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RESEARCH ARTICLE

LIVER CIRRHOSIS IN CHILDREN

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Abstract

Background : Liver cirrhosis is one of the major causes of hospitalization and mortality in children. A wide spectrum of disorders including developmental abnormalities, infections, metabolic and genetic disorders can lead to liver cirrhosis in pediatric patients. Determination of its etiology is important for treatment, prevention of progressive liver damage, family counseling and prioritizing liver transplantation. The aim of this study is to evaluate etiological and prognostic aspects of liver cirrhosis in children at the pediatrics department at the university hospital center of Marrakech.

Methods : We included all cirrhotic children under the age of 15 who were hospitalized in the gastro-pediatric department at the University Hospital Center of Marrakech over a period from January 2012 to December 2018 in this retrospective study. The etiology of cirrhosis was determined based on clinical results, laboratory tests, imaging studies mainly by ultrasound and histopathological examination of the liver biopsy.

Results : A total of 78 cirrhotic children aged 1 month to 12 years with an average age of 3 years and 5 months, including 43 boys (55%) and 35 girls (45%) were enrolled in the study. The most common causes of liver cirrhosis were: 20 cases of Wilson's disease, biliary atresia in 16 cases, 5 cases of glycogenosis, 3 cases of PFIC, 2 cases of sclerosing cholangitis, 2 cases of tyrosinemia, 2 cases of alpha 1 antitrypsin deficiency, one case of hepatitis B, one case of autoimmune hepatitis, one case of cirrhosis on celiac disease and one case of hemochromatosis. In 31% of cases, the cause of cirrhosis was unknown.

Conclusion : Given the two most common pathologies of cirrhosis of the liver in children in this region of Morocco, we suggest an earlier diagnosis for these two pathologies.

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Introduction:-

Cirrhosis is a diffuse process characterized by progressive hepatic fibrosis, distortion of the hepatic architecture and formation of regenerative nodules,^{1,2} that is relatively uncommon in the pediatric age group.^{3,4} The characteristic feature of cirrhosis in children is the predominance of biliary cirrhosis and cirrhosis due to innate errors of metabolism.

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Complications of cirrhosis include jaundice, ascites, gastrointestinal variceal bleeding, and hepatic encephalopathy, whose presence is indicative of decompensated disease.⁸⁻¹⁰ Other reported complications include edema,¹¹ spontaneous bacterial peritonitis,¹² and hepatopulmonary¹³ and hepatorenal syndromes.¹⁴

For suitable treatment of liver cirrhosis the need for early diagnosis and etiological definition should be emphasized.¹⁵ Thus, the aim of this study is to report the causes of liver cirrhosis and evaluate its prognostic.

Materials and Methods:-

We included all cirrhotic children under the age of 15 who were hospitalized in the gastro-pediatric department at the University Hospital Center of Marrakech over a period from January 2012 to December 2018. Cirrhosis was diagnosed according to clinical, radiological, or histological criteria.

All patients were clinically examined and a data gathering form was completed that contained demographic, clinical and paraclinical data.

The etiology of cirrhosis was identified according to clinical, biological, radiological and in particular ultrasound results and based on histological data from the liver biopsy.

Within the framework of the etiological assessment, a panoply of assessment can be requested, among which we quote those available in our country:

1. Blood count, direct and indirect total bilirubin, Alkaline phosphatases, gamma glutamyl transferase, transaminases, Prothrombin level,
2. Electrophoresis of plasma proteins, if necessary alpha 1 antitrypsin weight determination,
3. TORCH serologies, hepatitis B and C serologies,
4. Ammonemia and lactatemia, chromatography of blood and urinary amino acids, determination of galactose 1 phosphate, testing for succinyl acetone in the urine,
5. Wilson disease assessment: ceruleoplasmin and 24 hour cupruria,
6. Autoimmune hepatitis tests: Anti-nuclear antibodies, Anti-smooth muscle antibodies, Anti-LKM antibodies,
7. abdominal ultrasound, X-ray of the dorsolumbar spine,
8. Ophthalmologic examination in search of posterior embryotoxon and Kayser Fleischer ring.

