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ORIGINAL ARTICLE

Adolescent gallstones—need for early intervention in symptomatic idiopathic gallstones

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Abstract

Background and aim Currently, there is a paucity of the literature describing the natural history of cholelithiasis (CL) and choledocholithiasis (CDL) in adolescent children. This study aims to analyse the changing demographics of paediatric and adolescent gallstones.

Methodology Retrospective review of all children (Age 0–18 years) presenting with symptomatic gallstones over the last 15 years (2002–2017) at a single tertiary institution. Demographics, diagnostic and therapeutic information were collected, with a 5-year median follow-up. Statistics were accomplished by Chi-squared analysis of trend and Student *t* test.

Results and discussions 188 children were seen with symptomatic CL. In the 0–11-year-old group, there were 13 females and 16 males (0.8: female to male ratio). There were 130 females and 29 males in the 12–18-year-old group (4.5:1 female to male ratio). The mean weight at presentation was 81.78 kg and the median age was 16 years. Idiopathic gallstones were found in 131 patients (82%). 137 required cholecystectomy (86%) and ERCP was required in 32 patients (20%). 48 adolescents (30.2%) with gallstones had an associated CDL, compared to six children (20%). All of the adolescent patients with CDL had idiopathic gallstones. Gallstone pancreatitis was noted in eighteen adolescents (11%) and one child (3%). We analysed the ideal time to operate on adolescent patients with symptomatic gallstones using the relationship between the length of delay from initial diagnosis to definitive management of CDL and incidence of complications. The analysis demonstrated that for every 10 days treatment was delayed, the risk of subsequent presentations with a symptomatic episode was increased by 5% ($p = 0.0004$).

Conclusion The current trend of gallstones in adolescent children seems to be a disease primarily of adolescent girls. Symptomatic idiopathic gallstones in adolescents are associated with high rates of common bile duct obstruction and pancreatitis and consequently warrant an early cholecystectomy for all adolescents.

Level of Evidence Level IV Treatment Study.

Keywords Gallstones · Adolescent · Complications · Children

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Introduction

The spectrum of gallstone disease in children and adolescents has changed over the last two decades, with numerous studies reporting both a greater prevalence and increased complications [1–3]. The reported prevalence of cholelithiasis (CL) has increased with current estimates ranging from 1.9 to 4.0% [4–8]. Complications of gallstones such as choledocholithiasis (CDL) and pancreatitis are considered uncommon in children. Conservative management of asymptomatic gallstones in children has thus been considered standard care [8].

There is scarce published data available on the current spectrum of gallstone disease in adolescents [3]. In the adult

population, there is a well-recognised link between obesity and gallstone formation and this trend is being increasingly recognised in adolescents [7]. The prevalence of obesity has increased by two times in children and tripled in adolescents in the past 30 years, with the percentage of obese adolescents (12–19 years) increasing from 5 to 18% [9–11]. Increasing rates of idiopathic gallstones have recently been reported in adolescent girls, with complication rates resembling those seen in adults [2, 5].

This single center retrospective study aims to analyse the changing demographics of symptomatic paediatric and adolescent CL and associations with obesity and gender. Further, we sought to describe rates of complications such as CDL and review optimal timing of surgery.

Method

All children aged 0–18 years presenting with symptomatic gallstones over the last 15 years (Jan 2002–Dec 2017) at a single tertiary institution were identified. The medical records of these children were reviewed retrospectively through our hospital information system. Our institution uniquely manages all children and adolescents in the same hospital; surgery in children over 16 years of age is performed by adult surgeons. Approval for this study was obtained from the local institutional review board.

Children were defined as aged 11 years or less; adolescents aged 12–18 years, to compare changing demographic measures such as sex and weight to previous studies [1]. We hypothesised that obese, adolescent children have higher rates of complications related to gallstones. The adolescent and the paediatric groups were further analysed in 5-yearly intervals.

