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ORIGINAL ARTICLE

Risk factors, Complications and Outcome of Pediatric Gall Bladder Stones in Aswan University Hospital

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ABSTRACT

Keyword: Gall Bladder Stones, cholecystectomy, choledocholithiasis

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Background: Pediatric gallstones have been increasingly diagnosed in the recent years, mainly due to widespread use of ultrasonography but still considered to be uncommon with prevalence between 0.13 and 1.9%. **Purpose**: study the possible etiology, presentation, complications and outcome of gallstone disease among children in Aswan governorate. **Methods:** This observational longitudinal study was performed on 24 cases diagnosed with gallstone below the age of 18 years old, from October 2022 to November 2023. **Results:** The mean age was 8.08 years with a female predominance (58.3%). Most cases were symptomatic (70.8%) with Fatty Food intolerance was (45.8 %). The most common risk factors were history of neonatal intensive care unit (NICU) admission (29.2%) and family history of gallstones (29.2%). Only one case (4.3%) developed complications (choledocholithiasis). Surgery (cholecystectomy) was needed in (70.8%) while (29.2%) of cases received medical management. (79.2%) of cases achieved complete improvement. **Conclusions:** Most cases were symptomatic at diagnosis. Important risk factors were history of neonatal intensive care unit (NICU) admission and family history. Complication rates were low. Cholecystectomy was needed in most of cases with excellent outcomes. Our findings went with that cholecystectomy remains the standard of care for symptomatic gallstones in children.

INTRODUCTION

The gallbladder is a small hollow organ about the size and shape of a pear. It is a component of the extra hepatic biliary system where bile is stored, concentrated and released into the duodenum during digestion. Bile is a fluid that is produced in the liver and is essential for the digestion of fats, the excretion of cholesterol and the presence of antimicrobial properties. Dysfunction in the physiology of the gallbladder and imbalances in the constituents of bile and biliary sludge secondary to gallbladder hypo kinesis can lead to the precipitation of gall stones (1). Bile consists of 5% organic and inorganic solutes involving cholesterol, amino acids, bile salts, bilirubin phospholipid, steroids, enzymes, porphyrins, vitamins, and heavy metals and ~95% water (2). There are 4 categories of gallstone according to gross appearance: whitish-yellow (cholesterol) gallstones, black pigment (calcium bilirubinate) gallstones, brown gallstones, and mixed gallstones that contain both cholesterol and calcium bilirubinate (3).

Gallstones have been progressively diagnosed recently, because of wide spread ultrasonography (US) use but considered to be uncommon in children. The gallstone disease prevalence among children is between 0.13 and 1.9% (4).

Risk factors for gallstone disease such as hemolytic disorders as (thalassemia major 20.3%, G6PD deficiency 14.3%, Hereditary Spherocytosis 5.7%), familial predisposition, obesity & hyperlipidemia 11.4%, cystic fibrosis 2.9%, total parenteral nutrition, hepatobiliary chronic disease, ceftriaxone usage 14.3%, neonatal intensive care unit (NICU) admission &neonatal sepsis 5.7%, abdominal surgery and idiopathic 28.6% (4,5,6).

This study is being conducted for the first time in Aswan aiming to study pediatric gallstone risk factors, composition, outcome and complications.

We aimed to study the possible etiology, presentation, complications and outcome of gallstone disease among children in Aswan governorate.

PATIENTS AND METHODS

This observational longitudinal study was carried out on 24 cases diagnosed – by ultrasonography -with gallstone below the age of 18 years old, from October 2022 to November 2023.

The study was done after approval from the Ethical Committee Aswan University Hospitals. An informed written consent was acquired from the legal guardians of the patients.

Exclusion criteria were all patients diagnosed with gallstone above the age of 18 years.

The following data was taken from all patients included: Medical history including age, sex, BMI, presentation (nausea, vomiting or fatty food intolerance, typical biliary colic, non-specific abdominal pain, and symptoms of complications as fever or jaundice due to cholecystitis, pancreatitis or choledocholithiasis), history of hemolytic disease, history of neonatal intensive care unit admission or prematurity, past medical history for prolonged use of Ceftriaxone and family history for gallstone.

Clinical examination (general and abdominal) including: Jaundice, pallor, fever, itching marks, abdominal tenderness, Murphy sign or organomegaly.

