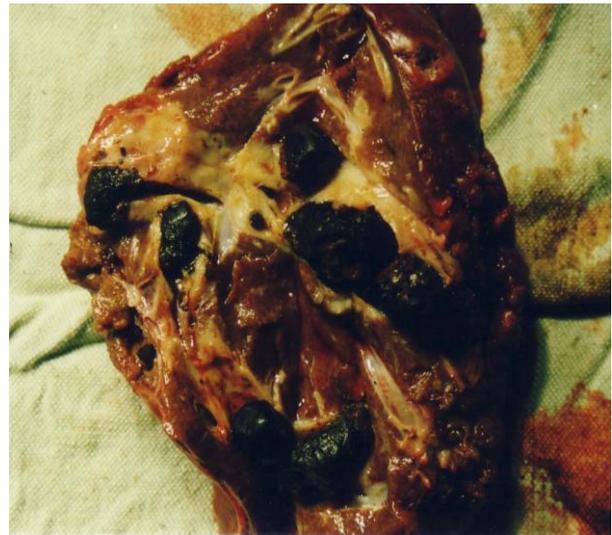
Currently, curative liver resection for hepatolithiasis is the preferred treatment; and left hepatectomy or left lateralsectionectomy is performed for left hepatolithiasis.<sup>9</sup> During the early 1990s, left lateral sectionectomy was performed in most centers; it is an easy operative procedure, with a shorter operating time and minimal intraoperative blood loss compared to left hepatectomy.<sup>10</sup> However when, Onish et al (2000) reported that B4 arises from the B3 duct in 24% of patients; and in such cases, B4 could be injured during left lateral sectionectomy<sup>11</sup>; this raised concern about injury to segment 4 bile duct during left lateral sectionectomy. In a comparative study; Kim YH et al (2005) while comparing the results of left lateral sectionectomy and left hemi

hepatectomy observed that incidence of bile leak was significantly higher in left lateral sectionectomy group.<sup>12</sup> Based on their observations they emphasized on the preoperative assessment of

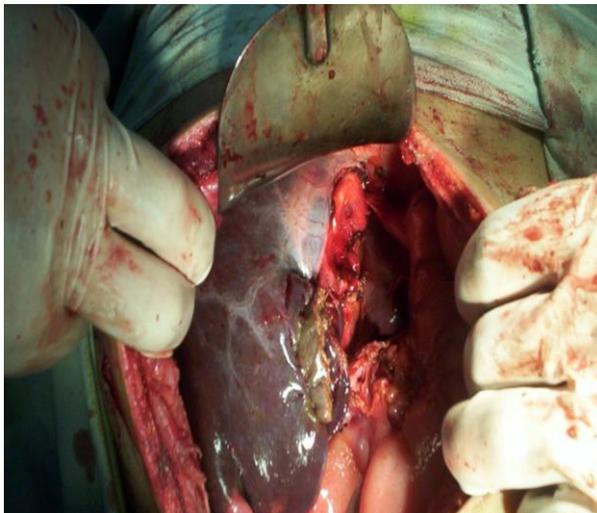
medial segmental bile duct anatomy and suggested that when the anatomy of medial segmental bile duct is not identifiable, a left hemi hepatectomy should be considered.



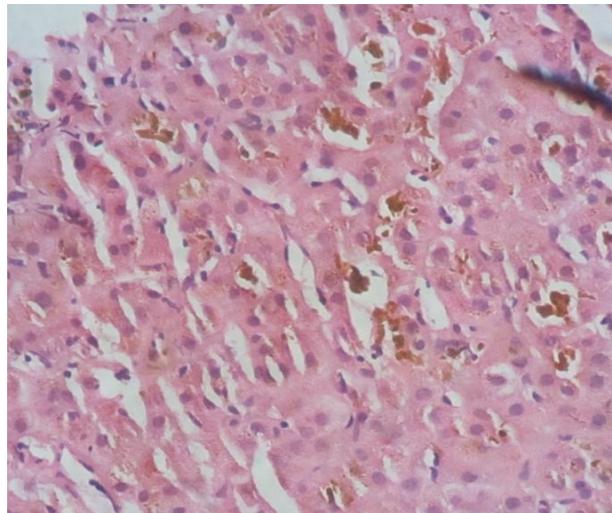
**Fig 1: ERCP picture showing type 3 LHD Anatomy with multiple stones in left hepatic duct.**