Results:-

Seventy eight (78) files were retained including 43 boys (55%) and 35 girls (45%). The age of our patients varied from one month to 12 years with an average of 3 years and 5 months.

Jaundice was the most frequent associated clinical sign (80% of cases), digestive hemorrhage was present in 60% of cases, pruritus in 3 patients. The clinical examination showed the presence of hepatomegaly in 90%, splenomegaly in 85% of patients, ascites in 60% of patients, collateral venous circulation in 85% of patients.

Biologically, cytolysis and cholestasis were present with varying degrees, liver function was disturbed in 70% of patients in our series with an average Prothrombin level of 37% ranging from an incoagulable Prothrombin level to 100%, the mean total bilirubin level was 169.4 mg/l predominantly combined with 143.6 mg / l.

The abdominal ultrasound showed a heterogeneous dysmorphic liver in 77 cases, a steatotic liver in one case.

At the end of the various investigations, an etiological diagnosis could be established in 69% of the cases, it was 20 cases of Wilson's disease, biliary atresia in 16 cases, 5 cases of glycogenosis, 3 cases of PFIC, 2 sclerosing cholangitis, 2 cases of tyrosinemia, 2 cases of alpha 1 antitrypsin deficiency, one case of hepatitis B, one case of autoimmune hepatitis, one case of cirrhosis on celiac disease and one case of hemochromatosis. In 31% of cases, the cause of cirrhosis was unknown.

Due to hepatocellular insufficiency and hemostasis disorders, liver biopsy puncture was only performed in 9 patients, confirming the diagnosis of cirrhosis and suggesting the cause in 3 cases: 3 cases of atresia of the bile ducts.

The death rate in our series was 33% with the main cause of gastrointestinal bleeding. All data were analyzed by SPSS for Windows (version 20.0).

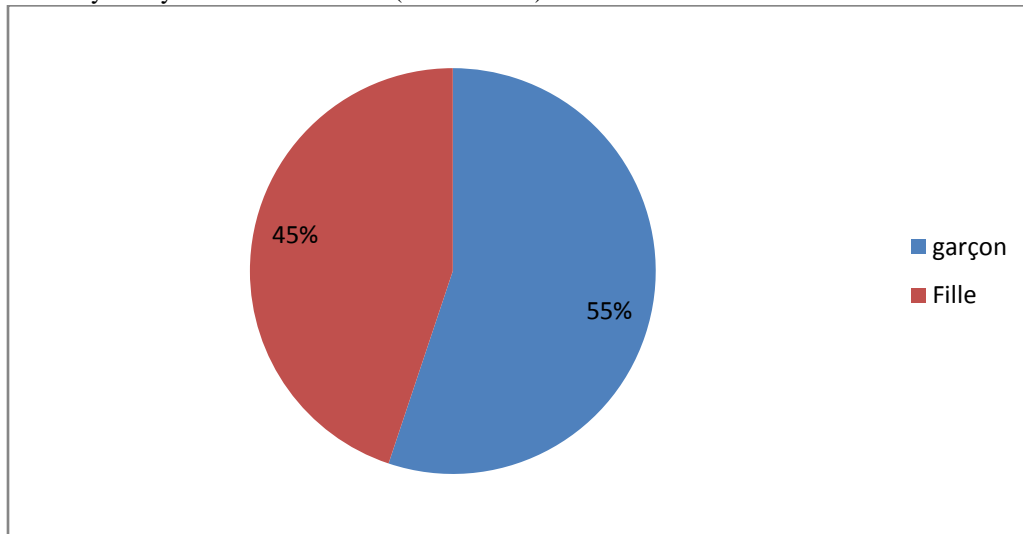


Figure 1:- Showing the distribution by sex.