Laboratory investigations including: (1) Basic lab tests: to all patients as CBC, reticulocytic count, Bilirubin, ALT, AST. (2) others related to etiology: as Hb electrophoresis, G6PD assay, osmotic fragility test, Coomb's test, lipid profile or sweat chloride test (if cystic fibrosis is suspected), as needed. (3) Labs to detect complications: as amylase, lipase if pancreatitis is suspected.

Abdominal Ultrasonography.

Symptomatic case is defined as the presence of biliary colic in the form of significant abdominal pain and other above-mentioned symptoms in the absence of complications identified (such as ascending cholangitis, common bile duct stones, acute or chronic cholecystitis, or pancreatitis). Data regarding the outcome of treatment modality given to the patient whether; laparoscopic cholecystectomy (surgical) or medical management (conservative management or chemical dissolution using ursodeoxycholic acid (UDCA)) was obtained and compared to each other.

Outcome (clinical, lab, ultrasound and surgical) was documented as complete improvement, partial improvement or non-response.

Statistical analysis

SPSS v20 (Armonk, NY: IBM Corp) was employed to conduct the statistical analysis. The quantitative data was expressed as median, range, mean and standard deviation (Mean ± SD). The Student t-test (t) for normally distributed data and the Mann-Whitney test (U) for comparison of nonparametric quantitative variables. Frequency and percentage (%) were employed to represent qualitative variables. The normality of the distribution was confirmed using the Kolmogorov-Smirnov test. A two-tailed P value of < 0.05 was regarded as statistically significant.

RESULTS

39 patients with gallstone were admitted to Aswan University Hospital 15 of them were excluded (9 cases didn't meet our inclusion criteria and 6 cases, their legal guardians declined to participate), so we were left with 24 cases involved in the study **(Figure 1).**

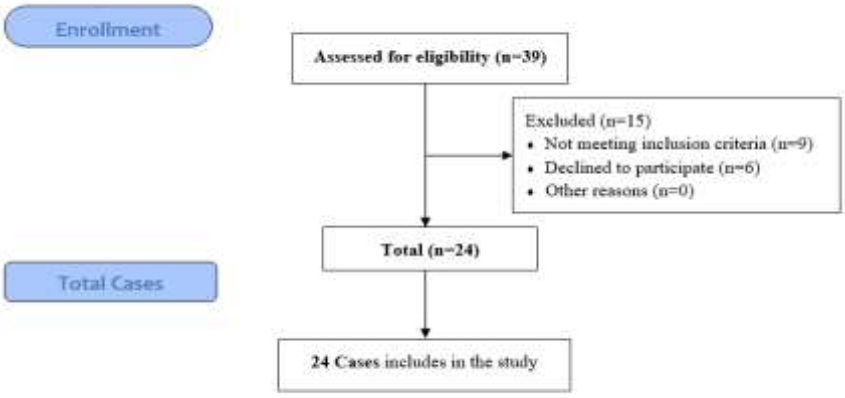

Figure 1: CONSORT flowchart.

The mean age was 8.08 (±4.05 SD) with range (1-15), among the studied cases there were 14 (58.3%) females and 10 (41.7%) males, and the mean BMI of the studied cases was 18.43 (±3.92 SD) with range (14.5-29.5) kg/m^2 as shown in **Table (1)**

Table (1): Distribution of the studied cases according to demographic data.

		Subjects (n = 24)	
Age	Range	1.0 – 15.0	
	Mean ± SD	8.08 ± 4.05	
		No.	%
Sex	Female	14	58.3
	Male	10	41.7
BMI	Range	14.5 – 29.5	
	Mean ± SD	18.43 ± 3.92	

Data are presented as frequency (%) unless otherwise mentioned, SD: standard deviation

Among the studied cases, there were 11 cases (45.8%) presented with fatty food intolerance, 10 cases (41.7%) with non-specific abdominal pain, 9 cases (37.5%) with vomiting, 7 cases (29.2%) asymptomatic cases, 6 cases (25%) with typical Biliary colic and 3 cases (12.5%) with jaundice as shown in **Table (2).**

Among the studied cases, the most common encountered risk factors were history of neonatal intensive care unit (NICU) admission (7 cases, 29.2%) and family history of gallstones (7 cases, 29.2%), followed by 4 cases (16.7%) with hyperlipidemia, 4 cases (16.7%) with history of ceftriaxone use, 3 cases (12.5%) with obesity, 2 cases (8.3%) with hemolytic disorder.

Among the studied cases there was one case (4.2%) experienced complications with choledocholithiasis.

