Available Online at http://www.recentscientificcom

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 15, Issue, 08, pp.4882-4886, August, 2024

International Journal of Recent Scientific Research

ISSN: 0976-3031

RESEARCH ARTICLE

GALLSTONE DISEASE AT THE SICKLE CELL RESEARCH AND FIGHT CENTER

Kanta M , Doumbia A, Coulibaly M,Goita A, Toure BA, Berthe D, Kene S, Keita I, Diabaté D, Coulibaly M, Baraika M.Ag, Sarro YS, Baby M, Guindo A

Mali

ARTICLE INFO

Article History:

Received 13th July, 2024
Received in revised form 20th July, 2024
Accepted 15th August, 2024
Published online 28th August, 2024

Key words:

cholelithiasis - Sickle cell disease – childs

ABSTRACT

Sickle cell disease is a very common hemoglobinopathy; it is the most common genetic disease with high mortality and morbidity worldwide. The high prevalence of cholelithiasis in sickle cell disease is supported by several studies. It varies from 9 to 15% in children with sickle cell disease [4] and would increase with age.

The main objective is to describe the clinical, biological and therapeutic data of cholelithiasis in children with sickle cell disease. This was a single-center study, with retrospective retrospective collection of data. The study took place from March 15, 2010 to December 31, 2020. All children aged 15 years or older presenting a major form of sickle cell disease who had undergone an abdominal ultrasound during the study period were included. Data were collected from patients' clinical data and entered into SPSS DATA software. The analysis was done by DATA.

The statistical test used was that of chi² with a significance threshold of $p<0.005$. Seventy sickle cell patients were enrolled according to our inclusion criteria. The average age of all sexes of the patients was 12 years and 8 months with extremes of 3 and 15 years. The female gender was in the majority with 51.4% of cases. The homozygous SS profile was the majority phenotype, i.e. 80%.

Abdominal pain is the most common (98%) revealing sign of cholelithiasis, sometimes associated with vomiting and nausea.

Thirty-four patients or 48.57% had microlithiasis, 28.57% had biliary sludge. A gallstone was found in 2 patients or 2.8% and 14 lithiasis clusters in 20%.

INTRODUCTION

Sickle cell disease is one of the most common genetic diseases in the world. Its prevalence continues to increase with nearly 120 million people carrying a sickle cell mutation worldwide. In mainland France, there are 6,000 to 7,000 people suffering from major sickle cell syndrome, with 250 new cases per year. Mali records 5,000 to 6,000 cases of sickle cell disease per year. It is a systemic genetic disease with two intertwined mechanisms: chronic hemolysis and vasoocclusion [1].

These two mechanisms are responsible on the pathophysiological level on the one hand for hyper bilirubinemia, iron overload and on the other hand for liver tissue damage; other known liver disease factors [2]. Nowadays, it is known that cholelithiasis is a frequent chronic complication in children with sickle cell disease. Abdominal pain crisis is one of the most common manifestations of sickle cell disease in children. Its cause is not always due to a vasoocclusive crisis and other complications must then be considered, including cholelithiasis, the diagnosis of which should be considered in the event of an exacerbation of cutaneous jaundice. Its frequency in sickle cell patients increases with age and the severity of the disease; in Jamaica, the prevalence is estimated at 12% in the 5-7 year old group and 23% in the 11-13 year old group [14]. In the pediatric hospital in Portugal, lithiasis represented 40.9% of chronic complications [27] Cholelithiasis can in turn lead to other complications: acute cholecystitis, cholangitis and acute pancreatitis and especially septicemia with a biliary origin [15]. Abdominal ultrasound examination should be systematic in sickle cell patients faced with an abdominal pain crisis and exacerbation of jaundice. The formation of gallstones is favored by the excessive production of bilirubin secondary to

*Corresponding author:**Mariam KANTA**

Mali

chronic hemolysis. They constitute one of the frequent chronic digestive manifestations during major sickle cell syndromes [3]. The high prevalence of cholelithiasis during sickle cell disease is supported by several studies. It varies from 9 to 15% in children with sickle cell disease [4] and would increase with age. According to a Congolese study, cholelithiasis represented 1.6% of causes of hospitalization. These gallstones are commonly encountered in adult sickle cell patients; their existence in younger subjects could be explained by the existence of systemic, local, grenetis and metabolic etiopathogenic abnormalities. The role of MDR3 as a cholelithiasis susceptibility gene has been described in two recent studies. On the one hand it was shown in a Japanese population and on the other hand in a pediatric series [5,6].

