Intrahepatic stones (IHS) have been described as early as the 16th century; however, the first detailed description of the disease in English literature was not until 1906. IHS is more prevalent in eastern Asia, with the highest incidence being in Taiwan, followed by China, Hong Kong, Korea, Malaysia and Japan. There also seems to be a high incidence in Brazil. On the other hand, the Western world and India have a low incidence of IHS.

In the Western world, IHS is generally thought to be secondary to stones originating in the gall bladder or primarily resulting from benign strictures, sclerosing cholangitis, choledochal cysts or malignant biliary tumors. In the East, however, IHS is regarded as a separate entity altogether. The majority of IHS is associated with recurrent pyogenic cholangitis (RPC). RPC affects both genders equally and has a peak incidence in the third and fourth decades of life. It is more common among people in the lower socio-economic class and those in rural rather than urban areas. The incidence of RPC in the East has been decreasing. The clinical features of RPC have been well documented. Yet, we are no wiser about the etiology of this disease.

An epidemiological study showed that the incidence of biliary tract disease among the offspring of Chinese and Japanese immigrants in the United States was similar when compared to the local population, suggesting that environmental rather than ethnic factors are involved in the pathogenesis of IHS.

The diet of the Orient, predominantly high in carbohydrate and low in fat and protein, has been implicated as an etiological factor for RPC. As saturated fat causes cholecystokinin release and relaxation of the sphincter of Oddi, a diet low in saturated fats could conceivably lead to biliary stasis, predisposing to IHS. A low-protein diet is also responsible for a decreased level of glucaro-1,4-lactone, a -glucuronidase inhibitor, potentiating the deconjugation reaction and leading to formation of calcium bilirubinate stones. The change in the diet pattern with economic development, to a high-protein, fat-based diet, may contribute to the decreasing incidence of IHS in the East. Recent studies from Korea report that presently about 40%-50% of IHS are of mixed variety, and some stones being pure cholesterol stones have lent support to the dietary theory.

Malnutrition associated with low socio-economic levels reduces immune ability, making subjects more prone to bacterial infections, which play a part in the pathogenesis of the disease. Bacterial infection is always present in RPC. Most commonly isolated bacteria are Gram-negative bacteria, including , and .

Another etiologic factor incriminated is biliary infestation by Clonorchis sinensis or Ascaris lumbricoides. Not only do they lead to inflammation resulting in injury of the biliary epithelium, the presence of parasitic fragments or their eggs can act as a nidus for formation of stones. Clinical and experimental data suggest that intestinal bacteria can pass through the portal system into the liver by bacterial translocation, secondary to intestinal mucosal lesions due to repeated parasitism. There has been a near eradication of these parasites in Japan and a low incidence of Clonorchis infestation in Taiwan, but a relatively high incidence of RPC persists in these places, casting some doubt on parasitic infestation as the main etiological factor for IHS.

IHS formation reported in a patient on long-term octreotide therapy and also in a patient who received ethanol injections as treatment for hepatocellular carcinoma suggests that biliary stones or sludge formation as a side effect of octreotide therapy and biliary injury due to alcohol injection are causative factors. Such factors, of course, are hardly operative in the vast majority of patients with IHS.

Intrahepatic stones could be in either or both lobes of the liver, associated with stones in the extrahepatic biliary tree. The left lobe is affected more commonly and in several cases is the only involved region. Whether the biliary anatomy of the left lobe has any role to play in this preponderance is up for debate.

The patients present commonly with abdominal pain and cholangitis. Charcot’s triad (jaundice, right upper quadrant pain, and fever with chills) is the form of presentation in about two-thirds of cases. Long-term biliary stasis with infection can lead to biliary strictures or liver abscess. Repeated cholangitic attacks can lead to atrophy of the affected lobe, secondary biliary cirrhosis, portal hypertension, and liver failure. Cholelithiasis is associated with a occurrence of cholangiocarcinoma.

Diagnosis is ultimately based on radiologic modalities, including ultrasonography, cholangiography (usually endoscopic, sometimes percutaneous), CT scan and MRI. Recently magnetic resonance cholangiopancreatography (MRCP) has been shown to be of higher sensitivity than ERCP in the diagnosis.
The management of IHS is dependent on the location of the stones, extent of involvement of the liver, and presence of associated complications. The management includes non-surgical means such as ERCP or percutaneous transhepatic stone removal with lithotripsy by mechanical, electrohydraulic or holmium laser methods. The non-contact methods for litholytic therapy include extracorporeal shockwave lithotripsy and ursodeoxycholic acid therapy. The surgical means include liver resection of the affected lobe, liver resection with hepaticojejunostomy and access loop creation, liver resection with biloenteric anastomosis including a duodenoojejunostomy for biliary access, and liver transplantation.

Prakash et al report in this issue of the Journal on the Indian experience with the management of IHS. Thirty-five patients treated over a period of 9 years were retrospectively analyzed. This report confirms the low incidence of IHS in India. Such a low incidence is in spite of a high prevalence of Ascaris infestation, poverty, poor environmental hygiene, and a high-carbohydrate, low-fat, low-protein diet leaves the proposed etiology of IHS on an even softer footing.

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References