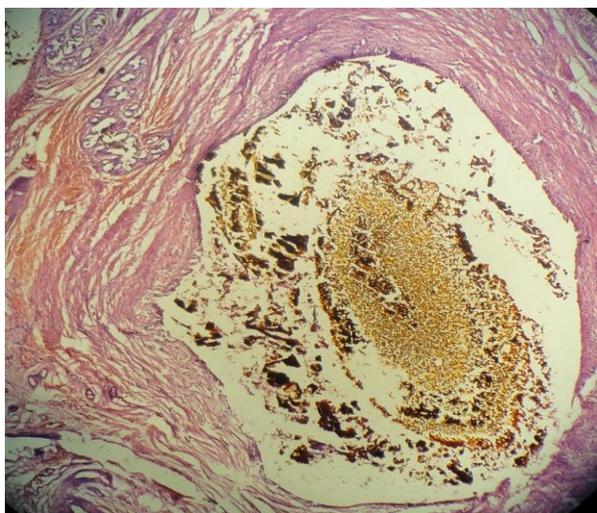
**Fig 2: Left lobectomy specimen showing multiple intrahepatic stones & dilated left intrahepatic biliary radicals**



**Fig 3: Picture showing right lobe of liver after completion of left lobectomy**



**Fig 4: Photomicrograph of a liver section showing intrahepatic cholestasis. (H & E X400).**



**Fig 5: Photomicrograph of a resected liver tissue showing a pigmented stone within a large bile duct with surrounding moderate periductal fibrosis. (H&E x100)**

Sun WB et al, recommended use of left hepatectomy for left hepatolithiasis because the duration of the operation, the intraoperative blood loss, and the postoperative complications were similar in patients who underwent left hepatectomy or left lateral sectionectomy, but they have not mentioned the indications for left lateral sectionectomy.<sup>9</sup> In another important study, Seung Eun Lee et al<sup>13</sup> recommended left lateral sectionectomy for the treatment of hepatolithiasis in the left lateral section without stricture or remaining or recurrent stones in B4. However in case where B4 joins lateral to the umbilical portion with dilatation of B4, left hemihepatectomy is ideal approach.<sup>13</sup> Not only is left hepatectomy more difficult to perform than left lateral sectionectomy, but left hepatectomy could result in the hepatic ducts that drain the caudate lobe being ligated, which would cause disturbances in biliary drainage of the caudate lobe. The right anterior sectoral bile duct or the right posterior sectoral bile duct drains into the left hepatic duct in 13% to 19% of cases.<sup>14,15</sup> In these cases, left hepatectomy could lead to injuries to the right anterior sectoral bile duct or the right posterior sectoral bile duct.

In our study, out of 80 left hepatic resections carried, Left lateral sectionectomy was done in 56 patients, left hemihepatectomy was done in 23 patients and left hemihepatectomy with caudate lobe resection was done in 1 patient. Cholecystectomy was included as part of left hepatic resections. Additional biliary drainage procedures done were choledochoduodenostomy (9 cases), t-tube drainage (6 cases) and hepaticojejunostomy (1 case). Exclusion criteria for isolated left hepatic resection was, the right anterior sectoral bile duct or the right posterior sectoral bile duct draining into the left hepatic duct. Human bile is sterile under normal conditions and in most series; there is almost 100% incidence of bacteria in the bile of patients with IHS. Polymicrobial infections are usually prevalent.<sup>10</sup> Most common are klebsiella sp, E.coli, pseudomonas sp, enterococcus sp and other beta glucuronidase producing bacteria. In our study Bacterial culture positive incidence of 100% was seen. Escherchia coli (41.25%), klebsiella (21.2%), proteus(12.5%), pseudomonas aerugenosa (8.7%) and Multiple organisms (16.2%).

