Gallbladder status among children with chronic hemolytic anemia attending Assiut University Children's Hospital

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Background
One among the numerous comorbidities of chronic hemolytic anemia (CHA) is bladder stones. The extensive use of abdominal ultrasound in kids documented raised detection rate of gallstones.

Aim and objectives
To see the frequency of gallbladder diseases among kids with CHA and to see the risk factors of gallbladder diseases among patients with CHA attending Assiut University Children's hospital.

Patients and methods
This cross-sectional study included 50 kids with CHA aged from 1 to 18 years, who were admitted to the Hematology Unit at Assiut University Children's Hospital (from the start of December 2018 to the end of November 2019). All patients were evaluated by full history, general and abdominal examination, laboratory assessment, and ultrasound findings to find the probable risk factors for gallstones.

Results
The age of patients ranged from 1 year up to 18 years. The commonest age of bladder diseases detection was at 6 years. Twenty-one (42%) cases had gallbladder diseases. Bladder diseases were symptomatic in –81 with abdominal pain in affected kids. Thalassemia major was recorded more frequently (72%) in the studied group with 20 and 8% reporting sickle cell anemia and spherocytosis, respectively. The frequency of blood transfusion had statistical significance with gallbladder affection.

Conclusion
From this study, it can be concluded that the type of hemolytic disease, frequency of blood transfusion, history of hydroxy urea intake, and splenomegaly were risk factors for gallbladder affection in children with chronic hemolytic disease.

Keywords:
gallbladder diseases, hemolytic anemias, stones

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Background

The prevalence of gallstones within the medical specialty population has been reported to be uncommon with a calculable overall prevalence of 0.13–1.9%. However, the inflated use of abdominal ultrasonography in recent years has led to increased rate of detection of gallstones [1].

Many etiological factors have been associated with gallstones in youngsters. Chronic hemolytic diseases are considered the foremost common cause. Different risk factors embody liver cirrhosis: chronic cholestasis, total parenteral nutrition, and ileal diseases such as ileal resection, Crohn's disease, cystic fibrosis, prolonged use of high-dose ceftriaxone, cancer therapy, family history, obesity, and congenital anomalies in the gallbladder [2]. One among the frequent comorbidities of chronic hemolytic anemia (CHA) is gallbladder stones. Chronic hemolysis causes increased bilirubin excretion and gallstone formation [3]. The foremost common types of gallstones associated with CHA are pigment gallstones. Even in cholesterol stones, a bilirubin nidus has been documented [4]. Thus, inflated bilirubin acts as a trigger within the formation of gallstones notwithstanding a stone or something of that sort [5].

Patients and methods

This study was a cross-sectional one that included 50 children with CHA aged from 1 to 18 years, admitted to the Hematology Unit at Assiut University Children Hospital (from the start of December 2018 to the end of November 2019). They consisted of 32 males and 18 females with age ranging from 1 to 18 years.

Clinical trial number: NCT03533322.

Patient evaluation

Initial diagnosis: all patients were evaluated in terms of age, sex, presenting symptoms (typical biliary colic, nonspecific abdominal pain, nausea, vomiting or fatty food intolerance, and symptoms of complications such as fever or jaundice), causative risk issues for gallstone, and different incidental diseases.

Laboratory assessment: complete blood count and liver function tests, and CRP specimen were collected and processed.

Radiological assessment: abdominal ultrasonography.

Ethical consideration: reviewing the proposal was carried out before beginning via the moral committee of Assiut Faculty of Medicine. The aim of the study was explained to every patient before starting of the process and written consent was obtained from those who were ready to participate in the study.

IRB NO: 17100515.

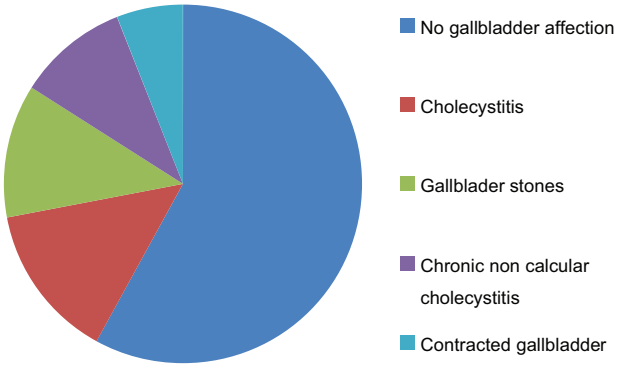
Statistical analysis

The data were tested for normality using the Anderson–Darling test and for homogeneity variances before additional applied mathematical analysis. Categorical variables were delineated by number and percent, wherever continuous variables were described by means and SD for parametric data and median (IQ) for nonparametric data. All analyses were performed with the IBM SPSS 20.0 software (Chicago, USA).

Results

Fifty kids with CHA were included; 42% have gallbladder affection as shown in Fig. 1.

Figure 1



Ultrasonography findings in 50 children with chronic hemolytic anemia according to gallbladder affection.

Their ages ranged from 1 to 18 years. It had been noted that 21 (42%) cases had gallbladder affection, of these 57.1% more than 6 years, 76.2% were males, 76.2% from rural areas and 23.8% with a positive family history of blood diseases (Table 1).

