

Gallbladder Disease in Children: A 20-year Single-center Experience

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Objective: Aim of this study was to examine the changes in incidence of pediatric cholecystectomies. **Methods:** Based on a review of hospital-records, children were divided into two groups regarding year of surgery (Group I: 1998-2007; Group II: 2008-2017) and their characteristics were compared. **Results:** Number of cholecystectomies increased from 11 to 34. Median age increased from 11 to 15.5 years and mean BMI increased from 19.2 kg/m² to 23.0 kg/m². Hereditary spherocytosis decreased from 63.6% to 11.8% ($P=0.001$) of indications for cholecystectomy, while proportion of cholesterol stones increased from 27.3% to 70.6% ($P=0.006$). Frequency of laparoscopic cholecystectomy increased from 36.4% to 85.3% ($P=0.001$). Duration of hospital stay shortened from 8 to 4 days ($P=0.008$). **Conclusions:** Number of pediatric cholecystectomies has significantly increased in the last 20 years, as well as average BMI of the observed population. This probably signifies a correlation between rising obesity rates and increase in frequency of symptomatic cholelithiasis in children.

Keywords: Association; Cholecystectomy; Hereditary spherocytosis; Obesity.

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In recent years, gallstone disease has been increasingly diagnosed in the pediatric population and the spectrum of pediatric biliary tract disease has been changing [1]. Until recently, the majority of pediatric gallstones were pigmented stones, related to hemolytic diseases such as hereditary spherocytosis [2,3]. In recent decades, the incidence of gallstone disease in children has risen, principally related to the epidemic of pediatric obesity [2,3]. Other than obesity, improved survival of critically ill neonates who have received long-term total parenteral nutrition or have underlying abnormalities resulting in short-gut syndrome is the new factor that may have led to an increased incidence of cholelithiasis in the pediatric population [3].

The objective of our study was to document the apparent increase in frequency of cholecystectomies in children, and to establish the epidemiological, demographic and clinical characteristics of children who underwent cholecystectomy.

METHODS

The case records of 45 children (12 males) who underwent cholecystectomy due to cholelithiasis from January 1998 to December 2017 at the Department of Pediatric Surgery, University Hospital of Split, were retrospectively reviewed. All patients with symptomatic cholelithiasis who underwent cholecystectomy younger than 18 years of

age were enrolled in the study. Preoperative MR cholangiography was performed in all of the patients. Intraoperative cholangiogram was performed only in patients with choledocholithiasis. The patients were divided into two groups (children who were operated on between 1998 and 2007 and children who underwent surgery between 2008 and 2017) and compared by demographic and anthropometric data, clinical findings, risk factors for the disease, indications for surgery, procedure type, treatment outcomes and complications. The patient data are summarized in **Table I**.

Statistical analysis: The data were analyzed using the Microsoft Excel for Windows Version 11.0 (Microsoft Corporation) and SPSS 19.0 (IBM Corp, Armonk, NY) software programs. Differences in median values of quantitative variables between the groups of patients were tested with Mann-Whitney U test. The Chi-square test was used for the statistical analysis of categorical data. All values of $P<0.05$ were considered to indicate statistical significance.

RESULTS

Out of 45 cholecystectomies, 11 (24.4%) were conducted in the first half of the study period (1998-2007) and 34 (75.6%) were conducted in the following 10 years (2008-2017), resulting in a 3.1-fold increase in the incidence of cholecystectomies ($P=0.002$). In both groups patients

TABLE I DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF CHILDREN UNDERGOING CHOLECYSTECTOMY, CROATIA.

Variable	1998-2007	2008-2017
<i>Baseline data</i>		
*Age, y	11 (10, 15)	15.5 (13, 16)
Male sex	2 (18.2)	10 (29.4)
#height, cm	144.7 (10.1)	169.5 (15.3)
#Weight	42.9 (16.8)	66.9 (18.7)
#BMI, kg/m ²	19.2 (3)	23.0 (5.1)
<18.5	1 (9.1)	8 (23.5)
18.5-25	8 (72.7)	11 (32.4)
25-30	2 (18.2)	10 (29.4)
>30	0	5 (14.7)
<i>Main indication for surgery</i>		
Biliary colic	4 (36.4)	17 (50.0)
Hereditary spherocytosis	7 (63.6)	4 (11.8)
Acute pancreatitis	0	7 (20.6)
Acute cholecystitis	0	4 (11.8)
Obstructive jaundice	0	2 (5.9)

All data in no. (%) except *median (IQR) and #mean (SD). All $P < 0.05$ for baseline data except sex difference. Indications for surgery all $P > 0.05$ except hereditary spherocytosis ($P < 0.001$).

were predominantly female (81.8% vs 70.6%). The median age was 11 (range 6-17) years in the period 1998-2007, with an increase to 15.5 (range 7-17) years in the period 2008-2017 ($P = 0.001$).

