RESEARCH BRIEF

Etiology and Outcome of Cholelithiasis in Turkish Children

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ABSTRACT

Objective: The aim of this study was to examine the etiology of gallstones in children and responses to ursodeoxycholic acid (UDCA) treatment.

Methods: 74 children with cholelithiasis were recruited, and underwent ultrasonography to detect gallstones. All relevant clinical information was recorded in a structured proforma.

Results: The commonest risk factor was a family history of gallstones. Most children responded to UDCA treatment in the first six months; children with hemolytic diseases showed no response to UDCA.

Conclusion: UDCA treatment may be useful before surgery in asymptomatic patients of cholelithiasis without hemolytic diseases.

Keywords: *Cholecystectomy, Gallstone, Ursodeoxycholic acid.*

The reported incidence of gallstones and bile sludge in children is 1.9% and 1.46%, respectively [1]. In symptomatic patients, a cholecystectomy is performed. Ursodeoxycholic acid (UDCA) treatment dissolves gallstones in 19–37% of pediatric cases [2]. There is no consensus on the most appropriate medical or surgical treatment of pediatric gallstones.

This study investigated the demographic characteristics and symptoms of children with gallstones, underlying etiology, UDCA treatment response and cholecystectomy rates in two hospitals in Turkey.

METHODS

This was a retrospective study of children in whom gallstones were determined at an outpatient gastroenterology clinic between September 2009 and May 2016. Gallstones were detected by abdominal ultrasonography (USG) and separated into five groups according to the USG analysis: a

large single stone ≥1 cm, more than one gallstone, multiple millimetre-sized stones, bile sludge and microlithiasis (<3 mm) [3].

Data were collected on demographic characteristics, personal and family histories, underlying disease that might lead to stones, symptoms and laboratory findings. All the patients received UDCA treatment at a dose of 20 mg/kg per day at admission. The UDCA treatment was stopped in case of no treatment response after six months and in cases of failure to achieve complete dissolution by one year [4]. Treatment was continued in cases where gallstones were partially dissolved after six months [4]. A treatment response was considered complete dissolution of gallstones, as determined by USG. The patients underwent USG and laboratory examinations every three months. Ethical approval for the study was obtained from the ethics committee.

Chi square test, Student's *t* test and Mann–Whitney *U* tests were conducted for comparisons of variables using SPSS 19.0 using SPSS 19.0. Statistical significance was set at 0.05 in all tests.

RESULTS

These were 74 children (33 males, aged 2 mo-17 y) with mean (SD) age of 7.5 (4.3) y. Clinical findings on admission included abdominal pain (38, 51.4%), nausea (25, 33.8%), vomiting (21, 28.4%), lack of appetite (15, 20.3%), cholestasis (3, 4.1%), and acholic stool (1, 1.4%). Dehydration, acute pancreatitis and elevated transaminase levels were observed in 4 (5.4%), 2 (2.7%) and 10 (13.5%) cases, respectively. Asymptomatic gallstones were present in 29 (32.2%).

Risk factors and underlying diseases are shown in ***Table* I**. The mean (SD) follow-up duration was 17 (17.1) months, and duration of UDCA treatment was 9.7 (7.2) months (2–24 months). Gallstones disappeared within six months after treatment in 22 (29.7%) cases, and in 7 more by the end of 1.5 years. No change was observed in 45 (60.8%) cases. The average time to the resolution of gallstones was 4.9 (3.3) months. Adverse reactions (vomiting and abdominal pain) occurred in only one patient (1.4%).

A cholecystectomy was performed in 21 (28.4%) cases, mostly laparoscopically, except for patients with choledochal cysts. Thirteen of the patients were asymptomatic. Of these, eight patients had a >1 cm gallstone, and five had multiple stones. Details of response to treatment are shown ***Table* II**.

DISCUSSION

Hematological diseases are reported to be the most frequent risk factor for gallstones, with a reported incidence of 8.9–50% [5,6]. In this study, a cholecystectomy was performed in 21 (28.4%) cases, most of whom were asymptomatic and had gallstones larger than 1 cm. These findings are similar to that in the literature [7].