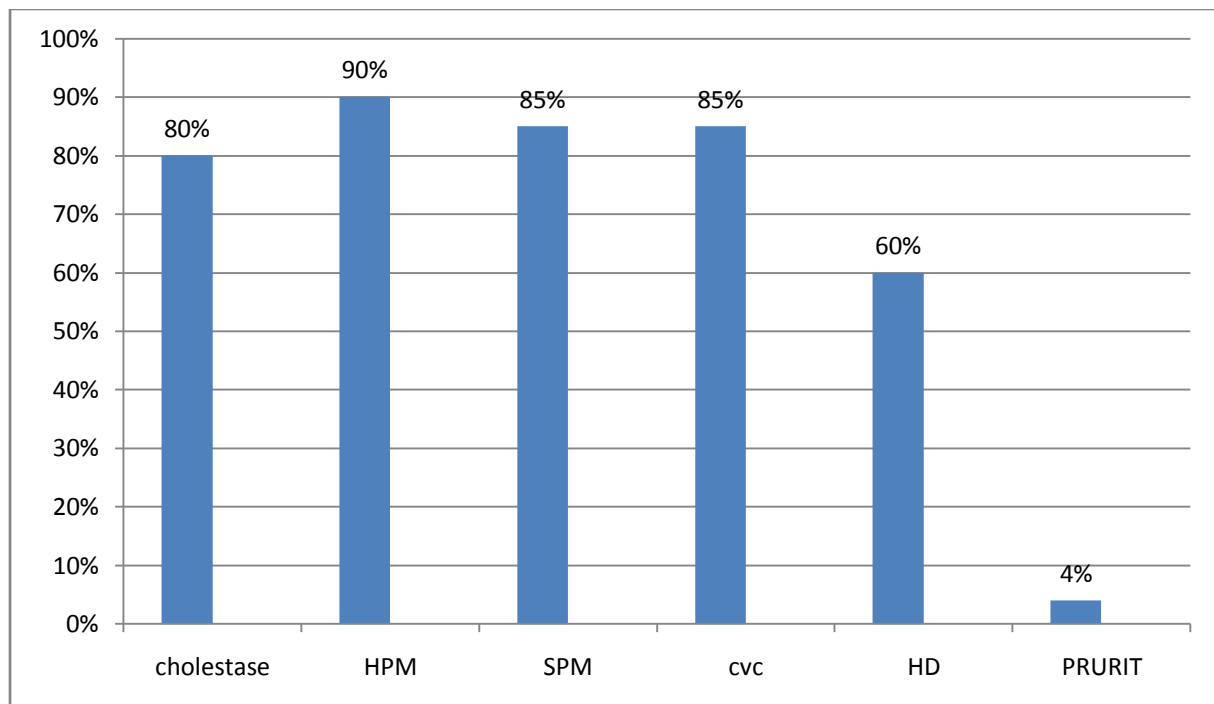


Figure 2:- Illustrating the frequency of functional and physical signs.