Primary objective

Describe the clinical, biological and therapeutic data of cholelithiasis in children with sickle cell disease Material and method The study was carried out at the Center for Research and Control against Sickle Cell Disease in Bamako. The Center for Research and Combating Sickle Cell Disease is located in the Point-G district, in commune III of the Bamako district. It is the first reference center for the treatment of sickle cell disease in Mali. It was created in 2008 thanks to political will supported by technical and financial partners (PTF) including the international cooperation of Monaco and the Pierre Fabre foundation.

Inaugurated on January 21, 2010, the CRLD began its activities on March 15, 2010 with the main objective of improving the quality and expectancy of life. Inaugurated on January 21, 2010, the CRLD began its activities on March 15, 2010 with the main objective: improve the quality and life expectancy of sickle cell patients.

Inclusion criteria:

Children with sickle cell disease presenting a major form of sickle cell disease aged 0 to 15 years in whom ultrasound of the gallbladder has revealed: cholelithiasis, biliary sludge; acute cholecystitis, or acute cholangitis.

Non-inclusion criteria

Children with sickle cell disease presenting a major form of sickle cell disease aged 0 to 15 years in whom ultrasound has not revealed any evidence of: cholelithiasis, biliary sludge, acute cholecystitis, or acute cholangitis

Operational definitions:

- Major form of sickle cell anemia: SS, SC, Sβ thalassemia
- Cholelithiasis: disease characterized by the presence of gallstones, a crystalline body formed by the concretion of normal or abnormal components of bile in the bile or in the gallbladder
- Bile sludge: this is a mucous material that contains lecithin crystals, cholesterol, cholesterol monohydrate crystals, calcium bilirubin and mucin threads.

This sludge can concentrate in the gallbladder and lead to the formation of stones, therefore we consider biliary sludge as a potential lithiasis.

- Acute stone cholecystitis: is an inflammation of the gallbladder wall more or less associated with an infection
- Acute cholangitis: acute infection of the common bile duct linked to the ampulla of Vater

Quételet index: the body mass index used to measure body fat reserves:
Overweight over 30
Ideal weight 18.5-25
Thinness: 16-18
4.7. Data collection, entry and analysis:
Data were collected from patients' clinical data and entered into SPSS DATA software.
The analysis was done by DATA

RESULTS

At the end of our study, seventy sickle cell patients were enrolled according to our inclusion criteria. Demographic and epidemiological characteristics are presented in Table (I); the average age of the patients was 12 years and 8 months with extremes of 3 and 15 years. The female gender was the majority with 51.4% of cases; the sex ratio (M/F) was 0.94. Clinically there was no history of obesity. On the other hand, 30% of patients had a previous history of lithiasis (table 2) On the ultrasound level, microlithiasis represented 48.67%, biliary sludge (28.7%), clusters of lithiasis (20%) and isolated gallstone (2.86%). (Table III)

Wall thickening was associated with cholelithiasis in 48.57%. Hyperleucytosis was observed in 100% of patients, mean free bilirubinemia 77.6 IU/l with extremes 14 – 480. Transaminases were elevated with an average level of 45 mg/l and 60 mg/l respectively for AST and ALT table (IV)

Table I distribution of patients according to sex and phenotype

Gender	Frequency (n)	Purcentage (%)
F	36	51.4
M	34	48.60
Phenotype erythrocytaire	Frequency (n)	Purcentage (%)
SS	56	80
SC	4	5.70
SB0	6	8.60
SB+	4	5.70

Table II distribution of patients according to clinical signs

Clinicals signs		Number	Percentage
Nausea	yes	47	67,1
	no	23	32,9
vomiting	yes	27	38,6
	no	43	61,4
Abdominal pain	yes	69	98,6
	no	1	1,4
fever	yes	58	82,9
	Non	12	17,4

Table III distribution of patients according to ultrasound signs

Ultrasound signs	Number	Percentage
Microlithiasis	34	48,67
Bile Mud	20	28,57
Lithiasis cluster	14	20
Isolated gallstone Total	2 70	2,86 100

Table IV: distribution of patients according to associated ultrasound signs

Ultrasonore Signs	Number	Percentages
Wall thickening	34	48,57
Hyper vascularization Liquid péri vesicular	4 15	5,71 21,43

Table V distribution of patients according to biology data

Paramètres biochimiques	Rate AVERAGE *	Gap kind	There median	minium	Maximin
Bilirubine Conjugated biluribineé(mmol/l)	41.31	25.11	35.50	1.25	122.0
Bilirubine Libre (mmol/l)	77.67	70.60	67.15	14.60	480.0
ALAT (mg/l)	59.74	60.26	43.00	14.00	487.0
ASAT(mg/l)	45.81	70.60	33.20	12.50	586.0

Table VI Distribution of patients according to blood count data

Paramètres cliniques	Minimal	Maximal	Moyenne	Écart-type
Age de survenu des 1er signes (an)	0	13	2,32	2,48
Saturation moyenne en O_2 (%)	90,5	99	96,29	2,06
Nombre de CVO/an	1	6	3,26	1,67
Nombre d'hospitalisation/an	0	5	2	1,41

Lieu de décès	Nombre	pourcentage
Domicile	43	66,15
CRLD	13	20
Autre centre de santé	9	13,85
Total	65	100

DISCUSSION

Seventy cases of cholelithiasis were diagnosed during our study, including 36 girls versus 34 boys. This slight predominance would be linked to hormonal factors with the onset of puberty in Dakar Diagne, in a study carried out in 1999 and relating to cholelithiasis in 106 children with sickle cell disease, found 49 boys for 57 girls [12]. Parez found a sex ratio of 1 in a sample of 26 Parisian patients [13].

The average age of our patients was 12 years with a range of 3 to 15 years. In Senegal, Portugal and RCI, it was 10 and 13 years respectively [27]. These results are consistent with data from the literature which notes a prevalence increasing with age.

In children with sickle cell disease, it is 19% between 1 and 5 years old, 34% between 6 and 10 years old and 47% between 11 and 15 years old [7]. As described in the literature, lithiasis is much more common in homozygous sickle cell patients and this is linked to severe chronic hemolysis [8], but can also be observed in other sickle cell syndromes [9,18].

Clinical and paraclinical data

Nearly 80% of the children in our study were SS homozygotes and 5.7% were SC form sickle cell patients. According to Martins in Brazil in a study carried out on 107 sickle cell patients, 27 patients had cholecystitis, 63% of whom were homozygous (SS) [28] Abdominal pain was found in 98% of our patients. This rate was statistically higher than those of N'Doye Md in Senegal in 2002, and Plummer in Jamaica in 2006 who had respectively found a pain frequency of 68% and 21% [31;32] The average hemoglobin level was 7.6 g/dl with extremes of 3 and 12 g/dl. This result could not be compared due to the lack of a similar study. Hyperleucytosis was observed in 100% of patients. This hyperleukocytosis may be due to functional asplenia. Average free bilirubinemia 77.6 IU/l with extremes 14-480 Transaminases were elevated with an average level of 45 IU/L and 60 IU/L for ASAT and ALT respectively. The biological assessment is a poor indicator of the presence of stones in sickle cell disease. According to several authors, there is no statistically significant difference between the hemoglobin, hematocrit and reticulocyte levels of sickle cell patients with cholelithiasis and sickle cell patients without cholelithiasis (29;30)

The elevation of alkaline phosphatase and direct bilirubin would be good indicators for initiating retrograde cholangiography. This examination would facilitate the duration of the intervention [1] Our high figures could be explained by cytolysis caused by a simple hepatic vaso-occlusive crisis as described in the literature.

Abdominal ultrasound is the essential tool for detecting hepatobiliary pathologies in children. This examination allows you to visualize the stones but also the condition of the gallbladder and bile ducts. It can be sensitive when the ultrasound probe passes over the abdominal wall in the region of the gallbladder. Microlithiasis represented approximately 50% of cases associated with wall thickening. Abdominal ultrasound revealed a gallbladder with multilithiasis content in 61% of patients [34]. SUELL M N revealed in his study the presence of biliary sludge or lithiasis in 57% [35] Therapeutic data Eleven children out of seventy benefited from a cholecystectomy, i.e. 7% including 36% by laparoscopy, this figure is higher than that of N. PAREZ who found 2.3% [13] Laparoscopic cholecystectomy is the therapeutic method of choice in sickle cell patients due to its effectiveness and safety compared to traditional laparotomy surgery. Medical treatment based on antibiotic therapy combining at least two antibiotics of different classes was initiated in 100% of patients. Al-Mulhim et al used ampicillin, metronidazole, and gentamicin before surgery [30].

