

## **Cholelithiasis in children, a clinical, hematological and pathological study including chemical analysis of gallstones**

Dr Mushtaq Ahmad Bhat<sup>1</sup>, Dr Bashir Ahmad Bhat<sup>2</sup>, Dr Yaqoob Hassan<sup>3</sup>,  
Dr Anayatullah<sup>4</sup>, Dr Irshad Ahmad<sup>5</sup>

<sup>1</sup>Lecturer, Department Of General Surgery Government Medical College, Srinagar.

<sup>2</sup>Lecturer, Department Of General Surgery Government Medical College, Srinagar.

<sup>3</sup>Registrar, Department of General Surgery, Sher-i-kashmir Institute of Medical Sciences, Medical College, Srinagar

<sup>4</sup>Post graduate scholar, Department Of General Surgery Government Medical College, Srinagar

<sup>5</sup>Registrar, Department of General Surgery, Sher-i-kashmir Institute of Medical Sciences, Medical College, Srinagar

Corresponding Author: Dr. YAQOOB HASSAN

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### **Abstract:**

**Background:** Gallstone disease which has long been considered as an adult disease, is increasingly gaining recognition in the pediatric practice because of the significant documented increase in non-hemolytic cases over the last two decades. **Aim** The aim of this study was to evaluate the childhood cholelithiasis and its clinical, haematological, pathological aspects and the management.

**Methods:** The present prospective study was conducted in the Department of Paediatric Surgery, SKIMS, Srinagar over a period of two years. In this study 44 patients in age group of 2-14 years were included with ultrasound proved cholelithiasis. These patients were reviewed for demographic information, predisposing factors, presenting symptoms, laboratory findings, complications, treatment, stone analysis and histopathological characteristic of specimen.

**Results:** In our study of 44 patients, the mean age was 9.4 years with 21 males and 23 females. Most common symptom was pain abdomen. In our study, 10 patients (22.7%) had history of intestinal ascariasis, 11 patient (2.3%) had history of TPN (3 days), 4 patients (9.1%) had history of meconium ileus, 8 patients (18.2%) had history of ceftriaxone therapy (3-6 days) and 3 patients (6.8%) had positive family history of cholelithiasis in the first degree relatives. 4 patients (9.1%) had hemolytic disorder and rest of the patients had (47.7%) no risk factor or predilection for developing gallstones. 9 patients (20.5%) had single calculi in the gallbladder, 31 patients (70.5%) had multiple calculi and 4 patients (9.1%) had multiple calculi with splenomegaly. 38 patients (86.3%) had stone size <5mm while the rest of patients (13.7%) had stone size >5mm. The gall bladder specimen on histopathological examination showed chronic cholecystitis in 40 patients (93.0%), congested gall bladder in 1 patient (2.3%) and fibrotic inflamed gallbladder in 2 patients (4.7%). Stone analysis showed cholesterol stones in 25 patients (58.1%), pigmented stones in 13 patients (30.2%), mixed stones in 2 patients (4.7%) and 3 patients (7%) had calcium carbonate stones.

**Conclusion:** In children cholelithiasis is not uncommon and around two cases of cholelithiasis are admitted in pediatric surgery per 100 cases of total admission in our institution. The most common cause for cholelithiasis in children is idiopathic. Cholesterol stones are the most common stones in children with cholelithiasis followed by pigmented stone. Chronic cholecystitis is the most common histopathological findings in children with cholelithiasis. Cholecystectomy with open or laparoscope is safe and effective for cholelithiasis in children.