Among the studied cases there were 15 (62.5%) with right hypochondrial tenderness, 7 (29.2%) with murphy sign 3 (12.5%) with jaundice, 2 (8.3%) with pallor, 2 (8.3%) with organomegaly, 1 (4.2%) with itching markers and 1 (4.2%) with fever. As showed in **Table (2)**.

Table (2): Distribution according to history data, risk factors, complications, and examination data.

		Subjects (n = 24)	
		No.	%
Asymptomatic		7	29.2
Symptomatic		17	70.8
Typical Biliary colic		6	25.0
Non-Specific Abdominal pain		10	41.7
Vomiting		9	37.5
Jaundice		3	12.5
Fatty Food intolerance		11	45.8
Examination	Tenderness	15	62.5
	Jaundice	3	12.5
	Pallor	2	8.3
	Itching markers	1	4.2
	Fever	1	4.2
	Organomegaly	2	8.3
	Murphy sign	7	29.2
Hyperlipidemia		4	16.7
Hemolytic disorder		2	8.3
Obesity		3	12.5
Total parenteral nutrition (TPN)		0	0.0
Ceftriaxone usage		4	16.7
Neonatal intensive care unit (NICU)		7	29.2
Abdominal surgery		0	0.0
Hepatobiliary chronic disease		0	0.0
Cystic Fibrosis		0	0.0
Family history of gallstones		7	29.2
Complications	Cholangitis	0	0.0
	Choledocholithiasis	1	4.2
	Pancreatitis	0	0.0

Data are presented as frequency (%) unless otherwise mentioned

Table (3): Distribution of the studied cases according to labs.

		Subjects (n = 24)
Hb (mg/dl)	Range	8.5 – 15.3
	Mean ± SD	12.33 ± 1.57
Retic (%)	Range	0.3 – 3.6
	Median (IQR)	0.7 (0.5 – 1)
ALT (IU/L)	Range	11 – 154
	Median (IQR)	19.5 (15 – 30.5)

AST (IU/L)	Range	13 – 178
	Median (IQR)	24.5 (16.75 – 30.5)
T. Bil (mg/dl)	Range	0.1 – 5
	Median (IQR)	0.7 (0.38 – 1)
D. bil (mg/dl)	Range	0.06 – 4.2
	Median (IQR)	0.3 (0.2 – 0.53)
Cholesterol (mg/dl)	Range	136 – 245
	Mean ± SD	175.08 ± 27.44
Triglyceride (mg/dl)	Range	89 – 210
	Mean ± SD	127.79 ± 30.59

Data are presented as Mean ± SD, SD: standard deviation

Among the studied cases, there were 7 cases (29.2%) with medical management; 4 cases (16.7%) had conservative management and 3 cases (12.5%) received UDCA.

On the other side, 17 cases (70.8%) had surgical management; 8 cases (33.3%) underwent lap cholecystectomy as first choice management, 3 cases (12.5%) underwent conservative follow-up then lap cholecystectomy, 5 cases (20.8%) received UDCA and lap cholecystectomy and only one case (4.2%) had ERCP and lap cholecystectomy. **Table (4)**

Among the studied cases there were 19 (79.2%) with complete improvement, 3 (13.2%) with partial improvement and 2 (8.3%) with no response. **Table (4)**

Table (4): Distribution of the studied cases according to management, outcome.

Management		**Subjects (n = 24)**	
		No.	%
Medical	Conservative	4	16.7
	UDCA	3	12.5
Surgical	Lap Cho	8	33.3
	conserve + Lap	3	12.5
	UDCA + Lap	5	20.8
	ERCP + Lap	1	4.2
Outcome	Complete improvement	19	79.2
	Partial improvement	3	13.2
	No response	2	8.3

Data are presented as frequency (%) unless otherwise mentioned

There was a statistically significant relation between vomiting, fatty food intolerance, and murphy sign and the need for surgical management, while there was a statistically significant relation between organomegaly and medical management. **Table (5)**

Table(5): Relation between management and history data, risk factors, complications and examinations.