CDL was defined as the presence of gallstones in the common bile duct; this was identified using abdominal ultrasound (US), magnetic resonance cholangiopancreatography (MRCP), intraoperative cholangiogram or endoscopic retrograde cholangiopancreatography (ERCP). All patients were worked up for any underlying haemolytic disorders, or other abnormalities.

Demographic information such as age at presentation, sex and weight was recorded. The patient's medical history was also reviewed to identify any haematological conditions or intestinal problems. Diagnostic and therapeutic information such as laboratory and radiological investigations, intraoperative factors (type of procedure and use of intraoperative cholangiogram), post-operative complications and histopathological data were also collected. The first episode of uncomplicated biliary colic was an indication for elective cholecystectomy and urgent cholecystectomy/ERCP was offered only in complicated biliary obstruction. Follow-up was performed in all patients to the endpoint of data collection.

Statistical analysis compared patient groups using Chi-square test for categorical variables and Fisher's exact test where value for cell frequencies was <5, using Stata 15.1 (StataCorp, College Station, TX, USA). Continuous, normally distributed variables were compared using Student *t* test.

Results

188 children were seen at our institution with symptomatic CL during the 15-year study period, with a median follow-up time of 5 years. (Table 1).

There were 29 children aged 11 years or less and 159 adolescents aged 12–18 years.

Demographics (Figs. 1, 2)

143 females and 45 males (3.18: 1 ratio) presented with symptomatic gallstones. Out of these, there were 13 females and 16 males in the group of 0–11 years (ratio of 0.8 females to 1 male). In the group of 0–11 years, there was a failure to reject the null hypothesis that there is no difference in incidence of gallstone disease between males and females ($p=0.29$). In the group of 12–18 years, there were 130 females and 29 males (ratio of 4.5 females to 1 male) with a statistically significant result ($p<0.001$).

Children with gallstones (age less than 11 years)

There were 29 children diagnosed with symptomatic CL, with a median age of 8 years at presentation. The female to male ratio was 0.8 to 1. There were 24 children with idiopathic gallstones, four with haemolytic conditions (three with hereditary spherocytosis and one with pyruvate kinase deficiency).

18 of the twenty-nine children (62%) underwent cholecystectomy and 11 were managed non-operatively. CDL was noted in 6 children (21%) and pancreatitis was noted in one.

Adolescents with gallstones (age 12–18 years)

159 adolescents with CL were identified during the study period. This included 29 males and 130 females, with a male to female ratio of 1 to 4.5. The mean weight at presentation was 81.78 kg and the median age at presentation was 16 years. The median male weight was 85.0 kg (IQR 75.0–97.6), compared to 75.0 kg (IQR 60.0–100.0) in females. Idiopathic CL was found in 131 patients (82%); the following conditions were diagnosed in the remaining 25 patients: hereditary spherocytosis ($n=8$), haemolytic

Table 1 Demographics, aetiology and management of children and adolescents with gallstone disease

Characteristic	Children 0–11 years ($n=29$)	Adolescents 12–18 years ($n=159$)	Total ($n=188$)	p value
Demographic characteristics				
Male	16 (55.2%)	29 (18.2%)	45 (23.9%)	< 0.0001
Female	13 (44.8%)	130 (81.8%)	143 (76.1%)	
Ratio (female : male)	0.81:1	4.48:1	3.18:1	
Median male weight in kg (IQR)	22.8 (12.8–38.9)	85.0 (75.0–97.6)	75.0 (33.0–87.0)	
Median female weight in kg (IQR)	25.0 (9.1–32.0)	75.0 (60.0–100.0)	72.0 (51.5–93.2)	
Aetiology				
Idiopathic	24 (82.8%)	131 (82.4%)	166 (88.3%)	0.961
Haematological	4 (13.8%)	9 (5.7%)	13 (6.9%)	0.120
Other	0	1 (0.6%)	1 (0.5%)	
Complications				
Choledocholithiasis (CDL)	6 (20.7%)	48 (30.2%)	51 (27.1%)	0.299
Pancreatitis	1 (3.5%)	18 (11.3%)	19 (10.1%)	0.319
Management				
Operative				
laparoscopic cholecystectomy	18 (62%)	137 (86%)	155 (82%)	0.002
Intraoperative cholangiogram (IOC)	14 (78%)	119 (87%)	147 (95%)	0.004
Non-operative	11 (38%)	22 (14%)	33 (18%)	0.002
ERCP	1 (3%)	32 (20%)	33 (18%)	0.032
MRCP	6 (21%)	6 (4%)	12 (6%)	0.001

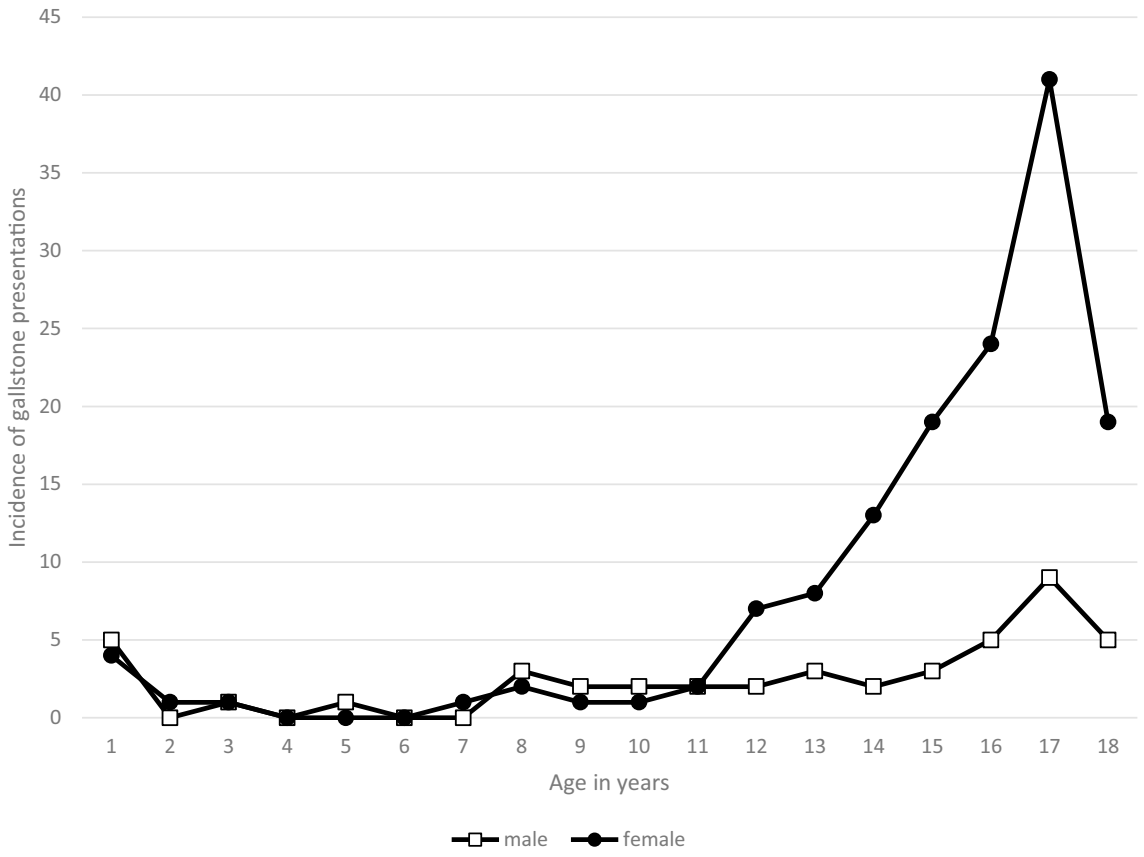

Fig. 1 Age distribution of gallstone presentations between genders

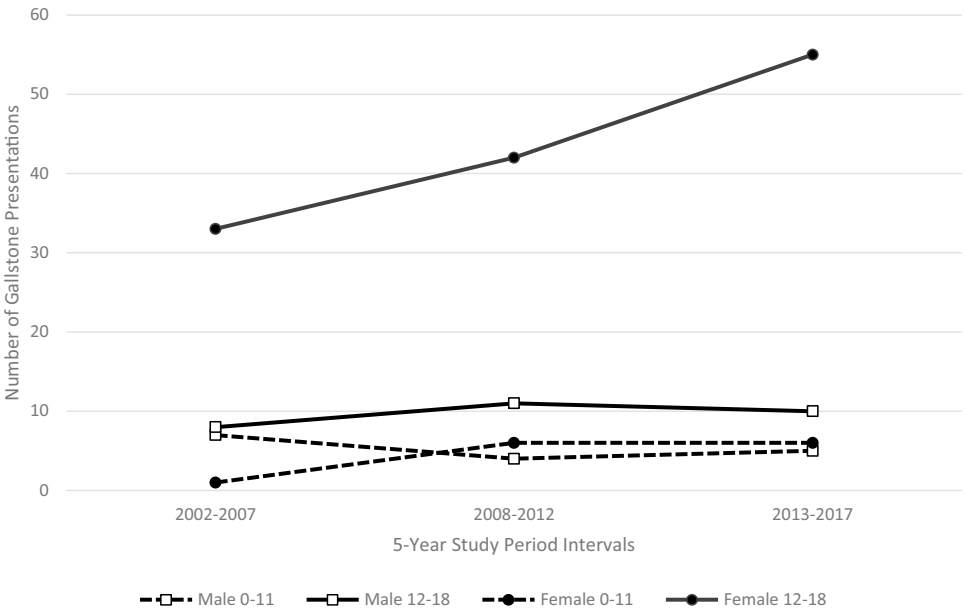

Fig. 2 Distribution of gallstone disease between male and female children and adolescents

anaemia (1), choledodochal cyst ($n=1$), pancreatitis (17). 137 required cholecystectomy (86%) and 22 had either been managed conservatively or not received an operation by the endpoint of data collection (14%). Median time from first diagnosis to cholecystectomy was 2 days (IQR 0–37). ERCP was required in 32 patients (20%). Of those who had a cholecystectomy, 87% (119) also had an intraoperative cholangiogram.

When plotted on the growth chart, 48% of adolescent females and 38% of adolescent males were above 90th centile for the age. 30% of the adolescent females were above the 97th centile.

Choledocholithiasis (CDL)

48 adolescents (30.2%) with gallstones had an associated CDL. This compared to six children (20%) who had an associated CDL. All the adolescent patients with CDL had idiopathic CL.

Pancreatitis

Pancreatitis attributed to gallstones was noted in eighteen adolescents (11%) and one child (3%). There were three cases of ERCP-induced pancreatitis. All cases were idiopathic, with the exception of one adolescent male with hereditary spherocytosis.

12 of these were adolescent females, with a median weight of 96.5 kg (IQR 64–119). 6 were adolescent males, with a median weight of 76.2 kg (IQR 53.3–85). In the group of less than 11 years, there was one 7-year-old female with a weight of 32 kg.

Delay in surgery

We analysed the ideal time to operate on adolescent patients with symptomatic gallstones using the relationship between the length of delay from initial diagnosis to definitive management of CDL and incidence of complications. A statistically significant result ($p<0.001$) was found, even with the relatively low ($n=27$) number of patients evaluated. The analysis demonstrated that for every 10 days treatment was delayed, the risk of subsequent presentations with a symptomatic episode was increased by 5%. Extrapolating from this, with an average delay of 53 days, patients are subjected to a 26.5% risk of re-presenting to emergency, potentially with serious complications.

