There is increasing evidence that Budd Chiari syndrome occurs when acquired predisposing factor(s) affect a susceptible individual with one or more underlying thrombophilic conditions. Geographical variations in disease pattern of Budd Chiari syndrome exist, which may reflect differing predisposing factors. We review a change in disease profile of Budd Chiari syndrome in India over the past three decades. While earlier studies from India reported isolated inferior vena cava (IVC) obstruction as the commonest disease type, this is a minority in more recent reports where a combination of IVC and hepatic vein obstruction is the commonest type. Longer duration of illness has been shown to be associated with IVC obstruction, and the recent change in disease profile in India may reflect earlier diagnosis of Budd Chiari syndrome. Poverty, malnutrition, recurrent bacterial infections and filariasis have been previously suggested as predisposing factors for IVC obstruction. Improvement in hygiene and sanitation may partly explain the recent change in disease profile of Budd Chiari syndrome in India. [Indian J Gastroenterol 2007;26:77-81]

Changes in environmental factors have been linked to changing epidemiology of a variety of diseases in India. Epidemics of tropical sprue are no longer seen in India (last reported epidemic was in the early 1980s), while sporadic tropical sprue has reduced (presumably due to improvement in hygiene and sanitation). The dramatic reduction in incidence of Indian childhood cirrhosis is attributed to change in feeding vessels (susceptible children received milk contaminated with copper that had leached out from brass vessels). In this review, we highlight a change in disease profile of Budd Chiari syndrome (BCS) in recent series from India and discuss possible reasons for this. Clinical pointers to recognize current disease presentation of BCS in India are also discussed.

Variations in profile around the world

The pattern of venous obstruction in BCS appears to vary in different parts of the world. It has been suggested that IVC obstruction is commoner in the Far East while hepatic vein thrombosis is commoner in the West. In a series of 157 patients with BCS from Japan, 93% had IVC obstruction and 7% had hepatic vein obstruction. In contrast, of 42 patients in the UK, 79% had hepatic vein obstruction, 17% had IVC obstruction, and 5% had combined obstruction. Membranous occlusion of vena cava (MOVC) has been described from Japan, South Africa, India, Nepal, China and USA. Hepatocellular carcinoma has been reported in 11%-48% of patients with MOVC (highest incidence in South Africa). In contrast, it has not been described as a complication of hepatic vein thrombosis, except for an association with Behçet’s disease-associated BCS (found in 5% of patients).

Disease profile in India is changing

IVC obstruction was the commonest disease pattern (38%-79%) in reports on BCS from three centers in India in the 1970s and ’80s (Table 1). The term coarctation of the IVC was described to emphasize the congenital theory of causation of IVC obstruction. In contrast, in 8 recent reports from India (Table 2), the commonest pattern of venous obstruction in BCS was combined hepatic vein and IVC obstruction (54%-64%) in 4 studies, isolated hepatic vein obstruction (42%-59%) in 2 studies, and isolated IVC obstruction in 2 studies (54%-82%). But for the two studies from Delhi and Kolkata, in all other recent studies (Table 2) isolated IVC obstruction was seen in only a minority of patients (0%-37%).

Thus, while reports in the 1970s and ’80s from India suggested that the disease pattern in

| Table 1: Pattern of venous obstruction in Budd Chiari syndrome in India in 1970s and ’80s |
|-----------------------------------|----------------|---------------|---------------|
| n                                 | 78             | 19             | 75             |
| Hepatic vein obstruction           | 26%            | 21%            | 32%            |
| IVC obstruction                    | 38%            | 79%            | 59%            |
| Combined obstruction               | 36%            | 0              | 9%             |
BCS was similar to that reported from the Far East (IVC obstruction being the commonest type), more recent reports suggest a change with combined hepatic vein and IVC obstruction as the commonest type (a position in between East and West).