	Management				**χ^2**	**p**
	Medical (n = 7)		**Surgical (n = 17)**			
History data	No.	%	No.	%		
Typical Biliary colic	0	0.0	6	35.3	3.294	0.070

Non-Specific Abdominal pain	1	14.3	9	52.9	3.048	0.081
Vomiting	0	0.0	9	52.9	5.929	0.015*
Jaundice	1	14.3	2	11.8	0.029	0.865
Fatty Food intolerance	1	14.3	10	58.8	3.962	0.047*
Risk factors						
Hyperlipidemia	1	14.3	3	17.6	0.040	0.841
Hemolytic disorder	1	14.3	1	5.9	0.458	0.498
Obesity	0	0.0	3	17.6	1.412	0.235
TPN	0	0.0	0	0.0	0.0	1.0
Ceftriaxone usage	2	28.6	2	11.8	1.008	0.315
NICU	3	42.9	4	23.5	0.897	0.344
Abdominal surgery	0	0.0	0	0.0	0.0	1.0
Hepatobiliary chronic disease	0	0.0	0	0.0	0.0	1.0
Cystic Fibrosis	0	0.0	0	0.0	0.0	1.0
Family history of gallstones	1	14.3	6	35.3	1.059	0.303
Complications						
Cholangitis	0	0.0	0	0.0	0.0	1.0
Choledocothilasis	0	0.0	1	5.9	0.430	0.512
Pancreatitis	0	0.0	0	0.0	0.0	1.0
Examinations						
Tenderness	3	42.9	12	70.6	1.627	0.202
Jaundice	1	14.3	2	11.8	0.029	0.865
Pallor	1	14.3	1	5.9	0.458	0.498
Itching markers	0	0.0	1	5.9	0.430	0.512
Fever	0	0.0	1	5.9	0.430	0.512
Organomegaly	2	28.6	0	0.0	5.299	0.021*
Murphy sign	0	0.0	7	41.2	4.069	0.044*

Data are presented as frequency (%) unless otherwise mentioned

There was statistically significant relation between hypercholesterolemia and the need for surgical management (P= 0.040).

There was high statistically significant relation between management with outcome as 100% of cases who underwent surgical management showed complete improvement while only 28.6% of cases with medical management achieved complete improvement. **Table (6)**

Table (6): Relation between management and outcome.

	Management				**χ^2**	**p**
	Medical (n = 7)		**Surgical (n = 17)**			
Outcome						
Complete improvement	2	28.6	17	100.0	15.338	<0.001*
Partial improvement	3	42.9	0	0.0		
No response	2	28.6	0	0.0		

Data are presented as frequency (%) unless otherwise mentioned

A significant relation was found between hypercholesterolemia and the clinical symptoms presence (p=0.028).

DISCUSSION

Gallstones are uncommon in the pediatric population, with an estimated overall prevalence of 0.13 to 1.9%. Nevertheless, the prevalence of gallstones has increased as a result of the heightened utilization of abdominal US recently (4).

In this research, the mean age of presentation was 8.08 years with a female predominance of 58.3% which agrees with the known higher incidence of gallbladder stones in females after puberty likely related to hormonal effects (7).

This also agrees with Zhang et al. who reported that, the gallbladder stones prevalence was higher among females than males (8).

In accordance, Todesco et al. reported an obvious prevalence in females (76.5%), with a median age of 14.1 years and a median BMI of 29 (9).

In the current study, most of the patients were symptomatic at presentation (70.8%) which matches the rate reported in other studies such as Enayet et al. (62.9%).

The most common symptoms were fatty food intolerance (45.8%), non-specific abdominal pain (41.7%) and vomiting (37.5%). While they reported that abdominal pain to be the most common symptom in 51.4%. Classical biliary colic tends to be less common as was seen in our study (25%) (4).

In contrary, Bhaumik, demonstrated that about 57.3% of their children with gallstones were asymptomatic (10).

In the present study, variable risk factors were associated with gall stone; the most common associations were history of NICU admission (29.2%) and family history of gallstones (29.2%) followed by 4 (16.7%) with hyperlipidemia, 4 (16.7%) with history of ceftriaxone use, 3 (12.5%) with obesity, 2 (8.3%) with hemolytic disorder.

Enayet et al. reported that many risk factors association hemolytic anemia was detected as a risk factor in 34.3%. Therapy with ceftriaxone was detected as a risk factor in 17.1% of cases. Chronic biliary disease in the cholestasis form was present in 8.6% of their cases. No risk factors were detected in 28.6% of cases (4).

Obesity has been detected to be a frequent risk factor in older children which agree with our study (11). Moreover, this agreed with literature where ceftriaxone usage was responsible for 6% and 27.3% of gallstones cases (12).