Some previous studies reported that UDCA had no effect on gallstones, whereas others reported that it had some effect [8]. Bogue, *et al*. [9] reported that an asymptomatic child could be treated safely without surgical interventions. Interestingly, in the present study, the gallstones were resolved in 20% of patients with larger stones (>1 cm). Although no stone analysis was conducted, these were most likely cholesterol stones, as these are the most common stones found in children without haematological diseases [10]. The lack of treatment response among the children with haemolytic diseases shows that black pigment stones are resistant to UDCA treatment.

There is no consensus on the indications for a cholecystectomy in asymptomatic paediatric patients [11]. A previous study reported longer operative times and post-operative stays, in addition to higher morbidity rates, among symptomatic patients who underwent a cholecystectomy than among asymptomatic patients [12]. Thus, as reported earlier, pediatric patients with gallstones who fail to respond to medical treatment should undergo a cholecystectomy, performed laparoscopically [13].

The present study has limitations common to retrospective studies. A controlled prospective study with larger numbers of patients is needed to provide additional evidence on the use of UDCA treatment for gallstones in children.

In conclusion, whether medical or surgical treatment should be recommended for gallstones remains a matter of debate, especially in pediatric patients. UDCA treatment was particularly effective in the first six months. Thus, UDCA can be recommended before surgery, especially in asymptomatic patients without haemolytic diseases.

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WHAT THIS STUDY ADDS?

- Most children with cholelithiasis experience a response to UDCA in the first six months, except those with hemolytic diseases.

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TABLE I UNDERLYING RISK FACTORS IN TURKISH CHILDREN WITH GALLSTONES (*N*=74)

#*Risk factors*	*n (%)*
*Blood diseases	6 (8.1)
Hemophilia	1 (1.4)
Spherocytosis	2 (2.7)
Prematurity	5 (6.8)
Familial hyperlipidemia	3 (4.1)
Ceftriaxone use	3 (4.1)
Total parenteral nutrition	13 (17.6)
Family history	11 (14.9)
Choledochal cyst	3 (4.1)
Oncological disease	4 (5.4)
Idiopathic	32 (43.2)

Thalessemia major and spleurocytosis – 2 each, 1 with haemophilia; 2 with obesity and 1 each with sepsis, trauma and cystic fibrosis.

TABLE II TREATMENT RESPONSE IN TURKISH CHILDREN WITH CHOLELITHIASIS (*N*=74)

	URSODEOXYCHOLIC	*ACID TREATMENT*		
Sizes of gallstones	*Received n (%)*	*mo duration mean (SD)*	*Responded n (%)*	*Underwent Cholecystectomy n (%)*
Larger than 1 cm	24 (32.4)	10.2 (7.9)	5 (20.8)	8 (33.3)
Multiple gallstones	5 (33.8)	11.7 (7.4)	7(28)	8 (32)
Multiple millimetre-sized gallstones	17 (23)	7.5 (4.7)	10 (58.8)	4 (23.5)
Bile sludge	5 (6.8)	3.6 (1.5)	5 (100)	None
Microlithiasis	3 (4.1)	11.6 (10.9)	2 (66.7)	1 (66.6)
Underlying disease				
Idiopathic	32 (43.2)	9.9 (6.9)	14 (43.8)	7 (21.9)
Haematological disease	6 (8.1)	7.4 (3.9)	1 (16.7)	1 (16.7)
Choledochal cyst	3 (4.1)	6 (5.1)	None	3 (100)
Drugs	4 (5.4)	10.7 (3.7)	2 (50)	2 (50)
Prematurity	5 (6.7)	14 (9.1)	None	2 (40)
Hypercholesterolemia	3 (4.1)	20 (6.9)	None	3 (100)
Total parenteral nutrition	13 (17.6)	10.5 (8.3)	3 (23.1)	5 (38.5)