Paediatric cholelithiasis: our experience at a tertiary care centre

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Abstract

Background: With increased incidence of symptomatic and asymptomatic gallstones in children, paediatric cholelithiasis has emerged as an important pathology in children. A retrospective study evaluates paediatric cholelithiasis and its management at a tertiary centre.

Objectives: To study the spectrum of paediatric cholelithiasis and its management issues.

Method: A retrospective study was conducted at a tertiary care on all patients of paediatric cholelithiasis (children less than 14 years) who were managed from April, 2017 to March, 2020. Data regarding demographic profile, clinical history, investigation results, management and postoperative outcomes were collected and analysed.

Results: Of the 52 ultrasound-confirmed cases of gallstones, 35 showed biliary and dyspeptic symptoms; while 17 were asymptomatic. Males outnumbered females; no child less than three years came with gallstones. No definite aetiology was found in 32 cases. Cholecystectomy was done in 40 patients (laparoscopic in 37 cases, open in three cases). Stone analysis revealed mixed stones (thirty cases), pigment stones (eight cases) and pure cholesterol stones (two cases). 10/17 cases of asymptomatic gallstones showed complete stone resolution from gallbladder on follow-up sonogram after six months; 5/17 showed no regression of stones (one symptomatic and rest four underwent elective surgery due to parental anxiety); 2/17 cases were lost to follow up. No major complication was seen.

Conclusions: Of the 52 ultrasound-confirmed cases of gallstones, 32.7% were asymptomatic and 61.5% had no definite aetiology. Of the asymptomatic cases 58.8% showed complete stone resolution from gallbladder on follow-up sonogram after six months

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Introduction

Recent trends show increased incidence of gallstones in childhood[1]. A population-based study showed a childhood gallstone prevalence of 1.9%, still less than that in an adult[2]. This can also be attributed to an increase in the use of ultrasonography (USG) in diagnosis. The cause, presentation and natural course of paediatric gall stone disease is known to be different than in adults. In a considerable number of cases, babies remain asymptomatic. Although the underlying pathology remains obscure in most cases just like in adults, haemolytic causes have been reported to have an important role[2,3]. This retrospective study was conducted to evaluate all children with gallstones for their symptoms, clinical features, natural course and outcome so as to emphasize the differences of paediatric gallstone disease from that of adults.

Objectives

To study the spectrum of paediatric cholelithiasis and its management issues

Method

All USG-confirmed paediatric cases of cholelithiasis managed at a tertiary care centre from April, 2017 to March, 2019 were studied retrospectively. All children less than 14 years old with gallstones on USG were included in study and divided into two groups. Group 1 comprised symptomatic patients who underwent surgery. Group 2 comprised asymptomatic patients who were followed up with periodic USG every three months and regular clinical monthly follow-up. If any of these patients became symptomatic, they were operated. Surgery was also considered if parents wanted to have it by choice when gallstones persisted on follow-up USG.

Ethical issues: Ethical clearance was obtained from the Indira Gandhi Institute of Medical Sciences, Sheikpura, Patna, India (036/IEC/IGIMS/2019).

Being a retrospective study, informed consent was not possible

Statistical analysis*:* Data regarding demographic profile, clinical features, aetiological factors, investigation results, including USG findings, natural course and management, were collected and analysed. For assessment of childhood obesity, we used the normative growth curves for boys and girls based on expanded body mass index (BMI) , considering the 95th, 120th and 140th percentile cutoff at any given age as the definition for class 1, 2 and 3 obesity respectively[4].

Results

A total of 52 USG-confirmed cases of paediatric cholelithiasis were seen. None of the patients were less than 3 years of age; the mean age of patients included in the study was 7.8 years and males were found to outnumber females. Table 1 describes the age and sex related characteristics of these patients.