In analyzing these data from India, a number of limitations need to be kept in mind. Three of the recent studies (Table 2) have only been reported in Abstract form. Population-based epidemiological data on BCS are lacking in India; available information is from hospital-based series. Consecutive patients were not studied in all series. On attempting to classify reports on BCS from India as per time periods (Tables 1 and 2), there is some overlap of study periods. The study period in the Chandigarh series was 1967 to 1991; thus it may not fully reflect current disease trends. Though most recent studies were done prospectively, three of the studies had primarily studied prothrombotic factors causing BCS and delineation of site of venous obstruction was not the primary aim. While in some of the recent studies, all patients underwent venograms, other reports used a combination of cross-sectional imaging and venogram to classify pattern of venous obstruction. The different imaging modalities used to map hepatic venous outflow tract could lead to differences in classifying type of venous obstruction in BCS.

Several attempts have been made to classify the disease pattern in BCS. Of late, disease classification is aimed at selecting appropriate treatment. Lack of uniform classification is another limitation in studying disease profile of BCS.

### Table 2: Pattern of venous obstruction in Budd Chiari syndrome in recent series from India

<table>
<thead>
<tr>
<th>Study period</th>
<th>Chandigarh 13</th>
<th>Mumbai 14</th>
<th>Lucknow 15</th>
<th>Vellore 16</th>
<th>Jaipur 17</th>
<th>Mumbai 18</th>
<th>Delhi 19</th>
<th>Calcutta 20</th>
</tr>
</thead>
</table>

### Possible reasons for recent change in disease profile in India

Venous thrombosis is a multi-factorial disease associated with a combination of inherited and acquired predisposing factors. Geographic variations in etiological factors may account for differences in pattern of venous obstruction in BCS. A prospective study of etiological factors in BCS from Delhi suggested that inherited prothrombotic factors were more important than acquired predisposing factors (cirrhosis, pregnancy, infection, oral contraceptive use, malignant neoplasm) in their study group. Inherited prothrombotic factors are often similar in BCS in India and the West.

Venous thrombosis of the vena cava could lead to membrane formation; thus, MOVC could be just a late presentation of IVC thrombosis. As shown in the Chandigarh study, longer the duration of illness prior to presentation, higher the likelihood of IVC obstruction (Tables 3 and 4). In that study, 100% of patients with >10 years of symptoms had IVC obstruction (Table 3). In the study on hepatopulmonary syndrome in BCS from Kolkata, wherein 82% of patients had isolated IVC obstruction, prolonged duration of illness (6-8 years) was noted (duration of illness was higher in those with abnormal contrast echocardiogram as compared to those with normal echocardiogram). Thus, previous reports of isolated IVC obstruction as the commonest type of BCS in India could be a reflection of delay in seeking medical care. Another possible reason is delay in making the diagnosis, often because the treating doctor has not considered this possibility.

### Table 3: Duration of symptoms correlated with pattern of venous obstruction in 177 Budd Chiari patients who underwent either vena cavaogram or percutaneous transhepatic venogram or both procedures (adapted from Reference 13)

<table>
<thead>
<tr>
<th>Duration of symptoms</th>
<th>Hepatic vein</th>
<th>IVC</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>28</td>
<td>24</td>
<td>67</td>
</tr>
<tr>
<td>&lt;6 mo</td>
<td>43%</td>
<td>4%</td>
<td>28%</td>
</tr>
<tr>
<td>6 mo – 5 y</td>
<td>50%</td>
<td>67%</td>
<td>48%</td>
</tr>
<tr>
<td>&gt;5 y</td>
<td>7%</td>
<td>29%</td>
<td>24%</td>
</tr>
</tbody>
</table>

### Table 4: Duration of symptoms correlated with pattern of venous obstruction in 119 Budd Chiari patients who underwent both vena cavaogram and percutaneous transhepatic venogram (adapted from Reference 13)

