Cholelithiasis in children 16 years and below in Basrah: Epidemiological and Clinical study

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ABSTRACT

Background: **Although compared with adults, cholelithiasis (or gallstone disease) is unusual in infants, and in children but it is certainly not rare. Gallstones currently are being recognized in children with increased frequency therefore, it should be studied more carefully in our locality as it represents a significant health problem.**

Method: **This is a retrospective hospital based study of children with gall stones aged 16 years and below who were admitted to the surgical wards of five major hospitals in Basrah city, during the period from first of January 2007 to 30th June 2012. Then children were studied for demographic criteria, past history, clinical presentation, hospitalization, and the treatment approach.**

Results: **The total number of the study population included in this study was 95children, the mean age of them was 11.7± 3.6 years (Range: 9 months - 16 years) and the male to female ratio was (1:1.4). The majority of the patients 46 patients (78%) were symptomatic at the time of diagnosis, while only 13 patients (22%) were asymptomatic, and the reported symptoms were: abdominal pain, fever, nausea, vomiting, and jaundice. Sickle cell disease (SCD), Thalassemia major and hereditary Spherocytosis were three major types of hemolytic disease that predisposed children to gallstones.**

Conclusions: **Sickle cell disease was the major predisposing factor and responsible for 59.3% of gall stone in this study, while Thalassemia and hereditary Spherocytosis were reported less frequently (6.8% and 1.7% respectively). No reported risk factor was seen in 32.2%. Surgery was performed for most of the patients; types of surgical approach were either open cholecystectomy (with or without splenectomy) or laparoscopic cholecystectomy.**

Key words: Cholelithiasis, Epidemiology, Child health

حصى المرارة لدى الاطفال بعمر ١٦ سنة فما دون بالبصرة: *دراسة وبائية و سريرية*

خلفية البحث: عند مقارنتها بالبالغين، حصى المرارة تعتبر اقل حدوثا في الاطفال والرضع لكنها بالتأكيد غير نادرة، حيث ان السنوات الاخيرة شهدت تسجيل حصى المرارة لدى الاطفال بشكل متزايد، ولذلك هناك حاجة ملحة لدراسة هذا المرض في مناطقنا كونها تمثل مشكلة صحية مهمة.

طرق العمل: اهتمت هذه الدراسة بتناول الاطفال المصابين بحصى المرارة الذين هم بعمر ١٦ سنه فما دون والذين سجلوا في الردهات الجراحية للمستشفيات الخمس الرئيسية في محافظة البصرة بالعراق للفترة الممتدة بين بداية شهر كانون الثاني ٢٠٠٧ حتى نهاية شهر حزيران سنة ٢٠١٢ بشكل متطلع للوراء، وكان العدد الكلي للمرضى قيد الدراسة ٥٩ مريضا. تمت دراسة العينة من ناحية المزايا الديموغرافية، التاريخ المرضي، الاعراض السريرية، مدة الرقود في المستشفى و اسلوب المقاربة العلاجية.

النتائج: تراوح عمر الاطفال الذين شملوا بالدراسة بين ٩ شهور و ١٦ سنة و كان متوسط الاعمار ١١,٧ ± ٣,٦ سنة، كما بلغت نسبة الذكور للإناث في هذه الدراسة حوالي ١:١,٤ . اغلبية المرضى المسجلين كانوا يعانون من اعراض سريرية لحصى المرارة (٧٨%)، بيد ان (٢٢%) من المرضى فقط تم تشخصيهم بشكل عرضي اي انهم لا يعانون من اي اعراض ناجمة عن حصى المرارة بشكل مباشر. ابرز الاعراض السريرية التي تم تسجيلها تتلخص بآلام البطن، الحمى، الغثيان، التقيئ واليرقان.

ابرز الحالات المرضية المسجلة التي جعلت المرضى قيد البحث عرضة لحصى المرارة كان فقر الدم المنجلي، فقر دم البحر الابيض المتوسط (الثلاسيميا) و كثرة الكريات المكورة الوراثي.

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الاستنتاجات: سجلت الدراسة ان ٥٩,٣% من المرضى كانوا يعانون من فقر الدم المنجلي فيما كان ٦,٨% و ١,٧% من اجمالي عدد المرضى يعانون من الثلاسيميا وكثرة الكريات المكورة الوراثي على التوالي. كان هناك ٣٢,٢% من المرضى لا يعانون من اي مرض حالة مسجلة تجعلهم عرضة لخطر الاصابة بحصى المرارة. كان خيار العلاج جراحيا هو الخيار الاكثر اتباعا في مقاربة الاطفال قيد الدراسة وتنوع الخيار الجراحي بين استئصال المرارة (مع او بدون استئصال الطحال) و بين استعمال الجراحة المنظارية لاستئصال المرارة.