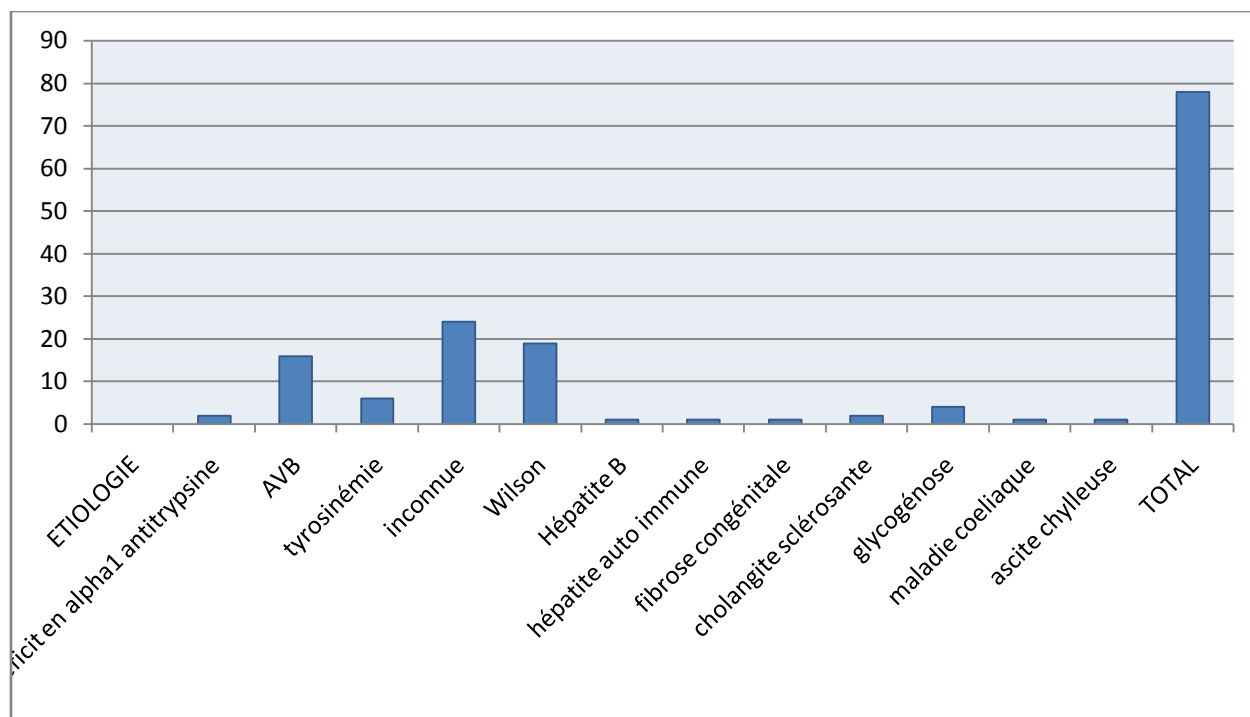


Figure 3:- Illustrating the distribution by etiology.

Discussion:-

Liver cirrhosis is the most common hepatic cause for hospitalization in adults' gastroenterology and hepatology wards and also the third leading gastrointestinal causes of death in Iran.¹⁶ Although rather uncommon and multifactorial in etiology, liver cirrhosis is a severe and often rapidly fatal disease in pediatric patients. There is little epidemiological information regarding etiology of liver cirrhosis in children and it's change over time.

The most common causes of liver cirrhosis in a study in central southern Iran were Wilson's disease (20.7%), biliary atresia (17.9%), cryptogenic cirrhosis (13.2%) and autoimmune hepatitis (11.3%)⁹.

Recently this center has become an active pediatric liver transplant center in the Middle East region with more than 70 pediatric liver transplants annually, thus the high number of subjects with Wilson disease might be attributed to referrals from other parts of the country. In a recent study from Iran the most common hepatic diseases among inpatients were hepatitis B virus (HBV) and cryptogenic or non-alcoholic fatty liver disease induced cirrhosis.¹⁷ In another study from Southern Iran HBV infection was the major cause for cirrhosis and ascites was the most common complication in adult patients.¹⁸ The mean PELD/MELD scores in this study was 14.2 that is comparable with 15.5 in the Behroozian R et al series.¹⁹

In a Tunisian study on 36 girls and 35 boys with cirrhosis, jaundice and hepatomegaly were the most frequent clinical signs. Regarding the etiology of cirrhosis, biliary causes (including biliary atresia, choledocal cysts, and progressive familial intrahepatic cholestasis) were diagnosed as the most frequent (40%), causes followed by metabolic diseases that included hepatorenal tyrosinemia, Wilson disease (17%) and post-hepatitis cirrhosis (17%). In 27% of cases, no etiology was found.²⁰ The authors concluded that etiological diagnosis in children with cirrhosis was a problem in their country because of the lack of availability of some specific tests.²⁰ In Iran, the main indications for liver transplantation in children were reported as Wilson disease (20.3%), cryptogenic cirrhosis (16.7%) and autoimmune cirrhosis (14.5%),²¹ which agreed with the results of this study.

In a study from Northern India on 235 children with hepatobiliary disorders, acute hepatitis (28%), chronic liver disease (36%) and neonatal cholestasis syndrome (26%) were presented as the most common causes of liver disease. Chronic liver diseases included post-hepatitic cirrhosis (13%), Wilson disease (21%), autoimmune (4%), and non-Wilsonian metabolic diseases (16%).²²

In Brazil the most common causes of pediatric cirrhosis were biliary atresia (50%), autoimmune disorders (20.5%) and cryptogenic (17.6%).²³

The most common indications for liver transplantation in children in Argentina were biliary atresia (30%), fulminant hepatic failure (27%) and autoimmune cirrhosis (16%).²⁴

In Oman, progressive familial intrahepatic cholestasis (30%) as well as fibrocystic diseases of the liver and kidneys (21%) were the most common causes of liver cirrhosis.²⁵

These reports from developing countries recognized that metabolic disorders, cholestatic syndromes and autoimmune hepatitis were the most common causes of cirrhosis in children in these countries.

