ORIGINAL ARTICLE

Chronic liver diseases in the pediatric age

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ABSTRACT

Introduction: chronic liver diseases are a group of diseases that in the medium or long term produce structural and functional alterations in the liver, the affected child may suffer a spectrum of complications, with some similarities with respect to adults, but with notable differences.
Objective: to characterize pediatric patients with chronic hepatopathies seen at the Gastroenterology Service of the "José Luis Miranda" Hospital in the period from January 2019 to December 2020.
Methods: a cross-sectional descriptive study was conducted in pediatric patients with a diagnosis of chronic liver disease admitted to the Gastroenterology Department of the "José Luis Miranda" Hospital from January 2019 to December 2020. The population consisted of 32 patients.
Results: there was a predominance of patients younger than six months (50%) and female sex (59.39%). Among the causes of liver disease, atresia of the extrahepatic biliary tract was diagnosed in 18.75% of patients at term, with adequate birth weight. Hypertransaminasemia was present in 100% of cases as the predominant laboratory finding. The main treatments used were fat-soluble vitamins and bile salt chelators.
Conclusions: chronic hepatopathies were predominant in female children under six months of age. Extrahepatic biliary atresia, hepatotoxicity and Alagille syndrome were the main chronic liver diseases found.
Key words: chronic liver disease; pediatric patient, treatments

RESUMEN

Introducción: las hepatopatías crónicas son un grupo de enfermedades que a mediano o largo plazo producen alteraciones estructurales y funcionales en el hígado, el niño afectado puede padecer un espectro de complicaciones, con algunas similitudes respecto al adulto, pero con diferencias notables.
Objetivo: caracterizara los pacientes pediátricos con hepatopatías crónicas atendidos en el Servicio de Gastroenterología del Hospital "José Luis Miranda" en el período de enero de 2019 a diciembre de 2020.

Métodos: se realizó un estudio descriptivo transversal en pacientes pediátricos con diagnóstico de hepatopatías crónicas ingresados en el Servicio de Gastroenterología del Hospital "José Luis Miranda" enmarcado en el período enero de 2019 a diciembre de 2020. La población quedó constituida por 32 pacientes.
Resultados: hubo un predominio de los menores de seis meses(50%) y del sexo femenino (59,39%). Entre las causas de hepatopatía la atresia de las vías biliares extra hepáticas se diagnosticó en el 18,75% de los pacientes a término, con adecuado peso al nacer. La hipertransaminasemia estuvo presente en el 100% de los casos como hallazgo de laboratorio predominante. Los principales tratamientos empleados fueron las vitaminas liposolubles y los quelantes de sales biliares.
Conclusiones: las hepatopatías crónicas predominaron en el menor de seis meses, del sexo femenino. La atresia biliar extrahepática, la hepatotoxicidad y el síndrome de Alagille fueron las principales hepatopatías crónicas encontradas.
Palabras clave: hepatopatía crónica; paciente pediátrico, tratamientos

INTRODUCTION

Chronic liver diseases are a group of diseases that in the medium or long term produce structural and functional alterations in the liver, the pattern of response to cellular injury is variable. Hepatocyte lesions may be due to viral infection, drugs or toxins, hypoxia, immunological disorders, inborn errors of metabolism and congenital malformations of the liver or biliary tree.[1]
Children with chronic liver disease may suffer a spectrum of complications, with some similarities to adults, but with notable differences because they are more vulnerable as the etiology of liver disease is related to metabolic, cholestatic or infectious disturbances. The natural history of most chronic liver diseases, regardless of the etiology, means that many of them develop complications in their evolution or natural history, such as portal hypertension, ascites, esophageal varices and hepatic encephalopathy (the latter is less common in children than in adults). In addition, within the complications found, protein-energy malnutrition stands out because in the processes that occur with cholestasis there is difficulty for the absorption of fat and fat-soluble vitamins.[2,3,4]
Chronic liver diseases constitute a health problem of low incidence in the child population, but with a significant impact on the quality of life of sick children. Its diagnosis and treatment are usually a daily practice in the work of a Gastroenterology Specialist, but when the necessary training in its clinical behavior is not provided, it can become a difficult disease to control, accompanied by high morbidity and mortality and become a real health problem.[5]
The characterization of chronic hepatopathies in the "José Luis Miranda" Hospital in the study period represents the continuity of previous research on the subject in recent years, which has facilitated a better diagnostic and therapeutic approach to this type of diseases in the Gastroenterology Service, as well as the prevention of associated complications. The present research aims to characterize pediatric patients with chronic hepatopathies seen in the Gastroenterology Service of the "José Luis Miranda" Hospital in the period from January 2019 to December 2020.

