Caroli’s disease is a rare disease and has remained under-diagnosed in the past. Improved imaging modalities have increased the prospects of diagnosing Caroli’s disease. The condition is still quite often treated improperly due to lack of experience owing to the rarity of the pathology.

Present study was undertaken to evaluate our experience and the role of hepatic resection in the management of Caroli’s disease. Fourteen cases of Caroli’s disease managed during the last 15 years were analyzed for clinical presentation, diagnosis, management and outcome. The disease was localized to single lobe in 8 (57%) cases, out of which 7 underwent successful hepatic resection and all remained symptom free after the surgery. The remaining 6(43%) cases with diffuse disease remains a therapeutic challenge. One of these patients with associated congenital hepatic fibrosis presented with persistent haematemesis and underwent emergency modified Sugiura’s operation. Symptomatic control was achieved by repeated endoscopic clearances in the remaining 5 cases.

Hence, We conclude that hepatic resection remains the treatment of choice for localized disease and provides a chance of cure. The overall prognosis of diffuse disease remains poor and liver transplantation may be regarded as the only hope for cure.

**Key words:** Caroli’s disease, Hepatic resection, Liver transplantation, Caroli’s syndrome, Congenital hepatic fibrosis
operative cholangiography and percutaneous transhepatic cholangiography (PTC) were used where indicated. An upper GI endoscopy was carried out in one case of haematemesis.

The diagnosis of CD was made on basis of recurrent episodes of cholangitis, presence of intrahepatic stones, usually in absence of gallbladder and common bile duct stones, and typical radiological changes in intrahepatic bile ducts such as, multiple strictures with segmental cystic dilatations and retrieved stone analysis showing pigment (bilirubinate) stones. Final confirmation was made on histopathology of the resected liver specimen in cases of hepatic resection and liver biopsy in one case of CHF. The classical microscopic feature of CD is an ectasia of the intrahepatic bile ducts resulting in focal cystic dilatations separated by segments of nearly normal looking bile ducts. The epithelial lining is cuboidal with frank papillomatous appearance, like that of gallbladder, and containing bilirubin calculi. Another striking feature is the absence of any abnormality in hepatic lobules and a normal parenchyma surrounding the ducts. The characteristic lesions are found in large portal spaces that affect only the segmental bile ducts with infiltration of portal triads with mononuclear and polymorphonuclear cells but having no effect on the portal system in simple type of CD. Enlarged portal triads with abundant connective tissue and foci of bile ductules proliferation are present in cases associated with CHF. This type involves portal system consequently leading to changes of portal hypertension.

The initial management consisted of nasogastric aspiration, correction of fluid and electrolyte balance, broad-spectrum antibiotics, analgesia and correction of anemia and coagulation profile, where indicated. After basic diagnostic work up, endoscopic papillotomy with clearance of intrahepatic stones was tried and in case of failure of complete clearance, nasobiliary drainage was carried out to decompress the biliary tree. Once the cholangitis was controlled each case was evaluated and treatment option was individualized for every patient. The resected specimen of liver was sent for histopathology and stones were sent for analysis and microscopic examination to exclude the ova or parasites in the stone (Ascaris lumbricoides or Clonorchis sinensis). The cases diagnosed as Asiatic cholangitis were excluded from the study.

All operated cases were provided with standard post-operative care and monitored for any complication during the hospital stay, which was treated accordingly. All patients were regularly followed in outpatient’s clinic and check ERCP was performed in first two cases of hepatic resection at 6 months to 1-year period during the follow-up.

Results:
A total of 14 patients with the final diagnosis of CD were managed at Riyadh Central Hospital, Riyadh, Saudi Arabia, from 1988 to 2003. They were 9 males and 5 females with male to female ratio of 1.8:1. Only 2 were local residents and rest 12 were