CONCLUSION

This work confirms the frequency of gallbladder lithiasis in sickle cell patients with a slight female predominance. SS homozygotes are in the majority with 80%.

The clinicat manifestations are dominated by abdominal pain associated or not with vomiting.

The care is multidisciplinary; in our study only 7% of cases underwent surgery.

Acknowledgement and thanks to the Pierre Fabre foundation and Orange-Mali

References

1. Al-Salem AH, Qaisruddin S. The significance of biliary sludge in children with sickle cell disease. Pediatr Surg Int. Jan 1998;13(1):14-6.
2. Ngombe LK, Mukanya PK, Kanteng GW, Mulangu AM, Numbi OL. Cholelithiasis and sickle cell disease - about two observations in Lubumbashi (Democratic Republic of Congo). Pan Afr Med J [Internet]. July 20, 2015[cited-Nov15,2020];21.Availableat: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4575706/
3. Billa RF, Biwole MS, Juimo AG, Bejanga BI, Blackett K. Gall stone disease in African patients with sickle cell anaemia: a preliminary report from Yaounde, Cameroon. Gut. May 1991;32(5):539-41.
4. Al Talhi Y, Shirah BH, Altowairqi M, Yousef Y. Laparoscopic cholecystectomy for cholelithiasis in children with sickle cell disease. Clin J Gastroenterol. August 2017;10(4):320-6.
5. Jacquemin E, Devree M, Cresteil D et al. The wide spectrum of multidrug resistance deficiency: from neonatal cholestasis to cirrhosis of adulthood.Gastroenterolgy2001.120:1448 -1458
6. Shodo J, H. Susuki, Y. Sugiyans et al. Etiology significance of defect in cholesterol, phospholipid and bile acid metabolism in the liver if of patients with intrahepatic calculi. Hepatogy 2001-33: 1194 -1205.
7. Waligora J, Perlemuter L. Extra-hepatitis bile ducts. Anatomy notebooks.Abdomen. 3rd ed. Paris: Masson, 1975; 81p.
8. Franck H, Netter MD. Atlas of human anatomy translation Pierre Kamina.4th ed. Paris: Masson, 2007.
9. Olaf M.I intern at the Paris hospitals. the hypocratic collection National classification tests 2-258 cholelithiasis and complications.
10. Sanogo S D. Laparoscopic cholecystectomies in sickle cell disease. Thesis Medicine Bamako 2010; 54p; No. 56.
11. www.orpha.net[rare diseases/sickle cell disease]. Viewed 12/23/2020 9. Webb DK, Darby JS, Dunn DT, Terry SI, Serjeant GR. Gall stones in Jamaican children with homozygous sickle cell disease. Arch dis Child. May1989;64(5):693-6.
12. Diagne I, Badiane M, Moreira C, Signate-Sy H, Niamey O, Lopez-Sall P, et al. Cholelithiasis and homozygous sickle cell disease in pediatrics in Dakar (Senegal). Archives of Pediatrics. Dec 1999;6(12):1286-92.
13. Parez N, Quinet B, Batut S, Grimprel E, Larroquet M, Audry G, et al. Cholelithiasis in children with sickle cell disease: experience of a Parisian pediatric hospital. Archives of Pediatrics. 1 Oct 2001;8(10):1045-9.
14. Sarnaik S, Slovis TL, Corbett DP, Emami A, Whitten CF. Incidence of cholelithiasis in sickle cell anemia using the ultrasonic gray-scale technique. The Journal of Pediatrics. June 1, 1980;96(6):1005-8.
15. Séguier-Lipszyc E, de Lagausie P, Benkerrou M, Di Napoli S, Aigrain Y.Elective laparoscopic cholecystectomy. Surg Endosc. May 1, 2001;15(3):301-4.
16. Amazon.fr - Sickle Cell - Barnhart, M., et al - Books [Internet]. [quoted June 4 2021]. Available at: https://www.amazon.fr/Sickle-Cell-M-alBarnhart/dp/B0006WKNEU
17. Akamaguna AI, Odita JC, Ugbodaga CI, Okafor LA. Cholelithiasis in sickle cell disease: a cholecystographic and ultrasonographic evaluation in Nigerians.Eur J Radiol. Nov 1985;5(4):271-2.
18. Barrett-Connor E. Cholelithiasis in sickle cell ultrasound. pdf [Internet]. [cited May 17, 2021]. Available at: https://urgences-serveur.fr/IMG/pdf/echographie.pdf
19. Al-Mulhim AS, Abdulatif MM, Ali AM. Laparoscopic cholecystectomy in children with sickle cell disease. Saudi Journal of Gastroenterology. Jan 7 2006;12(3):130.
20. Chagnon S, Laugareil P, Blery M. Ultrasound appearance of gallstone lithiasis and its local complications. Radiol sheet. 1988;28(6):415-23.
21. Walker TM, Serjeant GR. Biliary sludge in sickle cell disease. J Pediatr. 00000000Sep1996;129(3):443-5.
22. Allou Bobole E. Contribution to the study of cholelithiasis in major sickle cell disease www. Wikipedia.org [sickle cell disease]. View 12/23/2020.
23. Galacteros F, Beuzard Y. Thalassemias and abnormal hemoglobins. In: Dreyfus B. éd. Hematology.3rd edition. Paris: Flammarion Medicine-Science; 1992.P359-93.
24. Abby C B, Sangaré A, Bougouma A, Meité M, Keita K, Djedje A T et al. Sickle cell biliary lithiasis.Rev Med Cote d'Ivoire 1986; 20;78:26-31.
25. Webb DKH, Darby JS, Dunn DT, Terry SF, Serjeant GR-Gall stones in Jamaican children with homozygous sickle cell disease.Arcn Dis Child 1989; 64:693-6.
26. N Parez, P. Bégué. Hepatobiliary complications in children. In: R.Girot, P. Bégué and F. Galacteros. Sickle cell anemia. Paris, JL Euronext, 2003: 177
27. Ines Vaz Silva Ana Filipa Reis Sickle cell disease in children: chronic complications and Cholelithiasis and its complications in sickle cell disease in a university hospital Raquel
28. . Alves Martins, Renato Santos Soares, Fernanda Bernadelli De Vito, Valdirene de Fátima Barbosa, Sheila Soares