METHODS

A descriptive, cross-sectional study was carried out from January 2019 to December 2020 in the Gastroenterology Service of the University Pediatric Provincial Hospital "José Luis Miranda" of Santa Clara City, Villa Clara Province.
The study population consisted of 32 patients with a clinical diagnosis of suspected and confirmed by the use of imaging techniques and diagnostic means of chronic liver disease in the aforementioned period.
Individual clinical histories, both hospital and outpatient, were reviewed and the statistical records of the Hospital were used as a secondary source in order to obtain the primary data in relation to the variables of interest in the study; the information was recorded in a form prepared for this purpose by the author and the research tutor. The information was collected in a database that included the variables of interest obtained from the guides prepared for the study.
Descriptive statistics were used to process the information by determining absolute and relative frequencies using the SPSS statistical software package, version 22.0 for Windows, and the nonparametric Chi-square test (x^2) was applied to corroborate the existence of association between variables or proportional differences between variables.
The information was presented in tables for better understanding.
Among the variables used in the study were age group, sex, causes of liver disease, gestational age at birth, birth weight, symptoms, signs or laboratory findings and treatment of the liver disease.
A commitment was made that the data obtained would be handled with discretion and professionalism, under the standards set forth in the Declaration of Helsinki, respecting the bioethical principles of Autonomy, Beneficence, Non-maleficence and Justice.

RESULTS

Table 1 shows that 50% of the cases were diagnosed in the age group of less than six months and that the female sex predominated (59.38%).

Table 1. Distribution of patients with chronic liver disease according to age and sex

Age group	Gender				Total	
	Masculine		Feminine			
	No.	%	No.	%	No.	%
< 6 months	8	18.75	8	31.25	16	50.0
6 - 11 months	2	6.25	0	0.00	2	6.25
1 - 5 years	1	3.12	6	18.75	7	21.88
6 - 9 years	2	6.25	1	3.12	3	9.37
10 - 18 years	2	6.25	2	6.25	4	12.50
Total	**15**	**40.62**	**17**	**59.38**	**32**	**100.0**

Source: clinical records

Figures 1 and 2 show the causes of hepatopathies according to gestational age at delivery and birth weight, respectively. Extrahepatic bile duct atresia

(18.75%), hepatotoxicity (15.62%) and glycogenoses (12.5%) were the most frequent hepatopathies at gestational age at delivery at ≥37 weeks. Among those with birth weight <2500 grams, a preponderance of Alagille syndrome was found (4, 12.5%).

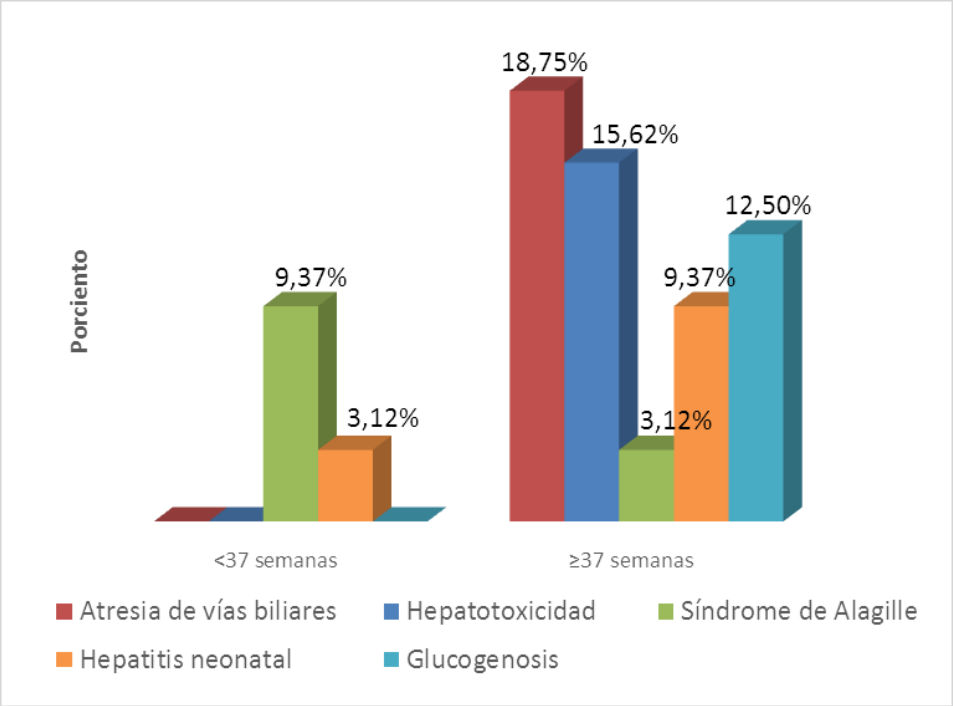

Figure 1. Chronic liver diseases according to gestational age at delivery
Source: clinical records