**Keywords:** Cholelithiasis, Childhood, Cholecystectomy

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### **I. Introduction**

Gallbladder calculi are relatively uncommon in children. However, the incidence of cholelithiasis has been increasing recently. Cholelithiasis in infancy is most often related to acute and chronic illness and hyperalimentation. Risk factors include abdominal surgery, sepsis, bronchopulmonary dysplasia, hemolytic disease, malabsorption, necrotizing enterocolitis and hepatobiliary disease. Other factors implicated include polycythemia, phototherapy and distal ileal resection. The immature hepatobiliary system of infants may predispose them to stone formation. Decreased hepatobiliary flow and immature bilirubin conjugation both contribute to stasis and sludge formation. Hemolysis and prolonged hyperalimentation are significant influences

in this age group. Up to one half of infantile gallstones, especially those associated with hyperalimentation may resolve spontaneously.<sup>(1)</sup>

Pediatric cholelithiasis was viewed as a disease of prematurity, usually related to the use of total parenteral nutrition, or in adolescence related to hemolytic disease. In one series, however, only 41% of children had hematologic disease, and 23% had no underlying illness or risk factor<sup>(2)</sup>. This observation is in keeping with other current reports that have suggested a higher incidence of non-hemolytic cholelithiasis in recent years.<sup>(3)</sup> Gallstones are four to ten times more frequent in older than younger subjects. Biliary cholesterol saturation increases with age, due to a decline in the activity of cholesterol 7 $\alpha$  hydroxylase, the rate limiting enzyme for bile acid synthesis<sup>(4)</sup>.

Genetic influence in gallstone formation is also suggested by familial clustering within populations. An increased frequency of gallstones was found among the relatives of gallstone patients as compared with families of controls. Familial dietary habits are not likely to offer an explanation of the increased familial incidence of gallstones, in view of the negative findings in spouses<sup>(5,6)</sup>.

Pregnancy, birth control pills, dehydration, and obesity have contributory roles. Early menarche has been shown to significantly increase incidence, perhaps because of the lithogenic effect of estrogen on bile. Racial and genetic influences in the adolescent age group are similar to those in adults.<sup>(1)</sup> Children may harbor cholesterol gallstones, black or brown-pigmented stones, or mixed-type gallstones. It has been demonstrated that there is a high incidence of calcium carbonate stones in children that are exceptionally rare in the adult population.<sup>(7)</sup>

The basic mechanism underlying the formation of gallstones is supersaturation with constituents in bile exceeding their maximum solubility. Additional factors contributing to gallstone formation are nucleation factors, bile stasis within the gallbladder and calcium in bile. Biliary cholesterol usually exists in a soluble single phase as micellar cholesterol. As the cholesterol concentration increases, cholesterol crystals begin to form.<sup>(8)</sup> Mucin and a soluble glycoprotein are potential nucleation factors. Prostaglandins stimulate the synthesis and secretion of bile mucin. Inflammation and other stimuli, which enhance prostaglandin secretion, increase the risk for gallstone formation. Biliary sludge, also referred to as microlithiasis, is a viscous gel composed of mucin, precipitates of cholesterol and calcium bilirubinate. Gallstone formation is usually preceded by the presence of biliary sludge. Therefore, sludge should be regarded as part of the spectrum of gallstone disease. Retarded or incomplete emptying of bile from the gallbladder can promote sludge formation.<sup>(7)</sup>

Ultrasonography is the diagnostic method of choice if gallstones are suspected. In children having gallstones diagnosed as a result of ultrasonography carried out due to different indication expectant treatment is recommended. Children presenting with typical clinical signs of gallstone colic need an operation<sup>(9)</sup> Children with gallstones and typical symptoms of right upper quadrant or epigastric pain with food intolerance should undergo cholecystectomy. Eighty-two percent of children with cholelithiasis and atypical symptoms have improvement with dietary manipulation. Pediatric patients with gallstones that are asymptomatic or associated with atypical symptoms can be safely followed without complications.<sup>(10)</sup>

## **II. Aims and Objective**

The aim of this study was to evaluate the childhood cholelithiasis and its clinical, haematological, pathological aspects and the management.