Also, in Japan the main causes of liver cirrhosis in children who underwent liver transplantation were biliary atresia (72.9%), cryptogenic (8.1%), Budd Chiari syndrome (5.4%), progressive familial intrahepatic cholestasis (5.4%), and Wilson disease (2.7%).²⁶

In a nationwide survey in Japan to evaluate the etiology of liver cirrhosis, the data from 33379 patients with liver cirrhosis were analyzed at 58 hospitals. The most common causes of cirrhosis were hepatitis B virus (13.9%), hepatitis C virus (60.9%), alcohol (13.6%), primary biliary cirrhosis (2.4%) and autoimmune hepatitis (1.9%).²⁷

In a center of southern Iran, Saberifiroozi et al. report in a study of 480 adult patients (mean age 39 ± 13 years; 68.1% men) on the liver transplant list that the most common causes of cirrhosis were cryptogenic (143; 29.9 %) and hepatitis B virus (127; 26.5%).²⁸

These studies have shown completely different causes of liver cirrhosis in children and adults, as the most common cause of liver cirrhosis in adults were viral hepatitis.

This study concluded that metabolic disorders (Wilson disease), cholestatic syndromes (biliary atresia) are the most common causes of cirrhosis in children in our area. Early diagnosis and determining the common causes of cirrhosis in are important for effective treatment and decreasing the rate of complications and mortality.

Conflict Of Interest :

The authors declare no conflict of interest related to this work.

References:-

1. Anthony P, Ishak K, Nayak N, Poulsen H, Scheuer P, Sobin L. The morphology of cirrhosisRecommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. *J Clin Pathol.* 1978;31:395–414. [PMC free article] [PubMed] [Google Scholar]
2. Malekzadeh R, Mohamadnejad M, Rakhshani N, Nasser-Moghaddam S, Merat S, Tavangar SM. et al. Reversibility of cirrhosis in chronic hepatitis B. *Clin Gastroenterol Hepatol.* 2004;2:344–7. [PubMed] [Google Scholar]
3. Romano F, Stroppa P, Bravi M, Casotti V, Lucianetti A, Guizzetti M. et al. Favorable outcome of primary liver transplantation in children with cirrhosis and hepatocellular carcinoma. *Pediatr Transplant.* 2011;15:573–9. [PubMed] [Google Scholar]
4. Keller PD, Nute Jr WL. Cirrhosis of the liver in children: A clinical and pathologic study of forty cases. *J Pediatr.* 1949;34:588–615. [PubMed] [Google Scholar]
9. Pinzani M, Rosselli M, Zuckermann M. Liver cirrhosis. *Best Pract Res Clin Gastroenterol.* 2011;25:281–90. [PubMed] [Google Scholar]
10. Seyed Mohsen Dehghani,¹ * Mohammad Hadi Imanieh,² Mahmood Haghighat,³ Abdorrasoul Malekpour,⁴ and Zeinab Falizkar⁵; Etiology and Complications of Liver Cirrhosis in Children:Report of a Single Center from Southern Iran. *Middle East J Dig Dis.* 2013 Jan; 5(1): 41–46.
11. Dehghani SM, Haghighat M, Imanieh MH, Tabebordbar MR. Upper gastrointestinal bleeding in children in Southern Iran. *Indian J Pediatr.* 2009;76:635–8. [PubMed] [Google Scholar]
12. Solà E, Watson H, Graupera I, Turón F, Barreto R, Rodríguez E. et al. Factors Related to Quality of Life in Patients With Cirrhosis and AscitesRelevance of Serum Sodium Concentration and Leg Edema. *J Hepatol.* 2012;57:1199–206. [PubMed] [Google Scholar]

13. Cheong HS, Kang CI, Lee JA, Moon SY, Joung MK, Chung DR. et al. