

# Original Article

## Pediatric Cholelithiasis

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### ABSTRACT

Cholelithiasis and choledocholithiasis have been increasingly diagnosed in recent years in children. This may be because of increased use of ultrasonography in investigating children with unexplained abdominal pain and/or a genuine increase in the incidence of cholelithiasis due to increasing use of total parenteral nutrition, frusemide and phototherapy in the infants. Since Pediatric Cholelithiasis is being diagnosed with increased frequency, therefore, it's important that treating Pediatricians should have a basic understanding of disease and its medical as well as surgical management. This Review article describes the present management strategies for Cholelithiasis in pediatric age group.

**Keywords:** Cholelithiasis, Pediatric, children, cholecystectomy, gallstones, biliary sludge

Pediatric Cholelithiasis is being diagnosed with increased frequency. A population-based study of 4200 children estimated the prevalence of gallstones and biliary sludge in children at 1.9% and 1.46%, respectively.<sup>1</sup> This review describes approach to a child with cholelithiasis.

### Types of Gall Stones<sup>2</sup>

#### Cholesterol Gall Stone

- 21% of pediatric gall stones
- Cholesterol supersaturation of bile with stasis predisposes to cholesterol gallstone formation.
- Cholesterol stones are the most common type of stone in adults and adolescent girls.

#### Pigment Stone

- 51% of pediatric gall stones
- Black pigment stones are formed due to supersaturation of bile with calcium bilirubinate (48%).
- Black pigment stone are seen in hemolytic disease and TPN.

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- Brown pigment stone (3%) are seen in infection and biliary stasis
- Brown pigment stone are more common in Common bile duct.

#### Calcium Carbonate Stones<sup>3</sup>

- Rare in adults
- 24% of gallstones in children.
- Common in children with previous abdominal surgery or had required NICU care.

The remaining portion of gallstones in children consists of protein-dominant stones, which make up about 4% of gallstones in these patients.

### Special Stones

#### Microliths<sup>4</sup>

- Gallstones smaller than 3 mm
- Can form within the intrahepatic and extrahepatic biliary tree
- May lead to biliary colic, cholecystitis, and pancreatitis
- Can even persist after cholecystectomy
- Difficult to diagnose as they are often missed on ultrasonography.

#### Biliary Sludge<sup>1</sup>

- Biliary sludge is composed of mucin, calcium bilirubinate and cholesterol crystals.

- It is commonly associated with prolonged fasting, total parenteral nutrition, pregnancy, sickle-cell disease, treatment with ceftriaxone or octreotide.
- The natural history of biliary sludge is variable; it may resolve spontaneously or may progress to gallstone development.
- Persistent sludge may give rise to biliary complications (such as obstruction or infection).

**Aetiology of Gall Stone in Children (Table 1)<sup>5</sup>**

**Sex**

Boys and girls are equally affected in early childhood, but as in adults, a clear female preponderance emerges during adolescence.<sup>6</sup>

**Genetics<sup>7</sup>**

Gallstone disease represents a multifactorial condition and previous studies have identified the major genetic contributors to gallstone formation. Several Gall stone Disease predisposing gene variants have been reported, with most prominent effects being conferred by a common variant (p.D19H) of the hepatic and intestinal cholesterol transporter ABCG5/G8.

**Obesity<sup>8</sup>**

The increasing incidence of pediatric gallbladder disease parallels the rise in obesity in children.

**Table 1:** Aetiology of Gall Stones in Children

Aetiology of Gall Stone	%	Factors Associated
Idiopathic	30-40%	• No predisposing factor; may be obesity
Hemolytic	20-30%	• Sickle cell disease • Hereditary spherocytosis • Thalassemia major
Non hemolytic	40-50%	• TPN, prolonged fasting • Ceftriaxone • Ileal disease (like Crohn’s disease) or resection • Prematurity • Frusemide therapy • Cardiopulmonary bypass, • congenital biliary malformations, • PFIC, chronic liver disease, • cystic fibrosis, • OCP, teenage pregnancy