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Dis. Pattern</th>
<th>Operative procedure</th>
<th>Follow-up/Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20yrs/M</td>
<td>Left lobe</td>
<td>1.cholecystectomy, extended choledochotomy &amp; sphincteroplasty</td>
<td>Symptom free 4yrs</td>
</tr>
<tr>
<td>2</td>
<td>42yrs/M</td>
<td>Left lobe</td>
<td>1.Left hepatic lobectomy, Choledochoduodenostomy &amp; Cholecystectomy 2.T.vagotomy, pyloric exclu. &amp; Roux-en-Y gastrojej.</td>
<td>Symptom free 3 yrs</td>
</tr>
<tr>
<td>3</td>
<td>37yrs/M</td>
<td>Both lobes</td>
<td>Repeated ERCP clearances</td>
<td>Symptomatic control, 9 months</td>
</tr>
<tr>
<td>4</td>
<td>50yrs/M</td>
<td>Left lobe</td>
<td>Left hepatic lobectomy</td>
<td>Symptom free 6yrs</td>
</tr>
<tr>
<td>5</td>
<td>30yrs/F</td>
<td>Left lobe</td>
<td>Left hepatic lobectomy</td>
<td>Symptom free 3 months</td>
</tr>
<tr>
<td>6</td>
<td>11yrs/F</td>
<td>CD with CHF &amp; Nephrospongiosis portal hyperten.</td>
<td>Liver biopsy, Modified Sugiura's operation</td>
<td>Good control of haematemesis</td>
</tr>
<tr>
<td>7</td>
<td>37yrs/M</td>
<td>Rt. lobe</td>
<td>Repeated ERCP clearances</td>
<td>Symptomatic control</td>
</tr>
<tr>
<td>8</td>
<td>27yrs/F</td>
<td>Both lobes</td>
<td>Pt. refused for resection Initial management &amp; ERCP clearances</td>
<td>Went back to her country</td>
</tr>
<tr>
<td>9</td>
<td>40yrs/F</td>
<td>Both lobes</td>
<td>Repeated ERCP clearances 3 times in 2yrs</td>
<td>Symptomatic control, 2yrs</td>
</tr>
<tr>
<td>10</td>
<td>37yrs/M</td>
<td>Segmental (II&amp;III)</td>
<td>Segment II &amp; III resection Cholecystectomy and CBD exploration in other hosp.</td>
<td>Symptom free 2yrs</td>
</tr>
<tr>
<td>11</td>
<td>32yrs/M</td>
<td>Left lobe</td>
<td>Left hepatic lobectomy</td>
<td>Symptom free 1yr</td>
</tr>
<tr>
<td>12</td>
<td>60yrs/F</td>
<td>Both lobes</td>
<td>Cholecystectomy &amp; CBD exploration in other hosp. Repeated ERCP clearances</td>
<td>Symptomatic control, 6yrs</td>
</tr>
<tr>
<td>13</td>
<td>35yrs/M</td>
<td>Both lobes</td>
<td>Cholecystectomy 4yrs ago ERCP, refused treatment.</td>
<td>Went back to his country</td>
</tr>
<tr>
<td>14</td>
<td>29yrs/M</td>
<td>Left lobe</td>
<td>Left hepatic lobectomy</td>
<td>Symptom free 3yrs</td>
</tr>
</tbody>
</table>
foreigners; this distribution may be related to prevalence of the disease in these parts of the world. The age ranged from 11-60 years (mean 34.8 (+12) years). The age, sex, disease pattern, operative procedures performed, outcome and follow-up period are shown in Table 1.

The disease was localized in 8 (57%) cases, while diffuse in 5 (35.7%) and 1 (7.1%) case has CHF with predominant features of portal hypertension. The patients with localized disease (8) were considered suitable for hepatic resection; left lobectomy was performed successfully in 6 cases (Fig. 1 showing resected lobe of liver with intrahepatic stones) and segmental (segment II&III) resection in one, whereas one case involving right lobe refused surgery. The specimen histopathology confirmed the diagnosis of CD and none of the stones showed any evidence of parasitic infestation on microscopy.

One patient of diffuse CD with CHF presented with repeated episodes of haematemesis. This young girl underwent emergency modified Sugiura’s operation (Splenectomy, Gastroesophageal devascularization and esophageal transaction) to control relentless bleeding in spite of repeated sclerotherapies. The open liver biopsy confirmed the diagnosis of Caroli’s disease with associated congenital hepatic fibrosis. She was subsequently referred for liver transplantation. Among the remaining 5 patients of diffuse disease, one 60 yrs old local female in addition to outpatient visits and treatment had five admissions with cholangitis since her diagnosis 6yrs ago, every time treated with antibiotics and ERCP clearance. She was referred for hepatic transplant but because of her age (63yrs) and cardiac disease was refused for transplant. All other patients of diffuse disease including young girl with CHF were advised for transplantation but because of non-availability in early part of study or eligibility problems were unable to have transplantation and left to their native countries.