## **III. Material and Methods**

The study "Cholelithiasis in children, a clinical, hematological and pathological study including chemical analysis of gallstones" was a prospective observational study conducted in the department of paediatric surgery SKIMS, Kashmir, after obtaining approval from Institutional Ethical Committee, from October 2009 to August 2011. The study comprised of 44 pediatric patients who presented with cholelithiasis and its associated symptoms. The patients selected for the study were below 14 years of age of either sex.

Subsequent to hospital admission, the patients were evaluated on the basis of history, clinical examination and relevant investigations. Finer details like the demographic profile, and residential address were also noted in each case.

Detailed general physical examination and systemic examination was undertaken in each case to determine anemia, cyanosis, jaundice, lymphadenopathy, fever, etc. Examination of the chest, cardiovascular system, and nervous system was carried out to determine any associated disorder.

All the patients were subjected to complete haemogram, liver and kidney function tests, and x-ray examination of chest/abdomen. To detect gallstones, all patients were subjected to ultrasonography. Patients with any suspicion of hemolytic disorder, that is triad of anemia, cholelithiasis and splenomegaly were subjected to detailed hemolytic profile, which routinely included complete blood count with reticulocyte count, Reticulin production index (RPI), Peripheral Blood Film (PBF) for polychromasea, absolute eosinophilic count and Red Blood Cell (RBC) morphology, Lactic Acid Dehydrogenate (LDH), conjugated and unconjugated

bilirubin in particular. Further specialized available work up in form of plasma hemoglobin, sucrose lysis, and Hams test was also undertaken in certain cases.

All those patients who were diagnosed as having gallstones were categorized into two groups; patients with acute symptoms and those with chronic symptoms. The patients with acute symptoms were initially subjected to conservative treatment. Those who did not respond to conservative treatment or developed complications were subjected to emergency cholecystectomy or cholecystostomy. Other patients were treated with elective cholecystectomy (laparoscopic or open).

Subsequently gall stones removed at the surgery were sent for detailed stone analysis and histopathology of gall bladder specimen

Regular follow up of the patients was done two weekly for a period of one month to determine any subsequent complication and the resolution of the symptoms. Subsequently the patients were directed to follow-up after every two month or earlier if any problem was noted by the patient. Any complication noted during the course of follow up was entered into the proforma of the individual patient for record and further analysis of data.

#### IV. Results

The age range of patients in our study was 2 to 14years with the mean age of 9.4 years. There were 21 male (47.7 %) and 23 female children (52.3%) in our study.28 of our patients (63.6%) were from rural areas and 16 patients (36.4%) from urban area.(Table 1)

In our study, 14 patients(31.8%) were in the age group 2-5 and 30 patients(68.2%) in the age group of 6-14 and no patients below two years of age. Thus maximum numbers of cases were found in the 6-14 years age group.

Based on the clinical presentation 35 patients (79.5%) presented with pain abdomen, 23 patients (52.3%) with nausea, 19 patients (43.2%) with vomiting, 17 patients (38.6%) with post-prandial fullness, 5 patients (11.4%) with fat intolerance, 6 patients (13.6%) with itching, 15 patients (34.1%) with anorexia, 9 patients (20.5%) with fever, 6 patients (13.6%) with icterus and 4 patients (9.1%) with passage of high colored urine.(Table 2)

In our study, 10 patients (22.7%) had history of intestinal ascariasis, 11 patient (2.3%) had history of TPN(3days), 4 patients (9.1%) had history of meconium ileus, 8 patients(18.2%) had history of ceftriaxone therapy (3-6 days) and 3 patients (6.8%) had positive family history of cholelithiasis in the first degree relatives. 4 patients (9.1%) had hemolytic disorder and rest of the patients had (47.7%) no risk factor or predilection for developing gallstones.