**Ceftriaxone-Associated Biliary Pseudolithiasis<sup>9</sup>**

- Ceftriaxone induced biliary lithiasis or biliary sludge is reversible and disappears on discontinuation of therapy. That is why it is called ‘pseudolithiasis’.
- 40% of ceftriaxone is excreted in bile and can concentrate 20 to 150 times more than in serum and readily forms an insoluble salt with calcium (calcium-ceftriaxone) that precipitates in gallbladder.
- The risk factors for ceftriaxone pseudolithiasis are
  - o Hypercalcemia
  - o Renal failure (leads to increase biliary concentration)
  - o High dose (>2g or >200mg/kg/day)
  - o Long-term treatment
  - o Gallbladder stasis.
- Can be seen in 15% to 46% of patients on ceftriaxone therapy
- Usually appear after 6 days of therapy and disappear after 15 days of discontinuation of therapy
- Most cases are asymptomatic and detected on sonography
- Rarely can produce symptoms like pain abdomen, nausea, vomiting and biliary obstruction.
- Treatment
  - o In symptomatic cases, discontinuation of drug
  - o Asymptomatic cases- cessation of drug therapy is unnecessary if required for treatment

**Pathophysiology<sup>10</sup>**

Cholelithiasis primarily affects the gallbladder and may cause irritation of the gallbladder mucosa, resulting in chronic calculous cholecystitis and symptoms of biliary colic. If a gallstone obstructs the cystic duct, acute cholecystitis can occur, with distension of the gallbladder wall and possible necrosis and spillage of bile. If gallstones migrate from the gallbladder into the cystic duct and main biliary ductal system, further complications can occur, such as choledocholithiasis, biliary obstruction with or without cholangitis, and gallstone pancreatitis.

## Clinical Presentation<sup>10</sup>

The clinical presentation can be divided in three age groups. See table 2. They can be symptomatic or asymptomatic.

**Table 2:** Clinical Presentation of Gall Stone

Age Group	% of Gall Stone	Clinical Presentation
Infants <12 years	10%	Most of them have one risk factor Symptomatic- Jaundice, Transient acholic stool, abdominal pain and sepsis Asymptomatic incidental detection
Children (1-14 years)	40%	Typical biliary symptoms (40%-50%): right upper quadrant or epigastric pain with or without nausea, vomiting and fat intolerance. Non-specific abdominal pain (20%-30%). Acute abdomen (5%-10%): due to acute cholecystitis, pancreatitis or cholangitis. Asymptomatic incidental detection (20%).
Adolescents (14-18 yrs)	50%	Same as in children but right upper quadrant pain and fatty food intolerance are more common

## Physical Examination

- Pain in the Right Upper Quadrant(RUQ) is common.
- A Murphy sign (expiratory arrest with palpation in the RUQ) is thought to be pathognomonic.
- Look for hepatomegaly and splenomegaly, because they may be a clue to venous congestion or a hemolytic process that may be a predisposing factor for cholelithiasis.
- Obesity should also be noted on physical examination, because this can be a risk factor for the development of cholesterol gallstones.

## Investigations

The goal is to demonstrate evidence of gall bladder or biliary tract disease.

## Blood & Urine Analysis

- Complete blood count, Liver function test, gamma-glutamyltransferase (GGT), amylase, and urinalysis. Look for features of hemolytic anaemia in these results.

## Radiological Investigations

### Abdominal Ultrasonography

Ultrasonography of the RUQ is the study of choice in patients with uncomplicated cholelithiasis. Ultrasonography can be used to identify the location of the stone, gallbladder wall thickening, the presence of gallbladder sludge, and pericholecystic fluid. Enlargement of spleen suggest hemolytic anaemia.

### Radionuclide Scanning

Radionuclide scanning, such as with iminodiacetic acid (IDA) derivatives (eg, hepatoiminodiacetic acid [HIDA], diisopropyl iminodiacetic acid [DISIDA], and para-isopropyliminodiacetic acid [PIPIDA] scanning), is also used to assess gallbladder filling and bile excretion, particularly in response to cholecystokinin or a fatty meal.

### Cholangiopancreatography

In children with suspected hepatobiliary complications, magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) can help delineate the anatomy of the extrahepatic and intrahepatic biliary tract, identify the presence of ductal stones, and provide a therapeutic mode of removing a stone or decompressing the biliary tract. It is useful in small child in which choledochal cyst is suspected.

## Treatment

### Children (>1 years) and Adolescent Gall Stone

Can be divided into two groups

- Symptomatic children with typical symptoms (right upper quadrant or epigastric pain, nausea, vomiting and fatty food intolerance or complications)- early Laparoscopic cholecystectomy.<sup>11</sup> Symptomatic idiopathic gallstones in adolescents are associated with high rates of common bile duct obstruction and pancreatitis and consequently warrant an early cholecystectomy for all adolescents. The analysis demonstrated that for every 10 days treatment was delayed, the risk of subsequent presentations with a symptomatic episode was increased by 5% ( $p = 0.0004$ )<sup>11</sup>

- Asymptomatic children or children with nonspecific symptoms (non specific pain abdomen) - Follow up with USG surveillance and surgery if symptoms or complications develop.<sup>12</sup> However, this is controversial and some propose surgery for all gall stones.<sup>13</sup>

The spontaneous resolution rates of gall stone is higher in asymptomatic (17%) than symptomatic (6%) children.<sup>14</sup> In those children in which gall stone persists, there is no data about incidence of gall bladder cancer in follow up. As northern India has very high incidence of gall bladder cancer, there may be role of Cholecystectomy in young (20-30 Years old) with large gall stone.<sup>15</sup>

An exception is in children with sickle cell anemia, in whom laparoscopic cholecystectomy is currently recommended for asymptomatic gallstones, in order to prevent potential complications of cholelithiasis, which tend to be more common in children with sickle cell anemia.<sup>16</sup>

#### **Infant Gall Stones (Less Than 1 Years of Age)<sup>14</sup>**

- Most of them have one risk factors
- Most(80%) are asymptomatic
- Spontaneous resolution is common(34%), especially for idiopathic infants gall stones
- Complications are lower (5%) in comparison to (29%) in symptomatic children gall stones.
- Asymptomatic infants should be observed for spontaneous resolution.
- Symptomatic infants can also be observed for spontaneous resolution for 8- 12 months.
- Even for choledocholithiasis, an observation period of 1-2 weeks is recommended before active therapy as there is a chance of spontaneous resolution.
- Cholecystectomy is indicated for
  - o Symptomatic cholelithiasis persisting beyond 8-12 months
  - o With complications
  - o Radiopaque calculi.

#### **Ursodeoxycholic Acid Therapy**

- Ursodeoxycholic acid can be useful in the medical management of cholelithiasis. However, it has

not been approved by the US Food and Drug Administration for use in pediatric patients. Nevertheless, its use is well documented in other parts of the world.

- The only proven indication of UDCA is in radiolucent, noncalcified gallbladder stones less than 20 mm in diameter, when conditions preclude cholecystectomy.

It can be used in asymptomatic children with functioning gallbladder at dose of 15-25mg/kg/day in two divided doses although efficacy is doubtful and is not recommended by most authors.<sup>17</sup> The primary disadvantage with ursodeoxycholic acid therapy is the high incidence of gallstone recurrence.

#### **Laparoscopic Cholecystectomy**

Pre op orders

- Nil per oral for 6 hours
- Check blood reports(CBC, LFT, KFT, PT and viral markers)

#### **Intraoperative**

Standard Laparoscopic cholecystectomy is done by surgeon.

#### **Post operative Management**

- Analgesic and antibiotics as per surgeon order
- Orally allowed in evening or next day morning
- Discharge after day 1 commonly in children

#### **Complications<sup>18</sup>**

- Common bile duct injury and bile leaks
- Complications of hemolytic disease in patients who are at risk.
- Postcholecystectomy syndrome- rare.

#### **Long Term Implications of Cholecystectomy**

There is evidence to suggest an increased risk of intestinal cancer after cholecystectomy. The risk may be higher the closer to the duodenum and perhaps more so in women.<sup>19</sup> There is also a similarly increased risk of gall bladder cancer and colon cancer in those with cholelithiasis who have not had cholecystectomy.<sup>15,20</sup> There have been no studies

addressing the association between cholecystectomy or cholelithiasis and intestinal cancer in children—who because of their potentially longer lives might seem to be even more at risk.

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