<table>
<thead>
<tr>
<th>Duration of symptoms</th>
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Changes in acquired prothrombotic factors in India over time may partly explain the recent change in disease profile of BCS in India. Of 150 patients with IVC obstruction (at the hepatic portion) in Nepal, 89% belonged to the lower socioeconomic status and a majority were malnourished. In the same study, bacteremic episodes were documented in 35% of patients who had blood cultures tested, the commonest organisms isolated being *Escherichia coli* and *Staphylococcus aureus*. Progression of acute “thrombophlebitic lesion” of the retrohepatic IVC (often associated with bacterial infection) to chronic IVC obliteratorive lesion (stenosis or complete obstruction) has been reported from Nepal. A report from Chennai documented an adult filarial worm within pericaval fibrosis noted at autopsy in a patient with occlusion of retrohepatic IVC and terminal portion of all hepatic veins. Improvement in sanitation and hygiene and earlier treatment and prevention of bacterial infections and filariasis may partly explain the change in disease pattern of BCS in India. Oral contraceptive pill usage was associated with BCS in the West. In four recent reports from India (Table 3), oral contraceptive use was noted in 4 of 145 females with BCS. With the availability of safer contraceptive pills with lower estrogen content, the risk of venous thrombosis may decrease. Oral contraceptives are not likely to be a major predisposing factor currently for BCS in India as they are not the preferred method of contraception.

Recognizing current clinical presentation of BCS in India

Despite widespread availability of imaging modalities, the diagnosis of BCS is often delayed even now as the clinician did not consider the diagnostic possibility. Isolated hepatic vein obstruction usually presents with ascites, hepatomegaly, jaundice and/or esophageal/gastric variceal bleeding. Difficult-to-control ascites and ascites out of proportion to pedal edema should raise a clinical suspicion of hepatic vein obstruction. Abdominal pain is a prominent feature of acute presentation. Eliciting the abdomino-jugular reflux has been employed to ascertain patency of hepatic venous outflow tract at the bedside. However, there is considerable inter-observer variability in assessing central venous pressure at the bedside and the precision of this reflux as a clinical sign has not been studied.

Suprahepatic IVC obstruction can lead to ascites, hepatomegaly, jaundice and/or variceal bleeding (similar to isolated hepatic vein obstruction). Clinical signs caused by venous blood returning via alternative routes to the heart may also be present. This can manifest as distended tortuous veins over the abdominal wall (draining upwards), lower back and lower limbs, occasionally associated with stasis ulcers over the legs. Bilateral pitting pedal edema may be the sole presentation of chronic IVC obstruction. Bleeding scrotal varices have been reported in BCS. Infertility, attributed to chronic venous congestion of reproductive organs, is another presentation. The left testicular vein drains into the left renal vein, while the right testicular vein drains directly into the IVC. Thus, in a male patient with BCS, the presence of varicocele may be a clinical pointer to the extent of IVC block. Recurrent cough has been attributed to large intra-thoracic varicose veins pressing over the recurrent laryngeal nerve in IVC obstruction.

Clinical features of the different types of venous obstruction in BCS often overlap (Table 5). In a patient with isolated hepatic vein obstruction, extrinsic compression of the intrahepatic IVC by the engorged liver, especially by a hypertrophied caudate lobe, can lead to clinical features of combined hepatic vein and IVC obstruction. A patient with suprahepatic IVC obstruction can present with clinical features of isolated hepatic vein obstruction or of isolated IVC obstruction or both. A patient with combined block of hepatic veins and IVC presents with clinical features of either hepatic vein or IVC obstruction or both. Thus, a patient with refractory ascites due to BCS (Fig) could have isolated hepatic vein obstruction, isolated suprahepatic IVC obstruction or a combination.

Typically, post-partum BCS presents acutely as abdominal pain and ascites, usually 4-7 days
after childbirth. Fever, vomiting and jaundice may also be present. Less commonly, chronic presentation of BCS during pregnancy has been reported from India.

Rarely, BCS may present for the first time as acute liver failure with hepatic encephalopathy accompanying jaundice and ascites. Though BCS usually presents as symptomatic disease, less commonly asymptomatic disease is detected on imaging done for some other indication.

Portal vein thrombosis was noted in 25% of patients with BCS and causes refractory ascites with limited definitive treatment options. Case reports of venous thrombosis outside the hepatic venous outflow tract in BCS (sagittal sinus thrombosis, pulmonary embolism) highlight the underlying prothrombotic state.

The future

If measures like improving sanitation, better access to health care, better nutrition and reduction of infections play a role in the change in disease profile of BCS in India, the next question is: is the incidence of BCS in India decreasing? In the absence of population-based epidemiological data, this answer is not forthcoming at the present.

References

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drome: a study from Western India. *Hepatology* 2001;34(4 Pt 1):666-70.


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