Silva, search of predictive factors for adverse outcomes European Journal of Haematology 94 (157–161 Revista Brasileira de Hematologia e Hemoterapia Brazilian Journal of Hematology and Hemotherapy

29. Rennels MB, Dunne MG, Grossman NJ, Schuntz AD (1984) Cholelithiasis in patients with major sickle cell hemoglobinopathies. Am J Dis Child 138:66–67 19. Sarnaik S, Slovis T, Corbett DP et al (1980) Incidence of choMithiasis in sickle cell anemia using the ultrasonic grayscale technique
30. Al-Mulhim AS, Abdulatif MM, Ali AM. Laparoscopic cholecystectomy in children with sickle cell disease. Saudi J Gastroenterol. 2006;12(3):130.
31. N'DOYE MD, BAH MD, PAPE EN, DIOUF E, KANE O, BÈYE M, FALL B, KA-SALL B Perioperative management of laparoscopic cholecystectomy in children with homozygous sickle cell disease. Arch ped. Vol 15; No. 9; Pages 1393-1397.
32. PLUMMER J-M., DUNCAN ND, MITCHELL DI, MCDONALD AH, REID M, ARTHURS M. Laparoscopic cholecystectomy for chronic cholecystitis in Jamaican patients with sickle cell disease: preliminary experience. West Indian Med J. 2006; 55 (1):22-4.
33. A TRAORE. Laparoscopie cholecystectomies in sickle cell patients in surgery department A of the CHU du point G. Thesis of medicine 2013
34. SUELL MN, HORTON TM, DISHOP MK, MAHONEY DH, OLUTOYEOO, MUELLER BU. and al. Outcomes for children with gallbladder abnormalities and sickle cell disease .J.Pediatric.Nov2004; 145(5)617-21

How to cite this article:

Kanta M ,Doumbia A, Coulibaly M,Goita A, Toure BA, Berthe D, Kene S, Keita I, Diabaté D, Coulibaly M, Baraika M.Ag, Sarro YS, Baby M, Guindo A. (2024). Gallstone disease at the sickle cell research and fight center. *Int J Recent Sci Res*.15(08), pp.4882-4886.

****