Original Article

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Cholelithiasis in Childhood: A Cohort Study in North of Iran

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Abstract

Objective: Cholelithiasis rarely occurs in children but the increased use of ultrasonography has led to increased detection of gallstones in patients. The epidemiology and predisposing factors of cholelithiasis vary in different populations. The aim of this study was to describe the clinical presentation, predisposing factors and to evaluate management and outcome of patients referred to Amirkola Children's Hospital jn Babol.

Methods: This cohort study was performed on children with cholelithiasis referred during 2000 to 2011. Cholelithiasis was diagnosed with ultrasonography. The data was obtained based on history, physical exam, clinical and paraclinical investigations and analyzed by SPSS version 18. *P*-value <0.05 was considered being significant.

Findings: From the 66 patients with cholelithiasis, 39 (59.1%) were males. The mean age at diagnosis was 6.6±4.5 years. The most common predisposing factor included ceftriaxone therapy (27.3%), hemolytic diseases (13.6%), hepatobiliary diseases (7.5%) and cystic fibrosis (7.5%). In 30.3% of patients, no predisposing factor was detected. The most common complaint was abdominal pain (67%). Among the patients in whom abdominal X-Ray was performed, only 20% had radiopaque gallstones; 6 (9%) patients underwent cholecystectomy.

Conclusion: According to this study, ceftriaxone therapy and hemolytic diseases were the most common predisposing factors in children with cholelithiasis in our area and cholecystectomy had not been needed in most patients.

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Key Words: Cholelithiasis; Children; Gallstones; Cholecystectomy; Abdominal Pain

Introduction

Cholelithiasis is uncommon in childhood even though recent series show increased detection of this disease. In contrast to adults, the epidemiology of cholelithiasis in children is unknown, as most of the studies deal with a limited number of patients[1-3]. The frequency of pediatric gallstones documented in studies showed a prevalence of 0.2-1.9%[4,5].

The increased use of ultrasonography in diagnosis and monitoring of gastrointestinal and genito-urinary pathologies, has led to increased detection of asymptomatic gallbladder calculi[6-8].

The aim of this study was to review the clinical presentation, predisposing factor and outcome of gallstones in children through a cross-sectional study between 2000 to 2011 in a referral children's hospital in Babol, a northern city in Iran.

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Subjects and Methods

This cohort study was performed on children with cholelithiasis in Amirkola Children's Hospital from 2000 to 2011. Data on age at diagnosis, gender, clinical presentation, predisposing factors, ultrasonographic findings, gallstone density in abdominal X-ray, possible accompanying renal stone, were collected and management, follow up duration, and outcome recorded. We defined gallstones as echogenic foci in the gallbladder or bile ducts that produced posterior acoustic shadowing in ultrasonography. In some cases, abdominal X-ray was performed for determining opacity of gallstones when required. Related laboratory tests were done when needed.

Follow up was performed with ultrasonography focusing on persistence or resolving of gallstones. The data was analyzed by SPSS version 18 and a *P*-value <0.05 considered being significant.

Findings

Of all 66 patients 27 (40.9%) were females with the mean age at diagnosis 6.6±4.5 years (range 2 months to 17 years). There was no significant difference in the gender distribution (*P*=0.1). The most common predisposing factor for cholelithiasis was ceftriaxonee therapy (18 cases, 27.3%). Other risk factors are shown in Table 1.

Abdominal pain was the most common initial symptom (44 patients, 67%) that led to abdominal ultrasonography and detection of gallstones. Other symptoms or signs included vomiting in 23 (35%), fever in 11 (17%), diarrhea in 9 (14%), agitation in 4 (6%), hepatomegaly or splenomegaly in 4 (6%), jaundice in 3 (4.5%); 5 (7.5%) patients were asymptomatic and their gallstone was incidentally found in ultrasonography.

In 18 cases of ceftriaxone induced cholelithiasis, the stones dissolved within 1 month after cessation of therapy. Urolithiasis accompanying cholelithiasis was recorded in 3 cases (4.5%) 2 of whom had cystic fibrosis and 1 was obese. In all cases, ultrasonographic stone location was in gallbladder, simultaneous occurrence of stone in common bile duct (CBD) and cystic duct was seen in 2 and 1 patient respectively. In 19 (29%) patients the gallstones were solitary and in 47 (71%) multiple. Among 59 performed abdominal X-rays, 47(80%) had radiolucent gallstones. Most of patients underwent conservative treatment. Three patients who were asymptomatic and had

Table 1: Predisposing factors in children with gallstones

Predisposing factor		Frequency (%)
Pseudolithiasis (due to ceftriaxonee therapy)		18 (27.3)
Hemolytic diseases	**Major thalassemia**	4 (6.1)
	G6PD deficiency	3 (4.5)
	Fanconi anemia	1 (1.5)
	Eliptocytosis	1 (1.5)
Hepatobiliary disease	**Neonatal idiopathic hepatitis**	3 (4.5)
	Viral hepatitis	1 (1.5)
	Cryptogenic cirrhosis	1 (1.5)
Cystic fibrosis		5 (1.5)
Renal diseases	**Polycystic kidney disease**	1 (1.5)
	Nephrotic syndrome	1 (1.5)
	Neurogenic bladder	1 (1.5)
Endocrine diseases	**Congenital adrenal hyperplasia**	1 (1.5)
	Hyperlipidemia	1 (1.5)
Obesity		2 (3)
Metabolic disease		1 (1.5)
Down syndrome		1 (1.5)
Idiopathic gallstone		20 (30.3)
Total		66 (100)

radiolucent stones received Ursodeoxycholic acid (UDCA). Cholecystectomy was done in 6 patients (two cases of chronic abdominal pain, 1 case of cystic fibrosis, 1 case of major thalassemia and two cases of cholecystitis).