In our study 34 patients (77.2%) have under gone open cholecystectomy, 3 patient (6.8%) laparoscopic cholecystectomy, 4 patients (9.1%) open cholecystectomy with splenectomy and 2 patient (4.5%) have under gone open cholecystectomy with excision of choledochal cyst with hepaticojejunostomy and 1 patient (2.3%) was put on conservative management.The average hospital stay of the patients was 3.1 days for open cholecystectomy, 2 days for laparoscopic cholecystectomy, 4 days for open cholecystectomy with splenectomy and 7 days for open cholecystectomy with excision of choledochal cyst with hepaticojejunostomy. There were no major complications of surgery in our study except for minor wound infection in two patients and primary hemorrhage which delayed their discharge from the hospital.

The gall bladder removed at the surgery was sent for histopathological examination which showed chronic cholecystitis in 40 patients (93.0%), congested gall bladder in 1 patient (2.3%) and fibrotic inflamed gallbladder in 2 patients (4.7%).Based on the chemical analysis of the gall stones retrieved at the cholecystectomy 25 patients (58.1%) had cholesterol stones, 13 patients (30.2%) had pigmented stones, 2 patients (4.7%) had mixed stones and 3 patients (7%) had calcium carbonate stones.

| N:44     |           | n                 | %    |
|----------|-----------|-------------------|------|
| Age (yr) | ≤ 5       | 14                | 31.8 |
|          | > 5       | 30                | 68.2 |
|          | mean ± SD | 9.4 ± 4.4 (2, 14) |      |
| Gender   | Male      | 21                | 47.7 |
|          | Female    | 23                | 52.3 |
| Dwelling | Rural     | 28                | 63.6 |
|          | Urban     | 16                | 36.4 |

| Presenting Symptoms    | No of cases | %age |
|------------------------|-------------|------|
| Abdominal pain         | 35          | 79.5 |
| Nausea                 | 23          | 52.3 |
| Vomiting               | 19          | 43.2 |
| Post-prandial fullness | 17          | 38.6 |

|                               |    |      |
|-------------------------------|----|------|
| Fat intolerance               | 5  | 11.4 |
| Itching                       | 6  | 13.6 |
| Anorexia                      | 15 | 34.1 |
| Fever                         | 9  | 20.5 |
| Icterus                       | 6  | 13.6 |
| Passage of high colored urine | 4  | 9.1  |

## V. Discussion

Gallstone disease remains a serious health concern affecting millions throughout the world. Gallstone disease which has long been considered as an adult disease, is increasingly gaining recognition in the pediatric practice because of the significant documented increase in non-hemolytic cases over the last two decades.

The incidence of cholelithiasis in the pediatric population varies mostly according to age with some racial and cultural influence. Infants who have cholelithiasis tend to be patients who are ill, are receiving hyperalimentation and have prematurity, congenital anomalies and necrotizing enterocolitis as compounding risk factors. Children aged 1-5 years most frequently have hemolysis as the underlying conditions.<sup>(1)</sup>

A number of studies worldwide have been conducted to evaluate the gallstone disease in the pediatric age group. This present study comprised of 44 patients who presented with right upper quadrant abdominal pain and were found to have gallstones on ultrasonography. The age range of patients in our study was 2-14 years with a mean age of 9.4 years. In a study conducted by Kumar R, et al., the median age at presentation was 10 years. In studies conducted by S.Reif, et al. and J Deepak, et al, the mean age was 12.2 and 9.4 years respectively. The mean age at presentation of cholelithiasis in children was more or less similar with the results shown by Kumar R, et al, S.Reif, et al and J Deepak, et al.

In our study, 14 patients (31.8%) were in the age group 2-5 and 30 patients (68.2%) in the age group of 6-14 and no patients below two years of age. Thus maximum numbers of cases were found in the 6-14 years age group. Friesen et al, in a review of 693 children with gallstones reported that infants less than 6 months of age represented 10% of cases, 69% were in the age group 11-12 years, and 21% between 6 months and 10 years. This observation corresponds with our results.

