

CHOLELITHIASIS IN CROHN'S DISEASE

Incidence

- General Population:
 - Total prevalence 14 – 20%^{1,2}
 - Symptomatic prevalence 9 – 12%
- Patients with Crohn's disease:
 - Total prevalence 16 – 34%³
 - Symptomatic prevalence 14.9%⁴

Pathogenesis

- Multifactorial
 - Cholesterol **supersaturation**
 - **Increased nucleation/precipitation** of cholesterol monohydrate crystals
 - **Increased mucus** secretion
 - **Hypomotility** of gallbladder
- Cholesterol or Pigment stones?
 - Cholesterol stones account for more than 80% of gallstones in the Western world.
 - However, no good large studies have focused on stone analysis in Crohn's disease patients.
 - Increased prevalence of gall stones in Crohn's disease is thought to be related to **depletion of the bile salt pool** due to decreased intestinal reabsorption of bile salts in the diseased or resected terminal ileum and the resultant increase in cholesterol saturation in bile and the formation of cholesterol gallstones.^{5,6}
 - This is partially substantiated by animal and human studies which have suggested an initial increase in **cholesterol supersaturation**.⁷
 - However this increased saturation is not sustained because continual bile salt loss results in depression of 7 α -hydroxylase and an increase channeling of cholesterol into de novo bile acid synthesis instead to compensate for the intestinal loss.⁸
 - An additional risk factor for pigment gallstone disease has been suggested by **enterohepatic circulation of bilirubin** which is **enhanced** by ileal resection and excess colonic bile salt concentration.
 - Brink et al have shown that conjugated bilirubin is unconjugated in the large intestine and reabsorbed in the presence of excess colonic bile salts.⁹
 - This could theoretically predispose to **precipitation of pigment stones** if other factors, such as biliary stasis, B-glucuronidase activity, and ionized calcium concentration favoured an increase in the ionization products of calcium bilirubinate crystals.
 - These findings are supported by the increased unconjugated bilirubin levels found in the bile of Crohn's disease patients.
 - Controversy remains as to whether gallbladder motility is affected by Crohn's disease directly.
 - Several studies have demonstrated **decreased gallbladder contractility** in patients with Crohn's disease.

- Murray et al showed an impairment in fatty meal-stimulated gallbladder volume measured ultrasonographically in patients with ileal and ileocolonic Crohn's disease.¹⁰
- The mechanism behind the reduced contractility is still unknown.
- However, there is marked reduction in gallbladder contractility in patients on **total parenteral nutrition**.
 - Prevalence of biliary sludge and gallstones in Crohn's disease patients receiving TPN is up to 40% and many of the stones seen in these patients are pigment stones.^{11,12}

Risk Factors & Epidemiology

Crohn's Disease	General population
Age	Age
Gender	Female gender
Site of disease/ resection	Obesity
Duration of disease	Genetic predisposition
Extent of disease	
Previous number of resections*	

Treatment Options

- Therapeutic cholecystectomy
- Therapeutic ERCP
- Prophylactic cholecystectomy

Points for consideration:

- Prevalence of symptomatic cholelithiasis in patients with Crohn's disease similar to general population.⁴
- Prevalence of patients requiring cholecystectomy only 12.7% in the same study.⁴
- Only 10% of asymptomatic patients develop symptoms of biliary calculi, and 7% will require surgery.¹³
- Patients with >30cm of ileum resected were significantly more likely to require a cholecystectomy than patients with <30cm of ileum resected (8/25 vs 6/46; P = 0.056 Fisher's exact test)⁴

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