Table 1: ***Demography of patients***

Age Group *(years)*	Group 1 *(n=35)*			Group 2 *(n=17)*		
	Male	Female	Total	Male	Female	Total
0 to <5	02	01	03	04	03	07
5 to <10	14	06	20	05	02	07
10 to 14	04	08	12	03	0	03

Figure 1 gives the details of the natural course of the patients included in this study.

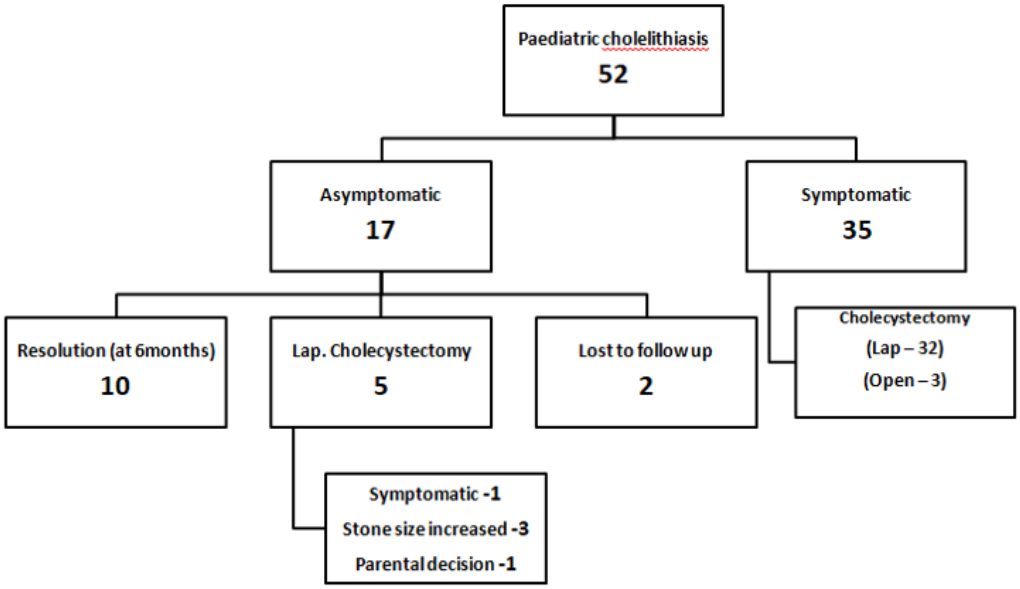

Figure 1: Presentation and natural course of paediatric gallstones

While most of them were symptomatic (67.3%), a sizeable number had no symptoms (32.7%) and were detected by chance on USG abdomen for some unrelated symptom.

Table 2 depicts the frequency of different symptoms observed in this study.

Table 2: ***Symptomatology of patients in Group 1 (n=35)***

Symptoms of gallstones	Number (%)
Vague abdominal pain	16 (45.7)
Pain in the right hypochondrium	10 (28.5)
Jaundice	03 (08.6)
Vomiting and dyspeptic symptoms	04 (11.4)
Pain in the right hypochondrium with fever	02 (05.7)

Among the symptoms, pain in the abdomen (26/35) was the most common complaint with which patients presented. Three children (8.6%) had a history of jaundice; two of them had common bile duct stone for which stone retrieval was done during endoscopic retrograde cholangiopancreatography (ERCP).

Table 3 shows the risk factors of paediatric cholelithiasis

Table 3: ***Risk factors of paediatric cholelithiasis (n=52)***

Associated risk factor	Number (%)	Group 1	Group 2
Family history of gallstones	06 (11.5)	05	01
Obesity	02 (03.8)	02	0
Prolonged use of antibiotics	07 (13.5)	03	04
Haemolytic disorder	02 (03.8)	02	0
Deranged lipid profile	03 (05.5)	03	0
No risk factors	32 (61.5)	20	12

We could not find any definite underlying aetiological factors in most of the cases (61.5%). In 6 cases (11.5%), the mother of the child had undergone cholecystectomy a few years back; 7 cases (13.5%) had a history of recurrent cough and cold for which they were given antibiotics on a number of occasions; sickle cell anaemia and thalassemia minor were each seen in one patient; deranged lipid profile (triglyceride in excess) was documented in 3 cases only (5.5%); two children were obese for their age. Forty patients (76.9%) were from urban area.