Discussion

The natural history of gallstone disease in adults is well known but there are currently no studies describing the natural history of cholelithiasis and choledocholithiasis in adolescent children. This article reviews the experience of 188 adolescent children over a 15-year period at our institution. Our experience is unique in that all children and adults are treated in the same hospital, allowing a wide capture of the current spectrum of paediatric and adolescent gallstones. The results from our study clearly indicate that paediatric gallstones most commonly occur in the adolescent female age group, concurring with similar studies [2, 7]. In comparison with historical series where haemolytic disease was the most common cause of paediatric gallstones, or results concur with recent studies showing that idiopathic gallstones are the most common cause of CL in children [1–3, 7].

Idiopathic gallstones seem to cause more complications than previously reported [12]; this is especially true in adolescent girls. The results from our study show that CDL occurs in 30% of adolescent children with idiopathic stones and pancreatitis occurs in 11%. This is much higher than the reported complication rate of symptomatic gallstones in adults, with an estimated incidence of CDL in 10–15% [13]. Recently, Herzog et al. demonstrated a similar phenomenon with complications occurring in 28/48 (58%) of their adolescent patients with idiopathic gallstones [2]. This implies that adolescent females with gallstones require early cholecystectomy and operative cholangiogram.

There is a clearly shifting demographic of adolescent gallstones illustrated by a sharply increasing prevalence of gallstone disease in post-pubertal females (Fig. 2). The reported increase of symptomatic gallstones seen in the adolescent population in this series has been reflected in other recent series [2]. The possible reasons for this increased incidence of gallstones in adolescent females are likely multifactorial: endogenous oestrogen, use of oral contraceptive medication and increased rates of obesity. Recent data suggest that these risk factors are increasingly reported [14–17]. Choledocholithiasis has been the most common complication of gallstones in adolescent children in this series, whereas some studies have reported pancreatitis as the most common [18, 19]. Biliary cholesterol saturation occurring secondary to hormonal changes during puberty [20, 21] may also contribute to the higher incidence of CDL in the current and other studies.

Our results indicated a clear trend towards obesity in the female adolescent cohort but lacked accurate BMI data as height is not uniformly recorded. This may be an explanation as to why these data are lacking in many retrospective studies. The relationship between obesity and gallbladder disease is well recognised and with the current obesity epidemic in adolescents, the obesity-related comorbidities are increasingly reported in the paediatric literature [14, 15, 21–25]. The pathogenesis of CL in obesity is multifactorial: hypersecretion of cholesterol and its subsequent precipitation in to bile along with gallbladder dysmotility appear to be the main causes suggested by the current literature [26–28]. Gallbladder hypomobility has been well reported during puberty [7]. The combination of these factors may contribute to the high incidence of CDL seen in this and other series [2].

We speculate that delay in surgery from the time of first presentation to definitive surgery may have increased the complications of gall stones in our adolescent population. A definitive answer will need randomised prospective study. We suggest that paediatric surgeons should consider early laparoscopic surgery in adolescent patients with gallstones rather than opt for a delayed definitive therapy.

The major strength of our study is incorporation of the entire paediatric-age spectrum of symptomatic gallstones, from infancy through to adult age, at the same center. The limitations of the present study include its retrospective design and lack of a standardised protocol as both adult surgeons and paediatric surgeons have been caring for adolescent children. Height data were not available for many patients, limiting interpretation of the weight data. A standardised approach would be ideal as it would allow consistent and appropriate therapy to be given to all patients. A multi-institutional prospective study should be undertaken to predict the natural course of this disease in adolescent children and further understand the role of obesity.

In conclusion, the current trend in gallstones in adolescent children seems to be a disease of primarily adolescent girls. Symptomatic idiopathic gallstones in adolescents are associated with a high rate of common bile duct obstruction and pancreatitis and consequently warrant an early cholecystectomy for all adolescents.

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