The numbers of male patients in our study were 21 and females were 23 in number. The male to female ratio in our study was 21:23 and this female predominance was found in all age groups. Pollak R, et al studied nineteen patients, seventeen patients were females and two male (8.5:1) and Robert W. Crichlow, et al. showed, females predominated in a ratio of 3.4:1. J Deepak, et al studied 22 patients (10 males and 12 females) with history of cholelithiasis. Our study also showed the female predominance, however the female predominance is lower than that of Pollak R, et al and Robert W. Crichlow, et al showed in their study. Our observation coincides with the observation of J Deepak, et al. The minute difference is not statically significant ( $p\text{-value} > 0.05$ ) and could be due to differing in sample size.

In our study, 3 (6.8%) patients had a positive family history of cholelithiasis in the first degree relatives. Aharon Klar, et al in their study had 7.5% of their patients with family history of cholelithiasis. The results are comparable with the observations of our study.

The most common presenting symptom of cholelithiasis in children in our study was pain abdomen (79.5%). In a study conducted by Pollak R, et al, found that the most common presenting symptoms of pediatric cholelithiasis was vague right upper quadrant or epigastric pain (95%). Kumar R, et al also found that the most common presenting symptom is the right upper quadrant pain<sup>(11)</sup>. Amira Bouraoui, Bayan, et al observed that the most common presenting symptom in pediatric cholelithiasis was pain abdomen<sup>(12)</sup>. These results are in accordance with the results found in our study.

Pediatric cholelithiasis was viewed as a disease of prematurity, usually related to the use of total parental nutrition (TPN), or in adolescence, usually to hemolytic disease. In our series, however, 4 children (9.1%) had hematologic disease, and 21 patients (47.7%) had no underlying illness or risk factor. This observation corroborates with other reports that have suggested a higher incidence of non-hemolytic cholelithiasis in recent years.<sup>(13)</sup> In their study, Kumar Rajendra, et al, studied 102 cases of cholelithiasis in children and found no cause in 66 patients (64%)<sup>(11)</sup> (idiopathic). Denise Herzog et al, studied 105 cases older than 2 years of age and about (50%) of these had idiopathic gallstone disease<sup>(12)</sup>. These figures corroborate well with the results found in our study. The present study demonstrate that generally held notion that hemolytic disease is invariably predisposing cause of cholelithiasis in children is not true, as majority of patients in our study had cholelithiasis of idiopathic type, even though they were specifically investigated for hemolytic disease.

In our series, 11 patients (25%) had a previous history of TPN administration. Joel J et al, studied 21 children that had history of TPN, 9 developed gallstones (43%)<sup>(14)</sup>. Bogue, Conor O, et al in their study showed TPN as a significant risk factor<sup>(15)</sup>. Friesen and Roberts,<sup>(16)</sup> reported that gallstones were associated With TPN in 29% of pediatric patients. Baily PV; et al observed infants and young children were affected more frequently who had history of TPN<sup>(17)</sup>. In our study, observations coincides with the observation of Friesen and Roberts, J Deepak, et al, Joel J et al. The observations of the present study about TPN administration as a risk factor is

statically significant ( $p$  value  $< 0.05$ ) thus patients receiving TPN administration should be followed by periodic USG examinations to look for cholelithiasis.

