INTRODUCTION:
Non cirrhotic portal fibrosis (NCPF) is a syndrome of obscure etiology, characterized by obliterator portal venopathy leading to portal hypertension, massive splenomegaly and well tolerated episodes of variceal bleeding in young adults, having near normal hepatic function. The lesion in NCPF is generally vascular, present in portal vein, its branches or in the presinusoidal area of liver. NCPF is also known by other names like idiopathic portal hypertension, hepatoporal sclerosis, obliterator portal venopathy of the liver and non cirrhotic intrahepatic portal hypertension.

HISTORICAL PERSPECTIVE:
In 1889 Benti of North Italy described a disease, characterized by congestive splenomegaly, anemia with or without gastrointestinal bleeding and ascitis. It was in 1956 some physicians in India drew attention to a clinical syndrome of portal hypertension distinct from cirrhosis. In 1962, Ramalingaswami and colleagues after a careful study of the autopsy material of some of these patients reported an entity of splenomegaly with non cirrhotic liver disease in North Indian patients. In 1969 the term NCPF was officially adopted at a workshop organized by the Indian council of medical research.

EPIDEMIOLOGY:
NCPF has been reported from all over the world, with maximum cases reported from India. World wide it accounts for 3-5% of all patients with portal hypertension, but in India it accounts for 15-20% of case of portal hypertension. Most studies from India have reported a male predominance of 2:1 to 4:1. NCPF is mainly a disease of young Indian men from low socioeconomic background. The mean age onset of NCPF patient varies from 25 to 35 years.

ETIOLOGY:
The etiology of NCPF is poorly understood. A number of hypothesis have been proposed. Clustering of the disease mainly in low socioeconomic class suggests that malnutrition, exposure to toxins and chemical or recurrent intestinal infections could possibly be responsible.

a. Infective hypothesis: NCPF seen mainly in patients from low socioeconomic background. Abdominal infection in early childhood lead to portal pyemia, pylephlebitis, resulting in thrombosis, sclerosis and obstruction of small and medium sized portal vein radicle.

b. Exposure to trace metals and chemicals: chronic exposure to arsenic, vinyl chloride monomer, copper sulfate, methotrexate, hypervitaminosis A, 6-mercaptopurine, azathioprine and corticosteroids can produced a histological picture similar to NCPF.

c. Immunological and immunogenetic hypothesis: NCPF patient shows a reduction is the suppressor / cytotoxic T lymphocytes, a decreased T4/T8 lymphocyte ratio and reduction in cell mediated immunity. There is familial aggregation and a high frequency of HLA-DR, associates in patients with NCPF.

Fig. 1 : Site of block in NCPF (3rd and 4th order intrahepatic portal vein radicle) and EHPVO* (Main or 1st order branches)
* EHPVO: Extra hepatic portal vein obstruction.
Non-Cirrhotic Portal Fibrosis

Pathology:

Gross pathology: Liver may be normal to markedly nodular. Nodularity when present is limited to subcapsular zone, in contrast to cirrhosis where it involves the center. Portal venous system shows prominent and dilated branches with marked sclerosis of the wall. Significant perivascular fibrosis along the portal vein and its branches is an important feature.

Microscopy: Histopathology shows patchy and segmental sub endothelial thickening of the large and medium sized intrahepatic branches of portal vein. These changes are most marked in medium sized portal venous 3rd and 4th order radicles. Emergence of new aberrant portal channels is quite characteristic of NCPF.

Ultrastructure: Shows widening of intercellular and disse's space with fibrogenesis in the perisinusoidal space.

Hemodynamics: Intrasplenic and portal vein pressure are markedly elevated in NCPF. Wedged hepatic vein pressure is normal or slightly raised. There is presinusoidal and perisinusoidal resistance to the flow of portal blood.

Clinical Features

Symptoms:

Patients are usually young and healthy, presents with one or more well tolerated episodes of gastrointestinal bleed. The other important symptom is a feeling of lump in the left upper quadrant of abdomen, due to enlarged spleen. It is not uncommon to see patient presenting with repeated attacks of left upper quadrant pain due to perisplenitis and splenic infection very rarely NCPF may present with glomerulonephritis or hypoxia.

Signs:

Splenomegaly is a constant feature. The size of spleen ranges from 4-15 cm with average being 8 cm below left costal margin. Liver enlargement is not striking. However liver is palpable 2 cm below the costal margin in about 55% of patients. Jaundice, ascitis, signs of liver failure are rare may occur transiently after an episode of hematemesis.