There was one intra-operative complication, iatrogenic injury to right hepatic duct that was identified during operation and repaired over T-tube. The patient had smooth post-operative course and had normal postoperative T-tube cholangiogram. T-tube was removed and patient was discharged 5 weeks post-operatively in good condition. There was no postoperative mortality. The commonest postoperative complication was chest infection in 2 cases, which was minor and self-limiting managed by chest physiotherapy. Among the delayed complications, one patient who had choledochoduodenostomy developed persistent epigastric pain, which on endoscopy found to have severe antral biliary gastritis. This patient ultimately required truncal vagotomy, pyloric exclusion and Roux-en-Y gastrojejunostomy two years after the first operation and remained symptom free ever since.

Follow-up ranged from 3 months to maximum of 6 yrs with average follow-up of 2.75 years. The overall symptom control was good and complete cure was achieved in all cases of hepatic resection. In spite of a very long study period, our follow up control was good and complete cure was achieved in all cases of hepatic resection cases were non-residents and due to their migration we were unable to maintain a long follow up with them.

Discussion:

The Caroli’s disease is a rare disease, with an estimated incidence of 1/1,000,000 cases.14 Owing to the rarity of disorder, the diagnosis is often delayed and lack of experience frequently results in inappropriate treatment. The typical presentation of disease by recurrent attacks of pain, fever and jaundice draws all attention to common bile duct, resulting in futile operations (Cholecystectomy, choleodoctomy, sphincteroplasty and biliodeigestive anastomosis) on CBD, as observed in world literature15-22 and also we did in our first case. That’s why, it is said that always remember the intrahepatic lithiasis (Caroli’s disease) if intrahepatic biliary tree is normal in a classical case of cholangitis.23,24

The current generation of diagnostic modalities has almost solved the problem of diagnosis. Today the pre-surgical diagnosis of CD can be established confidently with abdominal ultrasonography (US) and computed tomography (CT). The diagnostic US and CT features are multiple cystic dilatations of intrahepatic bile ducts which sometimes partially or completely surround the portal radicles giving rise to so called central dot sign.25-27 In addition, the associated lesions in other organs can also be demonstrated at the same time, as shown in Figure II. In spite of the risk of introduction of infection and occasional failure to outline the lesions due to stenosis or obstruction by stones or debris, the endoscopic retrograde cholangiopancreatography (ERCP) which outline the intrahepatic biliary tree showing classical picture of multiple saccular dilatation with intervening strictures, as shown in Figure III, remains the important diagnostic tool for preoperative evaluation as well as to follow the progression of the disease.28,29,30 Similarly the percutaneous transhepatic cholangiography (PTC) and operative cholangiography are useful diagnostic aids. Recently the use of magnetic resonance cholangiopancreatography (MRCP) is advised as it is free from the drawbacks of ERCP but because of non-availability in our center in initial part of study, it was not used. Nuclear medicine techniques, like Technetium-99m DISIDA, have been reported as being highly sensitive, noninvasive, inexpensive and safe but are nonspecific.31 Hence, CT scan and US may be regarded as more specific and best modalities for evaluating and making the diagnosis. Invasive procedures, like ERCP and PTC, for confirmation of the diagnosis remain the corner stones for the diagnosis of CD.

Precise delineation of the disease pattern and its differentiation from other conditions are of vital significance before selecting the therapy. The disease presents in a localized and diffuse form. Later is more common and usually associated with CHF. There is strong association between CD especially one with CHF and medullary sponge kidney.14-17 This was also observed in one of our cases, as shown in Fig. II. The reported incidence of localized or monolobar CD varies between 20-40% and more than 90% of these is confined to left lobe. The (57%) incidence of localized CD in present study is higher than the many reported figures.10,22,23 Higher incidence of localized CD has also been observed by M. Mercadier et al.18 This disparity may be due to different population under study but, to our knowledge no such study from this region is available for comparison.

The CD should be differentiated from recurrent pyogenic cholangitis (RPC), also known as cholangihepatitis or oriental or infestational cholangitis that is quite often seen in Far East. This condition can be distinguished from CD by typical radiological appearance on ERCP which in contrast to CD involve intrahepatic biliary tree mainly CBD, CHD and left hepatic duct just above the bifurcation and stricture-dilatations with marked smooth dilatations and excessive branching of intrahepatic ducts with prominent arrow-head formation,24-26 differentiate this from CD. In addition, hard stones, in contrast to soft stones of CD, are also mostly confined to intrahepatic ducts and in up to 50% of cases clonorchis infestation could be demonstrated. Dead clonorchis had been demonstrated in the center of stones.24 Similarly Ascaris ova have been found in the stones.23 All these evidences clearly points to infestational pathology rather than a congenital origin, hence the treatment is also different than CD.

