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ORIGINAL ARTICLE

Hepatobiliary disease in children and adolescents with cystic fibrosis☆,☆☆

Fernanda de S. Nascimento[a], Nelson A. Sena[b], Tatiane da A. Ferreira[c], Cibele D.F. Marques[d,e], Luciana R. Silva[f], Edna Lúcia S. de Souza[b,g,*]

[a] *Complexo Hospitalar Professor Edgard Santos, Salvador, BA, Brazil*
[b] *Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[c] *Complexo Hospitalar Professor Edgard Santos, Serviço de Pneumologia Pediátrica, Salvador, BA, Brazil*
[d] *Universidade Federal da Bahia (UFBA), Faculdade de Medicina, Salvador, BA, Brazil*
[e] *Complexo Hospitalar Professor Edgard Santos, Programa de Residência Médica em Gastropediatria, Salvador, BA, Brazil*
[f] *Universidade Federal da Bahia (UFBA), Serviço de Gastroenterologia e Hepatologia, Salvador, BA, Brazil*
[g] *Universidade Federal da Bahia (UFBA), Faculdade de Medicina, Departamento de Pediatria, Salvador, BA, Brazil*

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KEYWORDS
Mucoviscidosis;
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Abstract
Objectives: The aims of the study were to determine the frequency of hepatobiliary disease in patients with CF and to describe the sociodemographic, clinical, and laboratory profile of these patients.
Methods: This was a retrospective, descriptive, and analytical study of 55 patients diagnosed with CF fibrosis, aged between 3 months and 21 years, followed-up from January 2008 to June 2016 in a referral center. Medical records were consulted, including sociodemographic, clinical and laboratory data, including hepatobiliary alterations, imaging studies, genetic studies, liver biopsies, and upper digestive endoscopies.
Results: Hepatobiliary disease was diagnosed in 16.4% of the patients and occurred as an initial manifestation of CF in 55.6% of these cases. The diagnosis of hepatopathy occurred before or concomitantly with the diagnosis of CF in 88.9% of the children. All patients with hepatobiliary disease were considered non-white, with a predominance of females (77.8%) and median (IQR) of 54 (27–91) months. Compared with the group without hepatobiliary disease, children with liver disease had a higher frequency of severe mutations identified in the *CFTR* gene (77.8% *vs.* 39.6%, $p = 0.033$) and severe pancreatic insufficiency (88.9% *vs.* 31.6%, $p = 0.007$).

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☆☆ Study carried out at Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil.

* Corresponding author.
E-mail: souza.ednalucia@gmail.com (E.L. Souza).

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Conclusion: The frequency of hepatobiliary disease was high, with a very early diagnosis of the disease and its complications in the studied series. A statistical association was observed between the occurrence of hepatobiliary disease and the presence of pancreatic insufficiency and severe mutations in the *CFTR* gene. It is emphasized that CF is an important differential diagnosis of liver diseases in childhood.

PALAVRAS-CHAVE
Mucoviscidose;
Hepatopatias;
Fígado

Doença hepatobiliar em crianças e adolescentes com fibrose cística

Resumo

Objetivos: Os objetivos do estudo foram determinar a frequência da doença hepatobiliar em pacientes com FC e descrever o perfil sociodemográfico, clínico e laboratorial destes.
Métodos: Trata-se de um estudo retrospectivo, descritivo e analítico de 55 pacientes com diagnóstico de fibrose FC, entre três meses e 21 anos, acompanhados de janeiro de 2008 a junho de 2016 em um centro de referência. Foi realizada consulta aos prontuários médicos, registrando-se os dados sociodemográficos, clínicos e laboratoriais, incluindo-se alterações hepatobiliares, exames de imagem, estudos genéticos, biópsias hepáticas e endoscopias digestivas altas.
Resultados: A doença hepatobiliar foi diagnosticada em 16,4% dos pacientes e ocorreu como manifestação inicial da FC em 55,6% destes casos. O diagnóstico da hepatopatia ocorreu antes ou concomitante ao diagnóstico da FC em 88,9% das crianças. Todos os pacientes com doença hepatobiliar foram considerados não brancos, havendo predominância do sexo feminino (77,8%) e mediana (I.I.Q) de idade de 54 (27-91) meses. Em comparação com o grupo sem doença hepatobiliar, as crianças com hepatopatia tiveram maior frequência de mutações graves no gene CFTR identificadas (77,8% vs 39,6%; p = 0,033) e de insuficiência pancreática grave (88,9% vs 31,6%; p = 0,007).
Conclusão: A frequência de doença hepatobiliar foi elevada, observando-se um diagnóstico muito precoce da mesma e de suas complicações na casuística estudada. Houve associação estatística entre a ocorrência de doença hepatobiliar e a presença de insuficiência pancreática e de mutações graves do gene CFTR. Enfatiza-se que a FC represente um importante diagnóstico diferencial de hepatopatias na infância.

Introduction

Cystic fibrosis (CF) is the most common lethal genetic disease in white individuals. Abnormal chlorine and sodium transport through the defective cystic fibrosis transmembrane conductance regulator (CFTR) protein causes an increase in the density of exocrine secretions, affecting several organs.[1]

The main clinical manifestations of CF are concentrated in the respiratory and gastrointestinal tracts. However, with the increase in the life expectancy of CF patients in the last decades, the prevalence of CF-associated hepatobiliary disease has increased and attracted more attention of patients, family members, and healthcare professionals.[2,3]

Usually, hepatobiliary manifestations associated with CF start at the end of the patients' first decade of life, and its prevalence ranges from 5.7% to 39%.[4–11] Hepatobiliary disease is the third leading cause of mortality in CF patients, preceded by deaths associated with pulmonary involvement and complications inherent to organ transplants.[12] Additionally, some studies have shown that patients with advanced liver disease are at risk of developing and/or exacerbating other extrahepatic CF manifestations, such as malnutrition, diabetes mellitus, hepatic osteodystrophy, and pulmonary disease, leading to increased morbidity caused by the underlying disease.[3,13] Thus, hepatobiliary disease has been considered a risk predictor of an unfavorable evolution and prognosis of CF.[14]

Few studies have been carried out on CF-associated hepatobiliary disease in the Brazilian population, being fundamental to know the disease particularities in Brazil, which has peculiar ethnic/racial characteristics in the different geographic regions. The objectives of the study were to determine the frequency of hepatobiliary disease in CF patients and to describe the sociodemographic, clinical, and laboratory profile of these patients.

Methods

This was a retrospective, descriptive, and analytical study of patients treated at a referral center in a university hospital. The records of all patients, aged 3 months to 21 years, followed-up between January 2008 and June 2016, with a diagnosis of CF confirmed by two positive sweat tests and/or