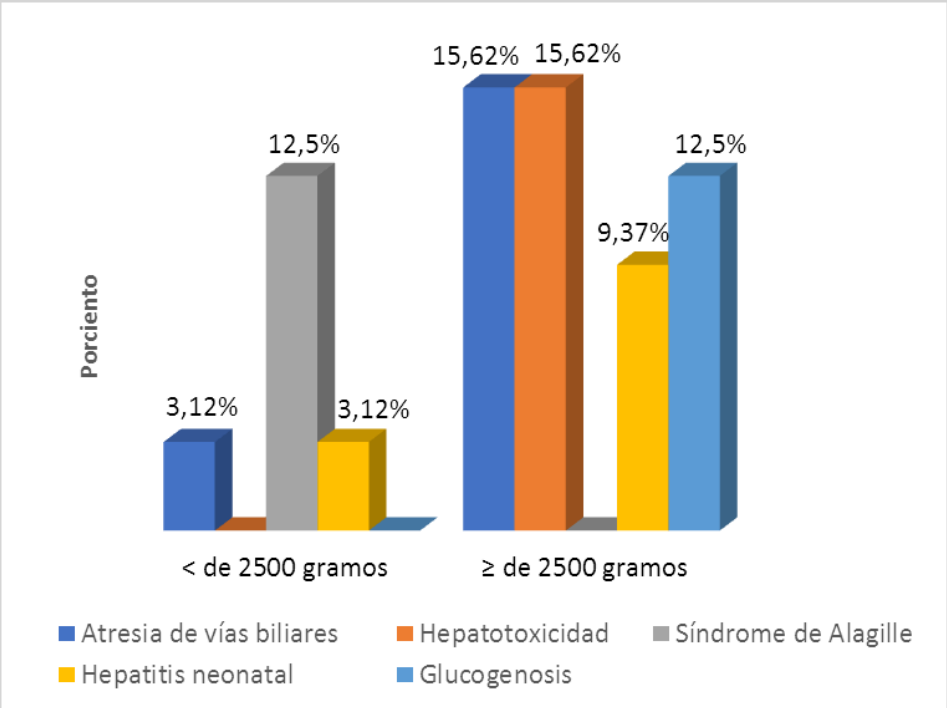

Figure 2. Chronic liver diseases according to birth weight
Source: medical records

The predominant symptoms or signs in patients diagnosed with chronic liver disease are listed in Table 2. The existence of more than one sign or symptom appeared in the same patient. Hypertransaminasemia was detected in all 32 patients (100%) and was the most frequent form; jaundice was observed in 14 children (43.75%).

Table 2. Predominant symptoms or signs in patients diagnosed with chronic liver diseases

Symptoms, signs and Laboratory findings	Total	
	No.	%
Jaundice	14	43.75
Hypertransaminasemia	32	100
Hepatomegaly	23	71.87
Upper gastrointestinal bleeding	1	3.12
Ascites	1	3.12

Source: clinical records

The variants of treatment applied to children with chronic liver disease were analyzed in Table 3. In all patients variants of pharmacological treatment were applied, in two children more than one variant was combined. Among the drugs, fat-soluble vitamins (43.75%) and bile salt chelators (34.48%) were the most frequently used. The most commonly used surgical technique was the Kasai technique, which was used in 15.63% of the infants.

Table 3. Distribution of patients with chronic liver disease according to treatment

Treatment		Total	
		No.	%
Pharmacological	Chelators of bile salts	11	34.48
	Lipid-soluble vitaminss	14	43.75
	Immunosuppressants	1	3.12
	Antibiotics	6	18.75
	Human albumin	2	6.25
Surgical	Kasai technique	5	15.63
	Hepatic-jejunal Roux-en-Y anastomosis	2	6.25
	Liver transplantation	1	3.12

Source: clinical records

DISCUSSION

Chronic liver diseases are a group of diseases of varied etiology that can be infectious, due to drugs or toxins, hypoxia, immunological disorders, inborn errors of metabolism, congenital liver malformations and decompensated respiratory diseases.[6]

In the present study it was found that there was a predominance of cases aged less than one year, half of them in the age group less than six months, with a discrete predominance of the female sex.

In some international studies it was found that the age at diagnosis was from 21 months to 12 years and nine months, with a mean age of seven years and seven months, a result that does not coincide with those of the present investigation.[6,7,8,9]

Other studies report that the most frequent age of diagnosis of chronic hepatopathies is less than one year in diseases such as biliary tract atresia and in the neonatal period in Alagille syndrome, which coincides with the present investigation, in which there was a predominance of infants younger than six months.[10,11]

Figures 1 and 2 show the causes of chronic liver disease according to gestational age at delivery and birth weight. A preponderance of biliary tract atresia was found, present in patients with a gestational age of 37 weeks or more and a birth weight greater than 2500g.