The most vital therapeutic consideration while planning the treatment of CD are cure or permanent relief of recurrent attacks of cholangitis and prevention of future development of cholangiocarcinoma. The incidence of cholangiocarcinoma is substantially high; the reported incidence varies between 7-14%.25,26,27 The carcinoma is believed to develop when biliary epithelium is exposed to long standing inflammation due to bile stasis, hepatolithiasis and recurrent bacterial infection leading to
epithelial hyperplasia-dysplasia and eventually carcinoma. While, a study by Parada et al on liver biopsy specimen of CD (without cholangiocarcinoma) has noticed several clonal chromosomal abnormalities. Although, uncertainty remains to be clarified that whether local or genetic factors are more important in development of carcinoma, the disease carries a significant risk of cholangiocarcinoma. The risk of malignant change is supposed to be higher in monolobar disease than diffuse forms, further suggesting more radical approach in localized disease. Even the squamous cell carcinoma has been reported as a complication of CD. Considering all these problems, when feasible resection of diseased part of liver seems the most suitable treatment.

Localized forms, which are generally confined to left lobe or occasionally to right lobe of the liver, are suitable candidates for hepatic resection. Currently, such resections can be performed with minimal morbidity and mortality, as observed in present study as well as in many other studies. Moreover, the excellent symptomatic relief during long term follow-up, as noticed in our cases of hepatic resection and also validated by others and eliminating the potential site for developing carcinomá uphold this therapeutic management. Such appropriate treatment is still often undertaken on a secondary basis either because of wrong initial diagnosis or when disease is recognized but inappropriately treated by sphincteroplasty or bilioenteric drainage procedures. We admit that we too did the same mistake in our first case and also added unnecessary drainage procedure in second case to safeguard the development of disease in the remaining liver which ultimately ended up in second operation. Furthermore, two of our cases had such operations in other hospitals before referral to us. This highlights the need for awareness about this pathology and its management strategies.

Panhepatic or diffuse forms of CD continues to be a greatest therapeutic challenge. Many types of external and internal drainage procedures have been tried but with limited success. The permanent external drainage method like Praderi’s operation or internal drainage procedures such as, Sphincteroplasty, Choledochoduodenostomy are not only ineffective but also attended by ascending cholangitis, thus should be avoided. Long limb Roux-en-Y choledochojejunostomy or hepaticojejunostomy are the favored method of internal drainage for CD and have lower incidence of such a risk. All these procedures remain inefficient due to specific pathology of CD, multiple intrahepatic stricture-dilations making these as inefficient drainage procedure. Mercadier has combined left sided resection with disimpaction of stones in right half of the liver and Roux-en-Y hepaticojejunostomy. Finally, permanent access hepaticojejunostomy, in which closed end of loop of Roux-en-Y hepaticojejunostomy is buried subcutaneously for ready access for ERCP or choledochoscopy and intermittent lavage of the diseased liver on an outpatient basis has been reported with good symptomatic control. For our own part, we did not use any of the above drainage procedures, as we believe that none of the above procedure provides permanent relief of symptoms or cure. Our reliance was mainly on endoscopic removal of intrahepatic stones using dormia basket or forgarty ballon catheters under cholangiographic control. Meticulous repeated clearance of ducts with prolonged antibiotic courses enabled us to achieve a worthwhile period of symptomatic control. However, the quality of life of these patients is severely impaired and long term survival remains poor. The patient with associated CHF, complicated by portal hypertension the picture is even more gloomy. The variceal bleeding should be managed by sclerotherapy or variceal banding but in case of failure of these methods, one should avoid shunt operations in patients who are possible candidates for liver transplantation. For the same reason, modified Sugiura’s operation was performed in our case. The only permanent cure in cases of diffuse CD is the liver transplantation that is why we did not use any major surgical intervention in these cases and relied on temporizing measures while waiting for liver transplantation.

Hence, it is concluded that where feasible, hepatic resections is the ideal management of localized Caroli’s Disease, which is not only safe but also provides the best chance of cure. Nonetheless, diffuse disease carries the poor prognosis and liver transplantation is the only hope for cure.
References