All initially symptomatic patients (35/52) had cholecystectomy. Of these 32 had laparoscopic cholecystectomy and in three patients, open cholecystectomy was needed. Among these three children, two had had a prior ERCP procedure done for the retrieval of concomitant common bile duct (CBD) stones while one case had excessive adhesions surrounding a perforated and inflamed gallbladder which forbade safe dissection by the laparoscopic method. The mean operating time was 42 minutes (range 30-65min).The average hospital stay was 2.3days (2-3days). Seventeen asymptomatic patients (32.69%) who were kept on regular clinical follow up had periodic USG done at the interval of every three months. In 10/17 cases (58.8%), we noticed complete resolution of stone from the gallbladder; 5/17 patients (29.4%) underwent cholecystectomy in due course of follow up while 2 cases, both being asymptomatic stopped follow-up.

Histopathology report of gallbladder specimens showed a spectrum of inflammatory changes ranging from acute cholecystitis (10%) to chronic cholecystitis (72.5%); while in seven cases (17.5%) it was found to be normal. However, these reports were non-specific and often did not correlate with intra-operative findings. On stone analyses, thirty children (75%) showed mixed stones; eight (20%) had pigment stones (6 - brown pigment stones and 2 - black pigment stones); pure cholesterol stones were found in only two cases (5%). Figure 2 depicts these findings. No major complication or mortality was observed in this study.

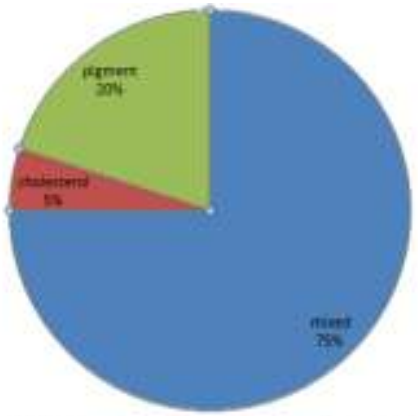

Figure 2: ***Different types of gallstones found in the study***

Discussion

Gallbladder pathologies are common in adults but recent trends also show an increase in their incidence in children[1]. Although Gibson reported the first case of paediatric cholelithiasis as early as 1737, it was found to be an uncommon pathology in children[5]. Recently however, several investigators have reported an increase in its frequency and the resultant cholecystectomy[6-9]. Incidence of gallstone disease in India is 0.3% with less than 0.1% in the 0–10 year age group[10,11]. Males and females are equally affected in early childhood, but a clear female preponderance emerges in adolescence[12,13]. In this study, we observed male preponderance with a male: female ratio of 1.36. In this study, mean age of presentation was 7.8 years and 67.3% of them were symptomatic. Bogue *et al* in their series reported that the mean age of patients was 8.23 years and 50.5% of the cases were asymptomatic at the time of diagnosis[9]. The detection of a significant number of asymptomatic gallstone patients can be attributed to the worldwide increase in the use of sonogram for evaluation of any abdomen related symptom.

Among symptoms, pain in abdomen, dyspepsia and vomiting are the frequent complaints with which most children present. Asymptomatic children usually have a diagnosis of gallstones when abdominal sonogram is done for some unrelated symptom. Around twenty five percent of kids with gallstones present with nonspecific abdominal pain[14]. The aetiology can be unknown or can be associated with risk factors, including haemolytic conditions. Recently, it has become evident that only

20% are related to recurring haemolysis[14,15]. However, Wesdorp *et al* reported 39% gallstones related to some haemolytic disease[2]. Factors related to development of gallstones and clinical presentation differ with age[2]. Risk factors for cholelithiasis, which we encountered in our study, were haemolysis, extended antibiotic use, obesity, hypertriglyceridaemia and family history of cholelithiasis. In 61.5% of cases, we could not find any underlying causes of gallstone formation.