The duration of follow up ranged from 1 month 6 years with a mean of 12.5±17.8 months in all 42 patients with ultrasonographic follow up. Resolution of stones was documented in 21 (50%) patients (18 patients after discontinuation of ceftriaxone therapy, 3 patients after receiving UDCA), in the remaining 21 (50%) patients there was no significant changes in the ultrasonographic appearance of stones in the gallbladder.

Three patients with cholelithiasis died, one because of end stage renal disease due to polycystic kidney disease (PKD), one because of renal failure and hemorrhage complicating thrombocytopenia associated with Fanconi anemia, and the last one because of metabolic disease (mitochondrial type).

Discussion

This is the first report of childhood cholelithiasis in northern Iran. Previous studies about pediatric cholelithiasis in our country are limited[9,10].

This study reviews the experience with 66 children with gallstones during a 12 year period. It is not possible to determine the incidence of gallstones in childhood because the total number of patients who had abdominal ultrasonography in this period is not available.

In most studies, the mean age of diagnosis ranges from 5 to 10 years[1,3,7-11]. In our study the mean age of diagnosis was 6.6±4.5 years. Some previous studies have shown a female predominance[12,13,14], while some others found a gender ratio of equal to 1 particularly in children <12 years of age[5,7,8]. In the present series 59.1% of patients were males and 40.9% females, this difference is not statistically significant.

In our study, the most common (27.3%) predisposing factor was ceftriaxone whereas in a multicenter study in Italy, ceftriaxone was responsible for only 6% of cholelithiasis cases[5]. This can be related to the widespread use of ceftriaxone in treatment of pediatric infectious diseases in our area.

Hemolytic diseases were the second predisposing factor (13.6%), however, in most studies the hemolytic diseases were the main risk factor for inducing cholelithiasis[7,8,15,16,17]. Cystic fibrosis (CF) was responsible for 7.5% of patients with cholelithiasis in our research. In some previous studies, same as in ours, CF was the significant risk factor for gallstones in children[13,18] while in more recent studies, CF was not a common risk factor[11,12]. In some studies, and in our study, idiopathic gallstones were more common than other causes of cholelithiasis[5,19]. In a multicenter study in Italy, hemolytic diseases, obesity and family history were common predisposing factors for inducing cholelithiasis[5] whereas in our study obesity was responsible for only 3% of patients and family history has not been evaluated.

In our experience, abdominal pain was the most common (67%) complaint same as in other studies[7-9,16,19,20]. 7.5% of our patients were asymptomatic whereas in a multicenter study 35.3% of patients were asymptomatic[5] compared to 80% of asymptomatic adult patients[21,22].

We found stones located mostly in gallbladder as seen in ultrasonography, whereas 3% of the patients had stones simultaneously in the common bile duct (CBD) and 1.5% in cystic duct. In other studies, gallstones were the most common finding in ultrasonography[8] whereas 15.8% of patients had stones in the CBD[23,24].

In children, more radiopaque gallstones have been noted in comparison with adults. In a study, 47% of stones were radiopaque[19]. In our series, 12 (20%) patients had radiopaque stones. In another study, 20.4% of stones were radiopaque[5]. Abdominal X-ray does not appear to be an initial investigation method for diagnosing children's cholelithiasis. Guidelines for management of cholelithiasis are available for adults, but little is known about management of childhood cholelithiasis[19,23].

Cholecystectomy is recommended for symptomatizing patients[8]. For non-symptomatizing patients, conservative management with periodical clinical and ultrasound follow up is recommended[24].

In our study, 6 (9%) patients underwent cholecystectomy and 3 (4.5%) patients received UDCA that dissolved gallstones during follow up

without relapse. In a study, 7.2% of patients responded to UDCA initially but in 50% of them stone recurred and cholecystectomy was performed on 35% of patients[5]. In another study, most of the children underwent cholecystectomy (13 of 19 patients)[8]. In a study 3.1% of asymptomatic patients and 59% of symptomatic patients' necessitated cholecystectomy[7], but in our study, most of the patients, received conservative management because the most predisposing factor for inducing cholelithiasis was ceftriaxone therapy where resolving stones occurred after discontinuation of the drug.

In this study, urolithiasis accompanying cholelithiasis was reported in 3 patients. Two of them had cystic fibrosis (CF); so, in our area, CF must be considered when urolithiasis and cholelithiasis are accompanying. CF is not only a predisposing factor for gallstones, but also predisposes patients to urolithiasis[20].

Conclusion

In conclusion, ceftriaxone therapy, hemolytic diseases, hepatobiliary disease and CF were the most common predisposing factors of cholelithiasis, and in 30% of patients, no predisposing factor was detected. In our series, cholecystectomy was required in a few patients.

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Conflict of Interest: None

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