Weng et al. reported several key risk factors associated with infantile gallbladder stones, including total parenteral nutrition (TPN) usage in 47%, diuretics in 49%, cephalosporins in 45%, cardiac surgery in 32%, and short bowel syndrome. In contrast, classically important risk factors like obesity and metabolic syndrome were strikingly uncommon in this cohort, seen in <1%, likely owing to the very young age. This extremely low rate could also possibly indicate under diagnosis of obesity in pediatric populations (13).

Todesco et al. reported that, none of their patients fell into these cases, although two girls were influenced by Rett Syndrome (9).

In the current study, family history of gallstones in 29.2% of cases, indicating a possible genetic contribution. Only one case (4.2%) had CBD stones while most did not have complications which agree with Sarrami et al. (5.6% choledocholithiais) (14).

Enayet et al. reported that, complications were documented in 20% of their cases, they detected choledocholithiasis to be more common; for the meantime, none of their cases reported acute cholecystitis or pancreatitis (4).

Choledocholithiasis was the most prevalent, followed by acute cholecystitis, according to Mora-Guzmán et al. The complication rate in infancy was low, at 9% (5 of 58), with equal rates of acute cholecystitis and bile duct obstruction from choledocholithiasis (15).

Weng et al. reported that, the complication rate in their patients was 22.4%, with 68.2% of complications assessed at diagnosis (13). The clinical course of pediatric gallstones is relatively benign, as evidenced by the complication rate of 7.1–27.7% reported by other authors (16,17).

In our study, among the studied cases, there were 7 (29.2%) with medical management; 4 (16.7%) had conservative management and 3 (12.5%) received UDCA. On the other side, 17 (70.8%) cases had surgical management; 8 (3.3%) underwent lap cholecystectomy, 3 (12.5%) with conservative follow-up then lap cholecystectomy, 5 (20.8%) received UDCA and lap cholecystectomy and only 1 (4.2%) case had ERCP and lap cholecystectomy.

As such, Hajong et al. reported 15 non-hemolytic gallstones cases that were managed by lap cholecystectomy. Of these, 13.3% were asymptomatic, 80% were symptomatic, and 6.7% had a complicated gallstone in the form of pancreatitis (18).

In a separate study, the primary indications for surgery in the pediatric population were choledocholithiasis (28%), symptomatic cholelithiasis (53%), and biliary dyskinesia (16%) (19).

Our findings contradict those of Enayet et al., who reported that LC was performed on seven of their patients. Six of these patients were diagnosed with choledocholithiasis, and one was diagnosed with a symptomatic gallstone accompanied by agonizing, typical right upper quadrant pain. Eighty percent of their cases were conservatively managed, with periodic clinical, laboratory, and US follow-up for 8 to 34 months (4).

In our study, among the studied cases there were 19 (79.2%) with complete improvement, 3 (13.2%) with partial improvement and 2 (8.3%) with No response.

This is consistent with the findings of Enayet et al., who reported that none of their cases developed complications. Additionally, two cases exhibited complete spontaneous resolution of gallstones, and eight cases exhibited resolution of symptoms and/or sonographic improvement (4).

In agreement, Weng et al. reported that expectant management was implemented in 61% of patients, and 62.5% of them achieved spontaneous resolution. The stone dissolution rate was not lower than that of the group that received ursodeoxycholic acid (UDCA). If resolution did not occur, the size of the stone decreased significantly following the use of UDCA (13).

Jeanty et al., who conducted a study on infantile cholelithiasis, observed complete resolution of stones in 25% of the cases. Gokce et al. reported spontaneous complete resolution in 50% of infantile cases and 19.8% in older children. This is consistent with the findings of the aforementioned studies (1,17).

In our study, there was high statistically significant relation between the presence of clinical symptoms and the outcome achieved.

Limitations: The sample size was relatively small. The study was in a single center. Difficulty to obtain stone chemical analysis as the test was not available not only in our centre but also in all governmental and non-governmental private facilities. The study was a descriptive study, results could differ in other study types.

CONCLUSIONS:

Most cases were symptomatic at diagnosis, with non-specific symptoms like abdominal pain and vomiting dominating over classical biliary colic. The most common risk factors were history for NICU admission and family history, rather than obesity or metabolic syndrome. Complication rates were low, with only a single case of choledocholithiasis observed. The majority of cases underwent cholecystectomy with excellent outcomes. Cholecystectomy remains the standard of care for symptomatic gallstones in children.

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