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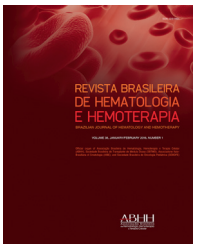

Original article

Cholelithiasis and its complications in sickle cell disease in a university hospital

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ABSTRACT

Introduction: The clinical manifestations of sickle cell disease are related to the polymerization of hemoglobin S. The chronic hemolysis caused by this condition often causes the formation of gallstones that can migrate and block the common bile duct leading to acute abdomen.

Objective: This study aimed to evaluate the profile of patients with sickle cell disease and cholelithiasis.

Methods: Patients with sickle cell disease were separated into groups according to the presence or absence of cholelithiasis. Socioepidemiological and clinical characteristics, such as gender, age, use of hydroxyurea and the presence of other hemoglobinopathies were researched in the medical records of patients.

Results: A hundred and seven patients with sickle cell anemia were treated at the institution. Of these, 27 (25.2%) had cholelithiasis. The presence of cholelithiasis was higher in the 11–29 age group than in younger than 11 years and over 29 years. No association was found for the presence of cholelithiasis with gender, use of hydroxyurea or type of hemoglobinopathy (hemoglobin SS, hemoglobin SC or sickle beta-thalassemia). Sixteen of the patients had to be submitted to cholecystectomy with 14 of the surgeries being performed by laparoscopy. Complications were observed in three patients and one patient died for reasons unrelated to the surgery.

Conclusion: A quarter of patients with sickle cell disease had gallstones, more commonly in the 11- to 29-year age range. Patients should be monitored from childhood to prevent cholelithiasis with preoperative, intra-operative and postoperative care being crucial to reduce the risk of complications in these patients.

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Introduction

Sickle cell anemia is caused by a mutation in chromosome 11 that results in the replacement of glutamic acid with valine at position 6 of the N-terminus of the globin chain. The clinical manifestations of sickle cell disease are directly associated with conformation changes in hemoglobin (Hb). In deoxygenation events (hypoxia, dehydration, stress, low temperature, acidosis, infection), because of the sickle shape of the red blood cells (hence the name), Hb S becomes relatively insoluble and aggregates into long polymers.[1–4]

Approximately 3500 people are estimated to be born with sickle cell disease in Brazil every year, with an estimated 25,000–30,000 people having sickle cell anemia and at least 7,200,000 people carrying the sickle cell trait. The prevalence of carriers of sickle cell trait ranges from 2% in the general population to 6–12% in African descents.[5]

As the cells are abnormal, they have a shorter life than normal red blood cells. Chronic hemolysis leads to continuous production of bilirubin, which is conjugated in the liver and excreted in the feces as urobilinogen; in large quantities, it may form calcium bilirubinate gallstones. Cholelithiasis can be detected even in under five-year-old children, but it is more common in adolescents and adults with sickle cell anemia. Gallstone migration can block the common bile duct leading to acute abdomen. Because of the potential complications and severity of this condition, early diagnosis is of paramount importance. Diagnostic imaging methods play a major role when managing patients with sickle cell anemia, particularly when evaluating complications. Early diagnosis and appropriate treatment increase survival and improve the quality of life of patients with sickle cell anemia.[6–8]

This study aimed to evaluate the profile of patients with sickle cell disease and cholelithiasis, the incidence of cases at the Fundação Hemominas in Uberaba (FHU) and the Hospital das Clínicas of Universidade Federal do Triângulo Mineiro (HC/UFTM) and the importance of early diagnosis for proper treatment.

Methods

This is a retrospective descriptive study. A computerized database was used to analyze patients with sickle cell disease referred to the FHU and to the HC/UFTM from 1995 to 2014. Diagnosis of cholelithiasis was performed by abdominal ultrasound and two groups of patients were formed: with and without cholelithiasis. The following absolute and relative data regarding some socioepidemiological characteristics were collected: gender (male, female), age (younger than 10 years, between 10 and 29 years, and older than 29 years), type of hemoglobinopathy (Hb SS, Hb S/beta-thal, and Hb SC) and use of hydroxyurea. The classification of the hemoglobinopathy was performed by electrophoresis on cellulose acetate at alkaline pH.

The data was first submitted to an analysis of absolute frequencies and percentages, and were organized in tables. An Odds Ratio was calculated in order to study the association between the characteristics of interest. The level of significance for all tests was set at 5%, and the data were analyzed using the statistical software InStat 3.0 (GraphPad Software Inc, La Jolla, CA, USA).

Results

One hundred and seven patients with sickle cell disease were followed up in the Hematology/Hemotherapy Services of the HC/UFTM and FHU during the study period. Twenty seven (25.2%) of the patients had cholelithiasis.

A mean prevalence of 25.2% was observed for the diagnoses of cholelithiasis. Of the 27 cases, 17 were investigated because of clinical symptoms, whereas ten patients were diagnosed during routine screening.

The percentage of cholelithiasis was higher in the 11–29 age group than in the age groups younger than 11 years and over 29 years (p-value = 0.018); the vast majority of the patients were diagnosed before 30 years of age, with an average age at diagnosis of 16 years. Only four cases were diagnosed after 30 years old.

There were no significant differences in frequency of cholelithiasis between males and females (29.3% and 22.0%, respectively; p-value = 0.400), between the group that used hydroxyurea and the group that did not use this medicine (32.4% and 21.4%, respectively; p-value = 0.215) and between Hb SS, Hb S/beta-thal and Hb SC groups (28.4%, 25.0% and 7.1%, respectively, p-value >0.05; Table 1). All Hb S/beta-thal patients were Hb S/beta^0.

Sixteen patients (59%) underwent cholecystectomy, fourteen patients underwent laparoscopic surgery, and two cases underwent open surgery. Although laparoscopy had been started in one of these two cases, laparotomy with emergency splenectomy was performed with satisfactory results due to excessive bleeding. Laparoscopy equipment was not available at the time of the procedure of the other patient.

Three cases (18.7%) of the 16 operated patients developed postoperative complications. One case required emergency splenectomy due to bleeding, and another patient was a choledocholithiasis carrier submitted to endoscopic retrograde cholangiopancreatography progressing to acute pancreatitis. The patient was treated with a good response and then videolaparoscopic cholecystectomy was performed without major complications. One patient progressed to death 30 days after surgery due to splenic sequestration.

Discussion

Cholelithiasis was significantly more prevalent in the 11–29 age group. These results suggest that this group should be made aware of the risk of gallstones, related symptoms, possible complications, and the need for regular follow-ups with routine preventive screenings. However, it should be highlighted that despite having found a higher occurrence in this group, the screening of lithiasis secondary to chronic hemolysis should be provided to all patients with sickle cell disease regardless of their profile in accordance with the Brazilian Handbook of Acute Events in Sickle Cell Disease.[9]

A study conducted at the Universidade de Campinas found a higher incidence of cholelithiasis in patients with sickle cell disease (45%), as well as predominance of younger patients

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