INTRODUCTION

Although compared with adults, cholelithiasis {or gallstone disease} is unusual in infants, and in children but it is certainly not rare.[1,2] Gallstones (GS) are relatively uncommon in blacks (except in Sickle cell disease), exceptionally common in selected groups of native Americans (especially the Pima Indians) and Hispanics, and frequent occurrence in white. Gallstones currently are being recognized in children with increased frequency, whether this increase in diagnosis is related to an increase in frequency of the disease or an increase recognition because of widespread use of ultrasonography (U/S) for abdominal complaints is unclear.[3] The incidence currently is reported to be 0.15% to 0.22% in children. In comparison, cholelithiasis is recognized in approximately 10% in adults.[4] Studies from Europe have shown an overall prevalence of gallstone disease of 0.13% to 0.2% in children.[5,6] In Japan, the prevalence of gallstone disease was reported to be less than 0.13% of children.(7)In India a prevalence of 0.3% was reported.[8] Gallstones are either cholesterol gallstones (pure or mixed) or pigmented stones (black or brown).[9,10] Etiologically, they are hemolytic (20% to 30%), non-hemolytic (40% to 50%), or idiopathic (30% to 40. [5,11] The clinical presentation of pediatric cholelithiasis is usually age dependant, and the most accurate diagnostic tool is ultrasonography which can detect stones, as small as, 1.5 mm.[5,12] Recently, laparoscopic cholecystectomy has become the treatment of choice in the surgical management of children with cholelithiasis.[13] The aim of this study is to show the demographic characteristics of children with cholelithiasis in Basrah, and to determine the clinical characteristics, predisposing factors and management of cholelithiasis in children in Basrah city.

PATIENTS AND METHODS

This is a retrospective hospital based study of children with gall stones aged 16 years and below who were admitted to the surgical wards of five major hospitals in Basrah city (Al-Sader teaching hospital, Al-Basrah Maternity and Children Hospital, Basrah Child Specialty Hospital, Basrah General Hospital, and Al-Mawani General Hospital), during the period from first of January 2007 to 30th June 2012. It's important to say that many clinical data were missing from patient's case sheets, including clinical reports, investigations and information about risk factors. This was the major limitation in the current study. Diagnosis of gallstones was based on ultrasonography finding of echogenic foci that produced acoustic shadowing in the gallbladder. Patients with bile sludge were excluded from the study. The total number of the study population included in this study was 59 children, they were divided into 3 age groups 1, 2 and 3 which were represent patients who were $\leq$ 5 years, 6-10 years, and 11-16 years old respectively. Then children were studied for demographic criteria, past history, clinical presentation, hospitalization, and the treatment approach. The data were analyzed using Statistical Package for Social Sciences (SPSS) version 17.0 and a P-value of < 0.05 was considered statistically significant.[14]

RESULTS

As shown in (Table-1), the frequency of children with gallstones increased with increasing age, it's clear that the majority of patients were aged more than 10 years old

which were 39 (66.1%). The mean age of the study population was 11.7 ± 3.6 years (Range: 9 months - 16 years), the mean age of females was 11.2 ± 4 years while the mean age of males was 12.4 ± 2.9 years with no significant difference between the mean age of males and females (P value = 0.222). The male to female ratio was (1:1.4).

Table 1. Distribution of the study population according to demographic characteristics

Age (years)	Sex		Total No. (%)
	Male No. (%)	Female No. (%)	
≤5	2 (8)	3 (8.8)	5 (8.5)
6 -10	4 (16)	11 (32.4)	15 (25.4)
11 -16	19 (76)	20 (58.8)	39 (66.1)
Total	25(100)	34(100)	59(100)

$X^2=2.170 df=2$ P-value=0.338

According to residency, 33 patients (55.9%) were from Basrah districts, while 29 patients (44.1%) were from Basrah city centre. The reported symptoms were: abdominal pain, fever, nausea, vomiting, and jaundice, this is shown on Figure (1) .