Association of gallstones with third generation cephalosporin therapy has been reported rarely in literature. Reversible ceftriaxone associated biliary pseudolithiasis was first reported by Schaad et al, in 1988. Parameters associated with pseudolithiasis were prolonged treatment (4-22 days), high doses and older patient age.<sup>(18)</sup> In our study eight patients had a previous history of ceftriaxone intake for a short duration of 4-7 days only. Ceftriaxone is commonly used antibiotics in admitted patients in our hospital. It constitutes a significant risk factor for developing gallstones and biliary sludge. Seven patients in our study had history of ceftriaxone intake in recent past and were symptomatic. One patient had history of ceftriaxone intake and was asymptomatic but USG examination performed for some vague urinary symptoms, documented biliary sludge. Subsequently that patient was followed by periodic USG. The patient remained asymptomatic with no biliary sludge on six month of periodic follow up with USG. Amber Mehmood et al<sup>(19)</sup> in their study showed that ceftriaxone is a risk factor for cholelithiasis. Araz N, Otran V et al reported 8 cases of cholelithiasis that had history of ceftriaxone administration.<sup>(20)</sup> Ozturk A, Kaya M et al, in their study showed that ceftriaxone had role in developing biliary sludge and pseudolithiasis<sup>(21)</sup>. These observations corroborate with results of our study. Thus patients having history of ceftriaxone intake for prolonged period should be followed by periodic USG to look for cholelithiasis.

Abdominal USG was done in all the patients in our study to detect gallstones. Sonographic diagnosis of gallstones was based on the presence of mobile echogenic foci and acoustic shadow in the gallbladder lumen. There were multiple stones in 35 (77.3%) patients and solitary in 9 (22.7%) patients. 38 patients (86.7%) had stone size of less than 5mm while the rest of the three patients had a stone size of more than 5mm. Forty of our patients had gallbladder wall thickness normal whereas four patients had gallbladder wall thickened.

USG is the diagnostic method of choice as same was suggested by Wewer AV et al<sup>(9)</sup>, Ganesh R et al. Thus any pediatric patient having history of pain abdomen should undergo USG abdomen to look for cholelithiasis.

The treatment of choice for cholelithiasis is cholecystectomy. 97.3% patients in the present study underwent cholecystectomy. The recovery was excellent after cholecystectomy in all cases. Willis A, et al, found that prognosis for recovery is excellent for pediatric cholelithiasis after cholecystectomy if there is no complicating systemic disease.<sup>(22)</sup> Wewer AV, et al, suggested that children presenting with gallstone colic need an operative intervention.<sup>(9)</sup> Bruch SW, et al, concluded in their study that children with gallstones and typical symptoms of right upper quadrant or epigastric pain with food intolerance should undergo cholecystectomy.<sup>(10)</sup> The results of our study are comparable with the results of above studies. In our study 93.0% patients (40) underwent open cholecystectomy and 6.8% of patients (3) had cholecystectomy done by laparoscopic method. With regards to complications we found no difference between the two methods.

Histopathological examination of the removed gallbladder in the present study showed features of chronic cholecystitis in 40 patients (93.0%) congested gallbladder in 1 patients (2.3%) and fibrotic inflamed gallbladder in 2 patients (4.7%). In a study conducted by Bakhotmah A<sup>(23)</sup>, features of chronic cholecystitis were found in 75% of his patients, while congested gallbladder and fibrotic inflamed gallbladder in 9.1% each<sup>(24)</sup>. Deepak Javare et al observed features of chronic cholecystitis in 83.3% patients on histopathological examination. Thus the most common feature on histopathological examination of removed gallbladder were chronic cholecystitis.

All the stones retrieved during surgery were sent for analysis by chemical methods. We found that 25 patients (58.1%) had cholesterol stones, 13 patients (30.2%) had stones composed of calcium bilirubinate and 2 patients (4.7%) had mixed stones. Calcium carbonate stone was found in 3 patients (7%). Analysis based on FTIR (Fourier transform infra-red micro spectroscopy) suggests that the composition of black and brown stones from both children and adults are similar. Black stones are rich in bilirubin. Brown stones are composed of varying amounts of bilirubin and cholesterol.<sup>(25)</sup> In contrast to adults, calcium carbonate gallstones are relatively common in children.<sup>(26)</sup>