Thalassemia major was recorded a lot of often 36 (72%) cases, 10 cases with sickle cell anemia, spherocytosis (20, 8%, respectively), from thalassemia cases; there were 13 cases with gallbladder affection, while there were eight cases of sickle cell anemia with gallbladder affection with (P = 0.009). It was ascertained that cases of gallbladder affection had a lot of frequency of blood transfusions with P value of 0.047. It had been ascertained that there was a statistically vital distinction between gallbladder affection and hydroxy urea intake with P value of 0.025 (Table 2).

It was observed that symptomatic cases in the form of abdominal pain was detected in 81% of affected cases (Table 3).

It was observed that there was statistically significant difference between gallbladder affection and splenomegaly with P value of 0.023 (Table 4).

Discussion

Our study was performed at the Hematology Unit of Assiut University Children Hospital during the period from the beginning of December 2018 to the end of November 2019.

In our study, 50 children with CHA were included; the mean age of children with CHA in our study was 5.94 ± 2.43 years, ranging from 1 to 18 years. An initial abdominal ultrasound reported that gallbladder

Table 1 Comparison between patients with affected or nonaffected gallbladder as detected by abdominal ultrasound with demographic data of studied children with hemolytic anemia

Parameters	Gallbladder affection (21 cases) [*n* (%)]	No gallbladder affection (29 cases) [*n* (%)]	*P*
Age (years)			
<6	9 (42.9)	19 (65.5)	0.111
≥6	12 (57.1)	10 (34.5)	
Sex			
Male	16 (76.2)	16 (55.2)	0.126
Female	5 (23.8)	13 (44.8)	
Residence			
Rural	16 (76.2)	21 (72.4)	0.764
Urban	5 (23.8)	8 (27.6)	
Family history of blood disease			
Positive	5 (23.8)	12 (41.4)	0.196
Negative	16 (76.2)	17 (58.6)	

Table 2 Comparison between patients with affected or nonaffected gallbladder as detected by abdominal ultrasound with a history data of studied children with chronic hemolytic anemia

History	Gallbladder affection (21 cases) [*n* (%)]	No gallbladder affection (29 cases) [*n* (%)]	*P*
Type of chronic hemolytic anemia			
Thalassemia major	13 (61.9)	23 (79.3)	
Sickle cell anemia	8 (38.1)	2 (6.9)	0.009*
Spherocytosis	0	4 (13.8)	
Age at diagnosis (months)			
<10	13 (61.9)	18 (62.1)	0.991
≥10	8 (38.1)	11 (37.9)	
Frequency of blood transfusion (months)			
<2	13 (61.9)	25 (86.2)	0.047*
≥2	8 (38.1)	4 (13.8)	
History of oral iron chelation agents			
Yes	11 (52.4)	16 (55.2)	0.845
No	10 (47.6)	13 (44.8)	
History of hydroxy urea intake			
Yes	7 (33.3)	2 (6.9)	0.025*
No	14 (66.7)	27 (93.1)	

Table 3 Comparison between patients with affected or nonaffected gallbladder as detected by abdominal ultrasound with symptoms related to gallbladder disorders in studied children with chronic hemolytic anemia

Symptoms	Gallbladder affection (21 cases) [*n* (%)]	No gallbladder affection (29 cases) [*n* (%)]	*P*
Abdominal pain			
Yes	17 (81)	3 (10.3)	0.000*
No	4 (19)	26 (89.7)	
Characters of pain			
Right hypochondrial	8 (47.1)	0	0.242
Epigastric	7 (41.2)	0	0.521
Diffuse	2 (11.8)	1 (33.3)	0.404
Vomiting			
Yes	8 (38.1)	8 (28.6)	0.482
No	13 (61.9)	20 (71.4)	

Table 4 Comparison between patients with affected or nonaffected gallbladder as detected by abdominal ultrasound with findings detected by abdominal examination

	Gallbladder affection (21 cases) [*n* (%)]	No gallbladder affection (29 cases) [*n* (%)]	*P*
Hepatomegaly			
Yes	16 (76.2)	24 (82.8)	0.723
No	5 (23.8)	5 (17.2)	
Splenomegaly			
Yes	9 (52.9)	24 (88.9)	0.023*
No	8 (47.1)	3 (11.1)	
Splenectomy			
Yes	4 (19.0)	2 (6.9)	0.223
No	17 (81.0)	27 (93.1)	

affection occurred in 21 children with CHA in the form of 14% had cholecystitis, 12% had gallbladder stone, 10% had chronic non-calcular cholecystitis, and 6% had contracted gallbladder from these 57.1% more than 6 years. This finding was consistent with Inah and Ekanem [6], in which cholelithiasis was reported in 12 patients giving a general prevalence of gallbladder calculi as 10%. No individual had developed gallbladder calculi in the first 10 years of life. The youngest sickle cell anemia patient with gallbladder calculi was 13 years old.

Many studies have shown that the prevalence of cholelithiasis in patients with sickle cell disease increases with age and affects 6% of patients before 15 years of age and more than 50% of young adults [7].