Laboratory Features:

Anaemia is seen in majority of patients, can be microcytic hypochromic due to GI blood loss or normocytic normochromic due to hypersplenism. Leukopenia (<4000/mm³) and thrombocytopenia (<50000/mm³) may be present because of hypersplenism. Bonemarrow is usually hypercellular. A state of mild compensated disseminated intravascular coagulation secondary to endotoxemia or porosystemic collaterals has been reported in fair proportion of patients with NCPF. LFT (Liver function test) usually normal or may be mildly deranged.

Imaging:

- USG (Ultra sonography): Portal and splenic veins are dilated and multiple collateral present at the splenic hilum. There is marked thickening of portal vein wall specially of intraheptic branches. There may be spontaneous lienorenal nut.
- Splenoportovenography: It shows dilatation of portal and splenic vein along with various collaterals.
- Hepatic venography and radio nuclide scintigraphy using 99mTc phytate or sulfur colloid shows high uptake.

Endoscopy: Esophagogastric varices seen in 85-95% cases. Anorectal varices seen in 90% cases.

Differential Diagnosis:

It includes:

1. EHPVO (Extra hepatic portal vein obstruction)
2. Compensated cirrhosis in the young
3. Tropical splenomegaly syndrome
4. Splenomegaly of myeloid syndrome

Table 1: Differentiating Features of NCPF, EHPVO, Cirrhosis

<table>
<thead>
<tr>
<th>No.</th>
<th>Parameter</th>
<th>NCPF</th>
<th>EHPVO</th>
<th>Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mean age</td>
<td>28</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>Sex M:F</td>
<td>2-3:1</td>
<td>2-3:1</td>
<td>4-5:1</td>
</tr>
<tr>
<td>3</td>
<td>GI bleeding</td>
<td>Infrequent</td>
<td>Infrequent</td>
<td>Frequent and</td>
</tr>
<tr>
<td></td>
<td>well tolerated</td>
<td></td>
<td>well tolerated</td>
<td>recurrent</td>
</tr>
<tr>
<td>4</td>
<td>Encephalopathy</td>
<td>Rare</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>5</td>
<td>Jaundice</td>
<td>Rare</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>6</td>
<td>Ascitis</td>
<td>Rare</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>7</td>
<td>Spider Nevi</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>Splenomegaly</td>
<td>&gt;7 cm</td>
<td>&lt; 7 cm</td>
<td>&lt; 5 cm</td>
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<tr>
<td></td>
<td></td>
<td>1-2 cm</td>
<td>&lt; 7 cm</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Hepatomegaly</td>
<td>Firm, smooth</td>
<td>Uncommon</td>
<td>Firm, irregular</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-2 cm</td>
<td></td>
<td></td>
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<tr>
<td>10</td>
<td>LFT</td>
<td>Normal</td>
<td>Normal</td>
<td>Deranged</td>
</tr>
<tr>
<td>11</td>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Gross</td>
<td>Normal/rarely</td>
<td>Normal</td>
<td>Shrunken,</td>
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<tr>
<td></td>
<td>microscopc</td>
<td>irregular</td>
<td></td>
<td>nodular</td>
</tr>
<tr>
<td>12</td>
<td>Site of block</td>
<td>Intrahepatic</td>
<td>Extrahepatic</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>presinusoidal</td>
<td>presinusoidal</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Pressure studies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Intrasplenic</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>b. Portal vein</td>
<td>High</td>
<td>Normal to</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>pressure</td>
<td></td>
<td>raised</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c. WHVP</td>
<td>Normal –</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>d. (wedged hepatic</td>
<td>Normal –</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>venous pressure</td>
<td>raised</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Long term survival</td>
<td>90-95%</td>
<td>90-95%</td>
<td>50-75%</td>
</tr>
<tr>
<td>(5 years)</td>
<td></td>
<td></td>
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</tbody>
</table>
5. Kala azar
6. Felty's syndrome

**MANAGEMENT:**

The majority of the patient present with variceal bleeding and the treatment therefore involves control of acute bleeding and prevention of rebleeding by medical and surgical means.

1. **Medical managements:** It includes emergent treatment, primary prophylaxis and elective treatment.

   a. **Emergent treatment:** Bleeding from esophageal varices ceases spontaneously in as many as 40% patients. Initial resuscitation with replacement of blood volume loss is done with blood transfusion and IV fluids specific treatment of bleeding lesion done by pharmacotherapy, endoscopic therapy or by balloon tube tamponade.

      i. **Pharmacotherapy:** Somatostatin, octreotide and terlipressin are the 3 drugs used in pharmacotherapy.