Stringer MD, et al, performed composition studies of gallstones by Fourier transforms infra-red micro-spectroscopy. Of the 20 children, 10 (50%) had black pigment stones, 2 (10%) had cholesterol stones, 1 (5%) had brown pigment stones, and 7 (35%) had calcium carbonate stones, the latter are exceptionally rare in adults. The composition of pediatric gallstones in his series differed from that found in adults.<sup>(27)</sup> Clemens Schafmayer, studied gallstone composition in Northern Germany. Only 2% of stones in their study were pigmented as compared to 91% of stones containing cholesterol as a main substance. Most of the patients in our study had cholesterol stones followed by pigmented stones. The gallstones in patients with nonhemolytic disease are usually made of cholesterol. These stones result when the bile cannot dissolve all of the cholesterol and some of the cholesterol solidifies into stone. These stones can be seen in older children and adolescents, although cholesterol stones are often typically seen, as these children get older and turn into adulthood.

There were no major complications of surgery in all of our patients, except for minor wound infection in two patients and primary hemorrhage in one patient which delayed their early discharge from the hospital. All the patients were discharged home after 2-7 days postoperatively, with an average in hospital stay of 3.98 days postoperatively. Darlene M. Miltenburg, et al,<sup>(2)</sup> observed that the overall complication rate following pediatric cholecystectomy was 9%. In his series, the complication rate was more than twice higher in emergency surgery than elective (16% vs. 6%). The complication rate in our study was 6.8%. Thus our observation more or less coincides with observation of Darlene M. Miltenburg, et al.<sup>(2)</sup> All surgeries in our study were elective cholecystectomies, and none of the surgery was undertaken in emergency.

All the patients were put on regular follow up every two weeks for a period of one month and subsequently after every month for a period of two years. During the follow up period we found no patient with recurrence of the symptoms or with the retained stones. Thus confirming the gratifying results following cholecystectomy.

## VI. Conclusion

In children cholelithiasis is not uncommon, and around 2 cases of cholelithiasis are admitted in pediatric surgery per 100 cases of total admission. The most common cause for cholelithiasis in children is idiopathic. Cholesterol stones are the most common stones in children with cholelithiasis followed by pigmented stone. Chronic cholecystitis is the most common histopathological findings in children with cholelithiasis. Cholecystectomy with open or laparoscope is safe and effective for cholelithiasis in children. We recommend that further community based larger studies are needed to establish risk factors for childhood cholelithiasis and prevention thereof in this part of country.