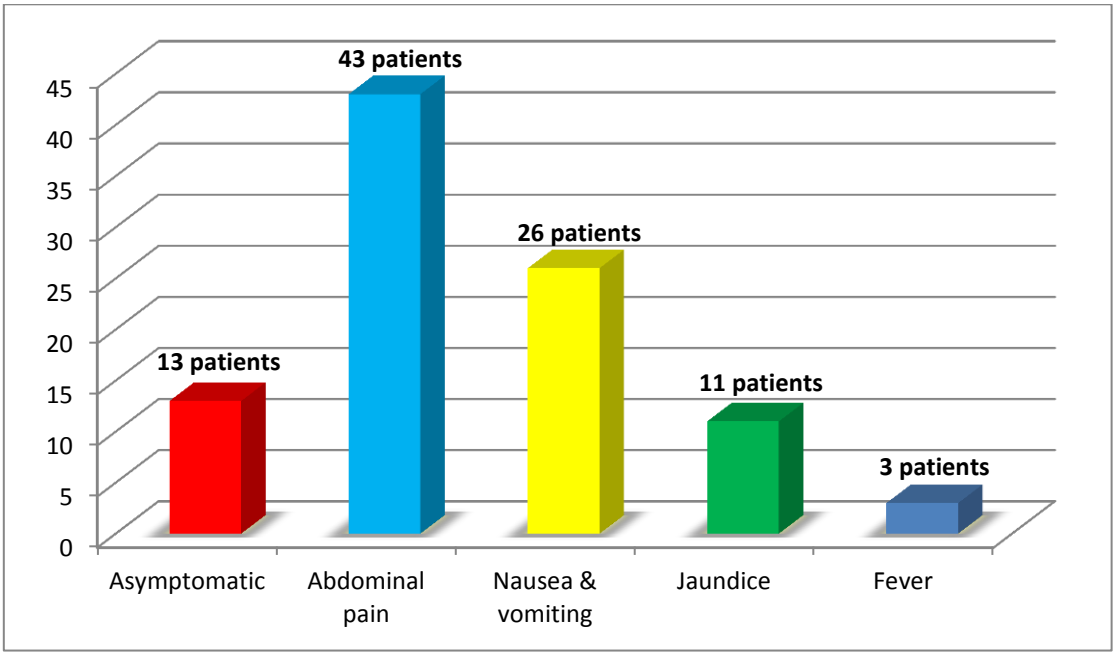

Fig 1. Clinical presentation of patients with gallstones

As shown, in (Table-2), in all age groups and in both sexes, the majority of patients were symptomatic at the time of diagnosis. Generally 46 patients (78%) were symptomatic, while only 13 patients (22%) were asymptomatic. No significant difference was found between symptomatic and asymptomatic patients regarding age and gender.

Table 2. Distribution of clinical presentation according to gender and age groups

Age Group	Symptomatic		Asymptomatic		P value
	No.	%	No.	%	
< 5 years	4	80	1	20	0.147
6-10 years	9	60	6	40	
11-16 years	33	84.6	6	15.4	
Total	46	78	13	22	
Gender					
Male	19	76	6	24	0.498
Female	27	79.4	7	20.6	

Sickle cell disease (SCD), Thalassemia major and hereditary Spherocytosis were three major types of hemolytic diseases that predisposed to gallstones disease.

Figure (2) shows that among children with gallstones who were aged 11-16 years, 22 (56.4%) of them had sickle cell disease, while 14 (35.9%) had no risk factor. 5.1% and 2.6% had Thalassemia and hereditary spherocytosis respectively. In patients who were aged 6-10 years, 10 (66.7%) had sickle cell disease, 3 (20%) had no reported risk factor and only 2 (13.3%) had Thalassemia. Finally, those patients who were aged 5 years and below, 3 patients (60%) had sickle cell disease in comparison with 2 (40%) who had no reported risk factor.