Biliary atresia is the most frequent chronic hepatopathy in pediatric age and affects one in every 18,000 newborns. It is a disease of unknown cause, but perinatal hepatic and biliary inflammation causing fibrosis of the extrahepatic bile duct with complete obstruction is described. Most cases with biliary atresia are born with a birth weight greater than 2500 g.[10] These findings are consistent with those of the present study and with those of another study which reports that biliary tract atresia is the most frequent chronic hepatopathy in the pediatric age group.[11]

Among patients with gestational age less than 37 weeks there was a predominance of cases with Alagille syndrome, all with a birth weight of less than 2500g. Alagille syndrome (mutation in one allele, JAG1 or NOTCH2 genes) is associated with low birth weight, facial features, systolic murmur due to hypoplasia of pulmonary arteries, renal hypoplasia, elevated liver enzymes and hypercholesterolemia.[10] These results coincide with those of the present investigation.

Another investigation describes Alagille syndrome as an arteriohepatic dysplasia, a highly variable autosomal dominant multisystemic condition, with an estimated frequency of one in 30 000-100 000, second in order of frequency among chronic liver diseases,[12] which does not coincide with the present investigation, in which hepatotoxic causes are in second place, which could be related to the multiple conditions that can cause toxicity to the hepatic gland.

Table 2 listed the symptoms, signs and laboratory findings that appeared most frequently among the patients studied. Hypertransaminasemia was a finding found in 100% of the cases, followed by hepatomegaly and jaundice.

There are several symptoms and signs that can be found in chronic hepatopathies in the initial stages, often non-specific, such as asthenia, intense anorexia, nausea, vomiting or epigastric pain. In chronic forms the clinical picture may be even more insidious, nonspecific or even asymptomatic, and there is often little correlation between the intensity of the symptoms and the severity of the liver disease.[13]

The most specific and well known symptoms of liver disease are hepatomegaly, jaundice, acholia, and choluria.[13]

Other symptoms suggestive of liver disease may be intense and generalized pruritus, especially in liver diseases with cholestasis, or symptoms such as telangiectasias, palmar erythema, endocrine disorders, malnutrition, ascites, splenomegaly and gastrointestinal bleeding from esophageal varices in case of portal hypertension, which may occur in more severe chronic liver diseases.[13]

Among the symptoms frequently found in children, jaundice, choluria, acholia, splenomegaly and hepatomegaly of increased consistency, with increased liver enzymes,[10] which coincides with the present investigation, when referring to jaundice and hepatomegaly among the symptoms most frequently found in these patients.

The treatment options used in patients with chronic liver disease are diverse and depend on the specific etiology that causes liver involvement. They can range from drug treatments to complex surgical techniques. Table 3 shows the different treatments used in these patients and highlights that all the infants used variants of pharmacological treatment; among the drugs, fat-soluble vitamins and bile salt chelators stand out as the most used in the study. The most commonly used surgical technique was the Kasai technique because it is used in the treatment of extrahepatic biliary tract atresia, the disease with the highest incidence in the study.

Close monitoring of nutritional status, fat-soluble vitamin supplementation requirements (vitamins A, D, K and E) and the use of porto-enterostomy (Kasai technique) are therapeutic options used in the treatment of biliary atresia. In Alagille syndrome, support treatment is suggested to avoid deficiencies of liposoluble vitamins in high doses, and nutritional support is essential, similar to that described in biliary atresia.[10] These therapeutic options coincide with those used in the present investigation.

Among the therapeutic options in chronic hepatopathies, the use of cytoprotectors such as ursodeoxycholic acid and choleretics such as cholestyramine, phenobarbital and rifampicin in short cycles stand out; the importance of nutritional support with diets enriched in medium chain triglycerides and liposoluble vitamins is also suggested,[14] which also coincides in part with the present investigation

CONCLUSIONS

Chronic liver disease predominated in the age group younger than six months and in females. Patients with a birth weight of 2500 grams or more and with an adequate gestational age predominated. Extrahepatic biliary atresia, hepatotoxicity and Alagille syndrome were the main chronic hepatopathies found in the study and presented at debut with jaundice, hypertransaminemia and hepatomegaly, mainly. All children received pharmacological treatment and seven required surgical treatment.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTION OF THE AUTHORS

ARR: conceptualization, data curation, research, visualization, writing original draft, writing (reviewing and editing).
RAD: research, writing (review and editing).
MCR: writing the original draft.
ÁLMV: conceptualization.
MLM: visualization.
IGV: data curation.