         Somatostatin is a synthetic, cyclic 14 amino acid peptide which is identical in structure and action to natural somatostatin. Somatostatin decreases portal blood flow by splenchnic vasoconstriction. It is given as slow IV bolus injection (3-5 min) of 250mcg, followed by continuous infusion at a rate of 250mg/hr.

         Octreotide, is a synthetic analogue of somatostatin administered as constant infusion at 50 mcg/hr. Terlipressin is a synthetic analogue of vasopressin given at a dose of 1000 mcg every 4-6 hrs.

      ii. **Endoscopic therapy:** It has the advantage of allowing specific therapy at the time of diagnosis. In acutely bleeding patients EVL (Endoscopic variceal ligation) and EST (Endoscopic sclerotherapy) are equally effective in 95% cases. In EVL a banding device attached to the tip of the endoscope is used to ligate varix using rubber bands. One to three bands are applied to each varix.

         **Endoscopic variceal ligation (EVL):** In EVL a banding device attached to the tip of the endoscope is used to ligate varix using rubber bands. One to three bands are applied to each varix.

         **Endoscopic sclerotherapy (EST):** The different sclerosants used are 1.5% sodium tetradecyl sulphate, cyanoacrylate, 5% ethanolamine oleate, absolute alcohol, 3% phenol in water and 5% phenol in oil. Gastric varices are seen in 25% of NCPF, can be managed with cyanoacrylate glue injection and rarely requires surgical intervention.

      iii. **Balloon tube tamponade:** Should be used only in massive bleeding as a temporary measure.

   b. **Primary prophylaxis:** Administered to patients at high risk of bleeding including large varices, red wale marking on varices and severe liver failure.

      i. **β-blockers:** Non cardioselective β blocker like propranolol and nadolol, which reduces portal and collateral blood flow, are used. Propranolol is usually started at a dose of 20mg every 12hrs and the dose adjusted every 3-4 days until a 25% reduction in resting heart rate occurs or the heart rate is down to 50/min. Nodalol dosing is half the daily dose of propranolol.

      ii. **Vasodilation:** Isosorbide mononitrate (ISMN) has been shown to reduce portal pressure gradient markedly in acute administration, but significantly less after long term administration.

      iii. **Combined therapy:** Involves both β-blockers and ISMN.

      iv. **Prophylactic EST:** no role in primary prophylaxis.

      v. **Prophylactic EVL:** shown to have an efficacy similar to β-blocker, but with increased adverse effect used in patients with grade III varices who have contraindication or can not tolerate β-blockers.

   c. **Elective Treatment:** Used for prevention of rebleeding.

      i. **β-blockers-** reduces the risk of rebleeding and are associated with prolongation of survival.

      ii. **EST:** Usually performed at weekly intervals; 4-5 session are required to eradicate the varices.

      iii. **EVL:** Considered as endoscopic treatment of choice for prevention of rebleeding. It is associated with lower rebleeding rates and lower frequency of esophageal strictures. Usually 2-4 sessions are required.

2. **Surgical managements:**

   It includes protosystemic shunt and devascularization procedure:

   a. **Protosystemic shunt:** Emergency shunt surgery is required in 5% cases shunt can be total or selective.

      i. **Total shunts-** portal blood is completely diverted to systemic circulation. The examples are - Central splenorenal shunt with splenectomy, Mesocaval shunt, Portocaval shunt.

      ii. **Selective shunts:** This decompresses the gastro-splenic-portal zone with maintained portal perfusion of the liver through hepato petal collateral. Encephalopathy is rare with selective shunts. The examples are - Distal spleno renal shunt (Warren
Non-Cirrhotic Portal Fibrosis

shunt), Distal spleno caval shunt, Gastroepiploic to left renal shunt, Left gastric vein to left renal vein shunt.

b. Devascularization procedure:” The indications are failed shunt, patient who have no shuntable vein or in emergency when shunt can not be performed.

E.g.: Sugiura devascularization.

INDICATION FOR SURGERY:

1. Failure of endoscopic therapy to control acute bleeding.
2. Recurrent bleeding.
4. Repeated splenic infection.
5. Patient who desires for one time treatment.

Surgical mortality after emergency shunt is 60%.

PROGNOSIS:

Prognosis for patients with NCPF is excellent, mortality from acute bleeding in NCPF is significantly lower than that observed in cirrhotic patients. 5 years survival rate is > 95%.

REFERENCES