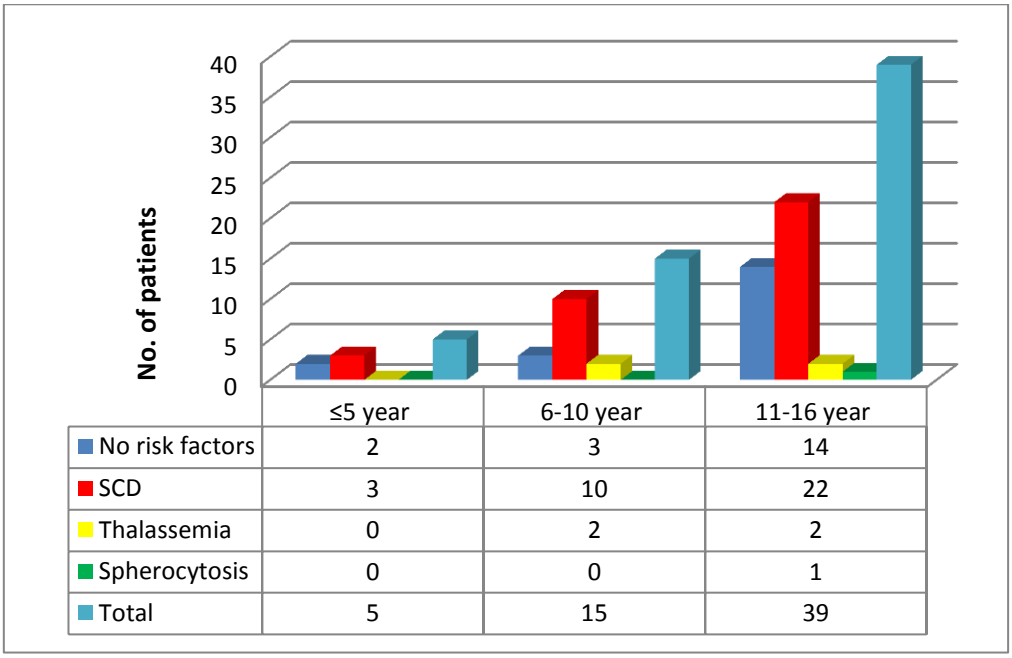

Fig 2. Distribution of gallstones risk factors according to age

On studying the distribution of gall stones risk factors according to gender, no significant statistical difference was reported, as shown on, (Table-3).

Table 3. Distribution of gallstones risk factors according to gender

Risk Factors	Male		Female		Total		P-value
	No.	%	No.	%	No.	%	
None	6	24	13	38.3	19	32.2	0.248
SCD	17	68	18	52.9	35	59.3	0.245
Thalassemia	1	4	3	8.8	4	6.8	0.630*
Spherocytosis	1	4	0	0	1	1.7	0.424*
Total	25	100	34	100	59	100	

*** Fischer Exact Test was used for analysis**

The diagnosis of gallstones in all cases was based on ultrasonography. Forty one patients (69.5%) had signs of chronic calculus cholecystitis, while only 4 patients (6.8%) had signs of acute calculus cholecystitis, and 14 patients (23.7%) had normal gallbladder containing gallstones. Among children who had single gall stone in ultrasonography, 90% had no risk factors, while only 2.6% of those with multiple gallstones had no risk factors with a high significant statistical difference ($p< 0.001$). 84.6% of children who had multiple gallstones were suffering from sickle cell disease, while only 10% of patients with a single stone on ultrasound scan had sickle cell disease with a highly significant difference (P value < 0.001). No significant difference was noted between number of gallstones and thalassemia or spherocytosis.

Table 4. Distribution of risk factors according to number of gallstones

Risk factor	Number of gallstones						
	Single		Multiple		Total		P value
	No.	%	No.	%	No.	%	
No risk factor	18	90.0	1	2.6	19	32.2	< 0.001*
Sickle cell disease	2	10.0	33	84.6	35	59.3	< 0.001*
Thalassemia	0	0	4	10.2	4	6.8	0.289*
Spherocytosis	0	0	1	2.6	1	1.7	0.661*
Total	20	100	39	100	59	100	

*** Fisher Exact Test was used for analysis**

All patients with multiple gallstones had Thalassemia or hereditary Spherocytosis, while none of those with single gallstone had Thalassemia or Spherocytosis. Surgery was performed for most of the patients; types of surgical approach were either open cholecystectomy (with or without splenectomy) or laparoscopic cholecystectomy. (Table-5), displaying types of treatment in study population and mean duration of hospitalization for each type of treatment, it shows clearly that there was a significant difference between duration of hospital stay and type of treatment (P value < 0.05).