Histologically<sup>16-18</sup> there is proliferation of bile ducts, and inflammatory cells, mostly polymorphonuclear leukocytes, infiltrate from the portal tracts well into the hepatic parenchyma, accompanied by local hepatocellular necrosis followed by suppuration in more severe cases. There is proliferation of fibrous tissue in the portal tracts, especially around the bile ducts. The intrahepatic ducts frequently show dilatation and stricture. They may contain pigmented stone, pigmented mud and debris, and may shed epithelial cells, exudates, and sometimes frank pus. Liver changes are common and can be quite severe.<sup>17,19</sup> The liver is usually enlarged and scarred with evident capsular adhesions. The papilla is usually hypertrophied<sup>17</sup>, fibrosed, and rigid but patent, allowing passage of a large dilator without difficulty.<sup>19</sup> In some cases there is periampullary stricture due to fibrosis and passage of stone. Dilatation of the extra hepatic ducts and large intrahepatic ducts such as the right and left hepatic ducts is observed in most patients (85-100%).<sup>20,21</sup> Dilatation of the intrahepatic biliary ducts tends to be disproportional, that is, central dilatation with rapid tapering toward the periphery.<sup>20</sup> The first and second divisions of the ducts are dilated, whereas the third and fourth divisions are not. The cause is not known, but periductal diffuse fibrosis may play a role. This pattern of bile duct dilatation is quite different from the dilatation caused by obstruction. In obstruction, the intrahepatic bile ducts are dilated diffusely instead of rapidly tapering peripherally. The dilatation of the extrahepatic duct generally is not related to the location of the stone.<sup>21</sup> Ducts both proximal and distal to the stone are dilated diffusely. Repeated passage of small pieces of stones through the sphincter of Oddi into the duodenum results in hypertrophy, ulceration, and stricture<sup>17</sup> and these changes may cause stenosis and proximal dilatation. However, localized stricture and resultant dilatation of the intrahepatic ducts are closely related to the location of stones. The left lateral segmental duct is affected earlier and more severely<sup>17,21,22</sup>, followed by the posterior segmental duct of the right lobe. This may be related to the more acute angulation of these ducts, resulting in less efficient drainage on this side of the biliary system.<sup>17,22</sup> Stricture along the extrahepatic ducts is very unusual.<sup>17</sup>

The stones in hepatolithiasis may be single or multiple and are composed mostly of bile pigment with variable calcification. They are dark brown or black and vary in consistency from claylike,

muddy material to concrete stones that are usually soft and friable.<sup>17,19</sup> Multiple stones are scattered in the intra or extrahepatic ducts or both with an occasional finding of packed bile ducts. Bile duct stones are present in about 75-80% of cases.<sup>17,19</sup> In the remaining cases, the biliary tree is infected recurrently in the absence of stone. Gallstones are found frequently, and including the cases of previous cholecystectomy, gallstones are present in about 50-70%.<sup>20-22</sup>

In our study; the gross examination of left hepatic resection specimens revealed left hepatic duct strictures in 75.0 % of patients. The detailed histopathological examination of the resected liver specimen revealed severe portal fibrosis in 43.7%, moderate portal fibrosis in 32.5% and mild portal fibrosis in 23.75% of patients. Severe periportal fibrosis was seen in 42.5%, moderate periportal fibrosis in 36.25 % and mild periportal fibrosis in 21.25% of patients. Severe portal and periportal inflammation was seen in 1.25% (each) of patients. Moderate portal and periportal inflammation was seen in 73.75% and 70.0% patients respectively. Mild portal and periportal inflammation was seen in 25% and 28.75% of patients respectively. Severe ductal proliferation was seen in 32.5%, moderate ductal proliferation seen in 35.0% and mild ductal proliferation was seen in 22.5% of patients. Cholestasis was seen in 83.75% and hepatic necrosis in 46.25%. cholangiocarcinoma was noted in only two patients with left intrahepatic duct stones. The association between cholangiocarcinoma and hepatolithiasis is well known. The incidence of carcinoma in the patients with hepatolithiasis ranges from 2.36% to 10.0%.<sup>4</sup> In the present study, cholangiocarcinoma was noted in only two patients (2.5%) with left intrahepatic duct stones which was comparable to the study discussed. Residual and recurrent stones are the most difficult problems encountered after surgery for hepatolithiasis; the incidence is 10% to 30%.<sup>23-25</sup> Seung Eun Lee, et al reported a residual and recurrent stone frequency of 8.9% and 6.7% respectively.<sup>13</sup>

In the present series, the frequencies of residual and recurrent stones after left hepatectomy or left lateral sectionectomy was 2.8% and 4.2% respectively. Out of these 3 patients were treated by Endoscopic retrieval of stones and 2 were subjected to bilioenteric bypass.

## CONCLUSION

Isolated left sided hepatic resection is an appropriate management for isolated left sided hepatolithiasis as it removes all intrahepatic stones along with the pathological bile ducts thus eliminating the chances of recurrent intrahepatic stones and the most unfavorable complication of disease i.e intra-hepatic Cholangiocarcinoma (IHCC).

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