In our study, there was statistically significant difference between gallbladder affection and type of hemolytic disease, frequency of blood transfusion, and history of hydroxy urea intake. Our results were supported by a study of Shahramian *et al.*[8] as they reported that the patients were transfused with a mean blood volume of 434.8 ± 136.5 ml every 2–4 weeks.

In our study, 33% of them had oral iron chelation agents. This finding is in consistence with Al-Kherbash *et al.*[9] on pattern and clinical profile of thalassemia among pediatric patients in which around 60.6% of the cases (66 cases) had received chelating therapy. This was also explained by the fact that majority of our studied children are thalassemic patients.

Our study showed that as regards symptoms and signs, 81% of gallbladder affected children with CHA had abdominal pain; 47.1% of them were in the right hypochondrium and 41.2% were epigastric. This finding was in agreement with Gumiero *et al.*[10] in which 46% had abdominal pain; 35.5% of them were in the right hypochondrium; and 24.5% were epigastric.

Our results were supported by a study of Enayet *et al.*[11] as they reported that 22 (62.9%) patients had symptomatic gallstones: abdominal pain was the most common presentation (51.4%), jaundice (28.6%), vomiting, nausea, and fatty food intolerance in 25.7, 11.4, and 14.3%, respectively. In our study, it was observed that there was statistically significant difference between gallbladder affection and hydroxy urea intake with *P* value of 0.025. This finding was in agreement with Khavari *et al.*[12] as they report that that if these patients had not been treated with hydroxy urea, we would probably have observed a significantly higher frequency of cholelithiasis, due to more hemolysis compared with patients not taking hydroxyl urea.

In our study it was observed that there was statistically significant difference between gallbladder affection and splenomegaly. This finding is in contrast with Shahramian *et al.*[8] as they report that there were significant differences between cholethiasis and splenectomized patients with thalassemia major. This was attributed to lack of follow-up and awareness of patients on the importance of surgical removal of spleen in such cases.

Conclusion

From this study, it can be concluded that the type of hemolytic disease, frequency of blood transfusion, history of hydroxy urea intake, and splenomegaly were risk factors for gallbladder affection in children with chronic hemolytic disease.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Gupta SK, Shukla VK. Silent gallstones: a therapeutic dilemma. Trop Gastroenterol 2004; 25:65–68.

2 Della Corte C, Falchetti D, Nebbia G, Calacoci M, Pastore M, Francavilla R, *et al.* Management of cholelithiasis in Italian children: a national multicenter study. World J Gastroenterol 2008; 14:1383–1388.

3 Currò G, Iapichino G, Lorenzini C, Palmeri R, Cucinotta E. Laparoscopic cholecystectomy in children with chronic hemolytic anemia. Is the outcome related to the timing of the procedure?. Surg Endosc 2006; 20:252–255.

4 Grünhage F, Lammert F. Gallstone disease. Pathogenesis of gallstones: a genetic perspective. Best Pract Res Clin Gastroenterol 2006; 20: 997–1015.

5 Duvaldestin P, Mahu JL, Metreau JM, Arondel J, Preaux AM, Berthelot P. Possible role of a defect in hepatic bilirubin glucuronidation in the initiation of cholesterol gallstones. Gut 1980; 21:650–655.

6 Inah GB, Ekanem EE. Sonographic diagnosis and clinical correlates of gallbladder stones in patients with sickle cell disease in Calabar, Nigeria. Open Access Maced J Med Sci 2019; 7:68–72.

7 Attalla BA, Karrar ZA, Ibnouf G, Mohamed AO, Abdelwahab O, Nasir EM, *et al.* Outcome of cholelithiasis in Sudanese children with Sickle Cell Anaemia (SCA) after 13 years follow-up. Afr Health Sci 2013; 13:154–159.

8 Shahramian I, Behzadmehr R, Afshari M, Allahdadi A, Delaramnasab M, Bazi A. Cholelithiasis in Thalassemia major patients: A report from the South-East of Iran. Int J Hematol Oncol Stem Cell Res 2018; 12:117.

9 AL-KHERBASH, Hala A. Pattern and clinical profile of thalassemia among pediatric patients attending the Yemeni Society Centers for Thalassemia and Genetic Blood Disorders in Yemen. The Scientific Journal of Al-Azhar Medical Faculty, Girls, 2017; 1.2:43.

10 Gumiero AD, Brandao MA, Pinto EA. Gallstones in children with sickle cell disease followed up at a Brazilian haematology centre. Arq Gastroenterol 2008; 45:313–318.

11 Enayet A, Afifi RA, Mogahed EA, El-Raziky MS, Abdellatif MAK. Gallstones in Egyptian infants and children: risk factors, complications and outcome: a single center experience. Egypt Liver J 2020; 10:1–7.

12 Khavari M, Hamidi A, Haghpanah S, Bagheri MH, Bardestani M, Hantooshzadeh R, Karimi M. Frequency of cholelithiasis in patients with beta-thalassemia intermedia with and without hydroxyurea. Iran Red Crescent Med J 2014; 16:e18712.