Kaechele V, *et al* investigated the role of obesity, female sex and pubertal development as risk factor for cholelithiasis[1]. In his study, he found gallstones to be unusual in pre-pubertal age group and obesity and female sex to be associated with a higher risk of gall stone formation, like in adults[1]. By contrast, we found a significant number of cholelithiasis patients to be in the pre-pubertal age group and only two of our children were obese. Males were more commonly involved in our series.

All laboratory results in cases of simple cholelithiasis were found to be within normal limits. They were however helpful to identify biliary obstruction and acute cholecystitis. We found elevated levels of serum bilirubin and alkaline phosphatase in the two cases of gallstones with associated choledocholithiasis. This can be explained by impedance of bile flow due common bile duct obstruction. Both these patients underwent a prior clearance of stone through ERCP procedure, followed by a subsequent attempt at laparoscopic cholecystectomy; unfortunately, the shrunken size of the gallbladder with significant inflammation and adhesions led to conversion to open cholecystectomy. Incidence of choledocholithiasis in paediatric age group is not known but in adult cases 3%-10% of the patients undergoing cholecystectomy will have common bile duct (CBD) stones[16].

USG of abdomen especially of hepato-biliary region remains the mainstay of diagnosis in cholelithiasis. Having a sensitivity and specificity exceeding 95%, it has high accuracy in detecting gallstones stones as small as 1.5mm; however, diagnosis of choledocholithiasis is imprecise with a reported sensitivity and specificity ranging between 50% – 75%[17]. One child with lump in right hypochondrium had an inconclusive USG; computed tomography scan of abdomen showed gallbladder perforation with lump formation. The most common intervention for CBD stones is endoscopic retrograde cholangiopancreatography (ERCP) followed by procedure to remove the stones[8,9].

Surgery is the best and only treatment for symptomatic gallstones. Laparoscopic approach remains the preferred approach compared to the open procedure with less pain, better cosmesis and shorter hospital stay[18]. Risks of laparoscopic cholecystectomy include CBD injury, bile leak, bleeding, wound infection, retained stones. Several series report minimal complication rates[7,12,18]. St Peter *et al*[19] and Tannuri AC, *et al*[20], in their studies reported no conversions, ductal injuries, bile leaks, or deaths. Reasons for converting from laparoscopic to open procedure may be too much inflammation around gallbladder, distorted and anomalous anatomy, difficult dissection in and around the Calot's triangle and constraints of space especially in paediatric patients. Kelley-Quon LI, *et al*[21] suggested that unlike in the adult, routine intraoperative cholangiogram in children may not lower the risk of bile duct injury during cholecystectomy. Thus, cholangiogram was not done in any of our patients. MRCP is useful in selected children to exclude choledocholithiasis and avoid intraoperative cholangiography[22].

Mean operating time of laparoscopic cholecystectomy in our study was 42 minutes (range 30-65min) at par with other series[18,23]. Proper pain management and wound care are the two most important goals of postoperative management[24]. With the majority of our patients having had a laparoscopic procedure with smaller wounds, both these problems were less frequently observed in our study. We aimed for early re-institution of oral feeds depending on the merits of the individual case and all these measures culminated in early discharge of the patients, mostly on the second postoperative day (mean hospital stay – 2.3 days). Langballe KO, *et al*[25] reported similar hospital stay in their study (91% of their patients were discharged within three days of surgery without readmission). Histopathology suggested chronic cholecystitis in most cases (72.5%). Pogorelic Z, *et al*[26], in their research paper mentioned that histopathology was suggestive of chronic cholecystitis in 79.8% cases and acute cholecystitis in 11.8% of cases. In 8.8% of cases, gallbladder was found to be normal.