## References

- [1]. Andre Hebra, MD, Melissa Miller, MD, Cholecystitis; 2006- WWW. EMedicine.com Specialities> pediatrics > Gastroenterology.
- [2]. Darlene M. Miltenburg, Randolph Schaffer III, Tara Breslin, and Mary L. Brandt. Changing Indications for Pediatric Cholecystectomy PEDIATRICS .2000;105, 6:1250-1253.
- [3]. Halpern, Z.; Vinograd. Z. Journal of Pediatric Gastroenterology & Nutrition. **1996**; 23; 147 -55.
- [4]. Bertolotti M, Bertolotti S, Menozzi D, et al. Ageing and bile acid metabolism: studies on 7 $\alpha$  hydroxylation of cholesterol in humans. In: paumgartner G, Gerok W, eds. Trends in bile acid research. Lancaster: kluwer Academic publisher, **1984**; 75-8.
- [5]. Danzinger RG, Gordon H, Schoenfeld LJ, et al. Lithogenic bile in siblings of young women with cholelithiasis. Mayo Clin Proc. 1972;47:762-6.
- [6]. Van Der Linden W, Simonson N. Familial occurrence of gallstone disease. Incidence in parents of young patients. Human Hered 1973; 23; 123-7
- [7]. Alexandre F Migala, DO, Hildegardo Costa, cholelithiasis; **2006**, WWW.eMedicine.com Specialities> Pediatrics > Gastroenterology.
- [8]. Aijaz Ahmed, Ramsey C. Cheung, Management of Gall Stones and their Complications. American Academy of Family physicians **2000**; 61, 6.
- [9]. Wewer AV; Hovendal CP; Paerregaard A Borneafdelingen, H. Gallstones in children. Ugeskr Laeger. **2005**; 167:2625-6.
- [10]. Bruch SW; Ein SH; Rocchi C; Kim PC The management of no pigmented gallstones in children. J Pediatr Surg. **2000**; 35:729-32.
- [11]. Rajendra Kumar, Kelly Ng uyen, Albert Shun. Gallstones and common bile duct calculi in infancy and childhood. Australian and New Zealand Journal of Surgery. Published online, **2001**; 70,3: 188 – 191
- [12]. Denise Heroz, Guylaine Bouchard. High rate of complicated idiopathic gallstone diseases in pediatric patients of Northern America. (World J Gastroenterol 2008 March; 14(10):1544-1548.
- [13]. Mc Evoy CF, Suchy FJ Biliary tract disease in children. Pediatr Clin North Am **1996**; 43:75-98.
- [14]. Roslyn JJ, Pitt HA, parenteral nutrition-induced gallbladder Disease: a reason for early cholecystectomy. Am J surg.
- [15]. Bogue, Conor O, Murphy. Risk factors of gallstones in children (Journal of pediatric Gastroenterology and Nutrition 50(3): 303-308 March 2010.
- [16]. Aharon Klar, David Branski, Yaacov Akerman, Michael Nadjari, et al. Sludge Ball, Pseudolithiasis, Cholelithiasis and Choledocholithiasis from Intrauterine Life to 2 years: A 13-year Follow-up, Journal of Pediatric Gastroenterology and Nutrition **2005** 40: 477-480
- [17]. Bailey PV, Connors RH, changing spectrum of cholelithiasis and Cholecystitis in infants and children. Am J surg. 1989; 158:585-8
- [18]. Schaad UB, Wedgwood-krucho J, Tschaepeler H. Reversible ceftriaxone-associated biliary pseudolithiasis in children Lancet **1988**; 2:1411-3.
- [19]. Amber Mehmood, Arif M K. Biliary stones: An atypical cause of abdominal pain in pediatric age group. (Department of Emergency Medicine and Section of Pediatric Surgery. The Aga Khan University Hospital, Karachi.)
- [20]. Araz N Okan V, Araz M, Demirci M. Pseudolithiasis due to Ceftriaxone Treatment for Meningitis in Children. Tohoku, Journal of Experimental Med 2007; 211(3): 285-90
- [21]. Ozturk A, Kaya M, Zeyrek D, Ozturk E, Kat N., S.Z. Ziylan. Ultrasonographic findings in Ceftriaxone: Associated biliary sludge and Pseudolithiasis in Children 2005, 46 :112-16 Department of Paediatrics & Paediatric Surgery, Sanliurfa, Turkey Correspondence
- [22]. Willis A. Wingert and Victor G. Mikity. Cholelithiasis and cholecystitis in children. Calif Med 1967; 107; 26-32
- [23]. Bakhotmah A. Mohammed, Symptomatic cholelithiasis in children: A hospital based review. Saudi Journal of Gastroenterology, **1999**, 12, 3, 1-8.
- [24]. St Peter SD; Keckler SJ; Nair A; Andrews WS; et al. Laparoscopic cholecystectomy in the pediatric population. Laparoendosc Adv Surg Tech. **2008**; 18:127
- [25]. Oleg Kleiner, Jagannathan Ramesh, Mahmoud Huleihel, A Comparative study of gallstones from children and adults using FTIR spectroscopy and fluorescence microscopy BMS Gastroentol. **2002**; 2:3.

- [26]. Sayers C; Wyatt J; Soloway RD; Taylor DR; Stringer MD Gallbladder mucin production and calcium carbonate gallstones In children. *PediatrSurg Int.***2007**; 23:219-23
- [27]. Lugo-Vicente HL Trends in management of gallbladder disorders in children .*PediatrSurg Int.***1997**; 12(5-6):348-52.