Table 5. Types of treatment in study population and mean duration of hospitalization for each type of treatment

Type of treatment	No.	%	Hospital stay (days) Mean ± SD	Median (days)	Range (days)	P- value
Conservative	7	11.9	2.3 ± 2.2	1	1 - 7	< 0.05
Laparoscopic cholecystectomy	24	40.7	3.1 ± 2.04	2	1 - 9	
Open cholecystectomy with Splenectomy	19	32.2	6.2 ± 2.01	7	3 - 11	
Open cholecystectomy without Splenectomy	9	15.2	5 ± 3	4	2 - 11	
Total	59	100.0				

DISCUSSION

Cholelithiasis (Gallstone disease) is relatively uncommon in infants and children. However many studies had shown an increasing number of children presented with gallstones,[3,5,6] this is might be due to increase detection of this condition by wide availability of ultrasonography for children and infants. [5] But it may be a true increase in the reported cases due to certain etiologies that have became more prevalent in recent years particularly chronic hemolytic diseases. Gallstones can occur in all age groups including infants (below the age of one year). In the present study (66.1%) of patients were aged 11-16 year. This may be explained partly by increased incidence of gallstones in patients with chronic hemolytic disease with increasing age. This finding also can partly be explained by the time at which cholesterol saturation in the bile increases.[4] In this study, more than half of patient were from Basrah districts (55.9%), this may be explained by that most patients with chronic hemolytic disease in rural areas, where the marriage between relatives is more. In Al-kwather's study (2004) in Basrah, the consanguinity rate was significantly higher among parents of patients with Thalassemia and sickle Thalassemia (69.9%).[15] The current study showed that the chronic hemolytic diseases were the most common predisposing factor for cholelithiasis, it accounts for 67.8% of patients. This result was less than what was reported in Saudi Arabia, in which the percentage of chronic hemolytic disease was 83.3%.[16] But it is consistent with the results of Wesdorp's et al study in which hemolysis accounted for almost 60%.[5] Another study in Canada (2010)[17] in which chronic hemolytic diseases accounted for 44% only. In the current study, about one third of patients (32.2%) were with no obvious risk factors for gallstones (idiopathic gallstones), while in Saudi Arabia, [16] and Amsterdam, [5] the idiopathic gallstones in children were reported to be (6.9% and 23% respectively). Patients who were suffering from gallstones without having specific risk factor were reported in many studies done in Italy, Canada, and India, those patients represented about 52.5%,52% and 77.3% respectively.[17,18,19] These differences in percentages may be explained by the differences in the study populations and the differences in the documentation systems in different countries. It's important to mention that obesity, as a risk factor, was not included in the analysis of this study because of missing data, this result in over-estimated percentage of idiopathic gallstones. In the present study more than half of patients (59.3%) had sickle cell disease, which is prevalent disease in Basrah city, this is less than what was reported in study of Saudi Arabia.[16] In the present study (60%) of children who were aged 5 years and below had

sickle cell disease, and the percentage of the children with gallstones who had sickle cell disease increased with increasing age. This percentage is more than what was reported by Wesdorp and Schweizer studies, which was ranged from 20% to 30% of patients.[5,11] The total parenteral nutrition (TPN), chemotherapy, malignancy is a risk factors for gallstones but were not seen in any patient in this study. In this study, the majority of children with gallstones were symptomatic (78%), this result was more than that reported by other studies in Italy (64.7%) and Canada (49.5%).[17,19] This may be explained partly by the absence of routine radiological screening by ultrasound for patients with haemoglobinopathies. In this study, most of symptomatic children presented with abdominal pain (93.4%), followed by nausea and vomiting (56.5%), fever was reported in (6.5%) of patients. These findings were consistent with that of Schweizer study.[11] Ultrasonography remains the most sensitive examination in diagnosis of gallstones in children as in adults.[21] The findings of this study regarding ultrasound scanning were consistent with results of other studies.[5, 22, 23] This may be explained by that most of gallstones remain asymptomatic until complications develop. In this study 88.1% were treated surgically which is a definitive treatment of gallstones.[4,9,10] From the total patients 40.7% were treated by laparoscopic cholecystectomy, with mean duration of stay in hospital 3.1 days, this duration was less that shown by another study in Saudi Arabia in which the mean duration was 5.9 days.[16] Laparoscopic cholecystectomy is confirmed to be a safe treatment for pediatric cholelithiasis.[19] It has advantages of being less invasive with lower morbidity and mortality and shorter hospital stay over conventional open cholecystectomy.[24] While open cholecystectomy was done for 47.4%, 32.2% patients of them were subjected to simultaneous splenectomy for hypersplenism, the mean of hospital stay was 6.2 days. The conservative treatment used in patients with acute calculus cholecystitis, and some patients may be due the refusal of child's parents for surgical interventions.

CONCLUSIONS

In conclusion this study found that sickle cell disease was the most frequent predisposing factor of cholelithiasis in children in Basrah, and the majority of children with cholelithiasis were symptomatic at time of diagnosis. This study also confirms that patients treated with laparoscopic cholecystectomy had less duration of hospital stay than those treated with open cholecystectomy.

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