What causes gallstones in young children? Possible reasons suggested include haemolytic disease, infectious aetiologies, metabolic causes, obesity, familial risks, dietary and environmental factors and medications; however, most of the cases are still idiopathic in several series[27,28]. Several early series had reported the higher proportion of pigment gall stones thereby strengthening the relation between haemolytic disease and gallstones[26,29]. Recent evidence also shows that an increased incidence of childhood obesity often parallels an increased incidence of childhood gallstone disease[28,30]. A recent trend has been the relative fall in the number of cases associated with haemolytic disease; this observation goes hand-in-hand with change in the spectrum of the type of stones from pure pigment

stones to mixed and pure cholesterol varieties[27]. Pogorelic Z, *et al*[26] described a similar shift in the composition of gallstones at their centre; in their study spectrophotometric analysis of gallstones removed from 1998-2007 showed 63.6% pigment stones, whereas from 2008-2017, 70.6% of gallstones were cholesterol stones. Our study also reflects this trend; mixed stones (75%) were exceedingly more common than pigment stones (8 cases) and pure cholesterol stone (2 cases).

With regard to gallstone sterols, gallstone disease of adolescent girls is similar to that of adults[31]. Composition of bile acids in paediatric gallstones remains different from adults[31,32]. Paediatric gallstones containing cholesterol less than 35% of the stone weight were called pigment stones whilst cholesterol stones contained it in excess of 35%. The brown pigment stone is characterized by calcium palmitate and cholesterol (10-35%) and the black pigment stone contains calcium carbonate with cholesterol (less than 10%)[32]. Reshetnyak VI, *et al*[33] made a significant remark regarding pathogenesis of gallstones that bacteria producing beta glucuronidase and mucus give rise to mixed and pigment gallstones, whereas bacteria producing mucus only or not producing any of these substance gives rise to cholesterol stones.

Asymptomatic paediatric gallstone cases are an important subgroup, comprising 4-24% in several series; these cases present with management related dilemmas[6,7,34]. Several investigators have reported regression of stones and sludge in infants and in children less than three years of age, thereby advocating non-operative follow-up with periodic USG abdomen[6,35]. Unfortunately, in our study we did not have any case less than three years of age. But, the phenomena of spontaneous resolution in asymptomatic cases can be observed in our study as well; 10/17 (58.8%) of asymptomatic gallstone patients in our series showed complete resolution on an abdominal USG after six months of diagnosis (three of them were stone-free after three months while it took six months in other seven patients). These patients were therefore not operated. 5/17 of the initially asymptomatic patients had surgery due to appearance of symptoms in one, increase in size of stones in three and parental insistence for surgery in one. Two of our patients in this group did not come for follow-up. No medications were given to any of the asymptomatic gall stone patients (analgesics, antibiotics or drugs to enhance bile flow).

Management of ultrasound confirmed but asymptomatic cases of paediatric cholelithiasis, is also a matter of debate today. Relevant literature suggest that asymptomatic cases of paediatric gallstones can be safely followed up; considering the low rate of complications observed in their series and the favourable natural history described in adults, they recommend an expectant management with periodic clinical and ultrasonographic evaluation[6,36-38]. Young age is a favourable factor for gallstone resolution; single stone, and stone size up to 5 mm were other factors that affect stone dissolution[35,39]. According to some other series, cholecystectomy is advised for all asymptomatic children more than 3 years of age if ultrasonography confirms that echogenic foci with shadowing are true stones and not echogenic sludge, to prevent complications of CBD obstruction, pancreatitis, perforation with bile peritonitis, and life-threatening sepsis[15,39]. There is a unanimous decision on symptomatic gallstones in children that it should be dealt surgically and laparoscopic cholecystectomy is the gold standard treatment for children as well[6-8,18,40]. Morbidity and mortality following cholecystectomy are expected to be relatively low in the paediatric age group. In our series there was no mortality or complications.

Conclusions

Of the 52 ultrasound-confirmed cases of gallstones, 32.7% were asymptomatic and 61.5% had no definite aetiology. Of the asymptomatic cases 58.8% showed complete stone resolution from gallbladder on follow-up sonogram after six months

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