The median body weight of children in the first group was 42.9 (IQR 27.25, 54.75) kg, while it was 66.9 (IQR 55, 79) kg in the second group ($P = 0.004$). In the first group the body weight of only 3 (27.3%) children was above the 90th percentile, while there were 14 (41.2%) such children in the second group, with 6 (17.6%) children above the 97th percentile ($P = 0.02$). The median BMI of children in the first group was 19.2 kg/m², with no obese children. In the second group, the average BMI was 23.0 kg/m², with 5 (14.7%) obese children ($P = 0.012$).

The most common indication for cholecystectomy in the first 10-year period was hereditary spherocytosis (63.6%), while biliary colic (50.0%) was main indication in the second 10-year period, followed by acute pancreatitis (20.6%), thus moving hereditary spherocytosis to the third place (11.8%).

The results of spectrophotometric analysis of gallstones removed during the first observed period showed a significantly greater proportion of pigment stones (63.6%), whereas in the second observed period the majority of gallstones were cholesterol stones (70.6%) ($P = 0.006$) (Table II).

DISCUSSION

Cholelithiasis in children used to be a rarity, but we have found that that is no longer the case: in our study there was a three-fold increase in the number of children who underwent cholecystectomy in the last 10 years compared to the previous 10-year period, thus affirming our hypothesis. The age median of children in our study has increased, while female sex has consistently prevailed in both observed periods. The median BMI of the observed children has increased in the last two decades, providing a significant between-group difference, with an even more significant proportion of children falling into the obese category. Spectrophotometric analysis of gallstones found in observed children's gallbladders revealed that cholesterol stones, which have been a rarity in the first observed period, have increased to a vast majority in the more recent decade.

Retrospective character is the main limitation of this study, although we have implemented multiple plausibility checks and cross validations in our data collection tool. Also, there is a relatively small number of patients included in the study, so further studies are needed to analyze the same parameters on a larger sample.

The increase in the incidence of cholecystectomies in the pediatric population was already recorded in multiple

TABLE II MANAGEMENT AND OUTCOME IN CHILDREN UNDERGOING CHOLECYSTECTOMY IN CROATIA.

Variable	1998-2007	2008-2017
*Laparoscopic surgery, n(%)	4 (36.4)	29 (85.3)
<i>Procedures, n(%)</i>		
Intraoperative cholangiogram	2 (18.2)	3 (8.8)
<i>Complications, n(%)</i>		
Bile duct injury	0 (0)	1 (2.9)
<i>Hospitalization (median, IQR)</i>		
#Hospitalization, d	8 (2, 11)	4 (2, 5)
Laparoscopic procedure	4 (2, 5.5)	3 (2, 5)
Open procedure	12 (2, 13)	10 (6, 12)
<i>#Type of gallstone, n(%)</i>		
Pigment	7 (63.6)	5 (14.7)
Cholesterol	3 (27.3)	24 (70.6)
Mixed	1 (9.1)	5 (14.7)
<i>Histopathology report, n(%)</i>		
Normal	4 (36.4)	3 (8.8)
Acute cholecystitis	0 (0)	4 (11.8)
Chronic cholecystitis	7 (63.6)	27 (79.4)

* $P < 0.001$; # $P < 0.05$.

studies carried out in the last three decades [2,6,7]. A suggestion was found in literature that the reason for such a rise could lie in the increasing use of abdominal ultrasound, with a consequent increase in the ability to identify gallstones and establish a diagnosis of cholelithiasis [6,8]. Some authors speculated that the most likely cause for this condition lied in the increase of average BMI of children with gallstones based on its increase in the general pediatric population [2,5,9-10]. In an attempt to additionally correlate excessive body mass with the increased incidence of cholelithiasis, the composition of gallstones found in observed children's gallbladders was compared to other studies, in which pigment stones were found to represent a vast majority [11,12]. However, these studies were conducted in the years accordant to the first period of our study, thus yielding results consistent with our findings in the said period. The prevalence of hereditary spherocytosis, and consequently, its proportion among the indications for cholecystectomy, strongly depends on geography, which makes it inappropriate for comparison [2,4-5,7,10]. However, the trend of decrease in the share of hereditary spherocytosis among the indications for cholecystectomy is consistent with the findings in many other published studies [6,13-15]. Children who do not suffer from haemolysis, and therefore, most likely do not have pigment but cholesterol gallstones, have a significantly higher BMI [10]. This relates high BMI to cholesterol stones, showing that the average BMI of children who underwent cholecystectomy probably increased on account of children who do not have a haemolytic anaemia, which fits the changes of the share of hereditary spherocytosis among the indications for the procedure.

In conclusion, this study suggests an association between rising obesity rates in the pediatric population and the increase in frequency of symptomatic cholelithiasis in children. If this hypothesis is proven by larger epidemiological studies, it would provide an impetus to efforts to prevent this risk factor with lifestyle changes.

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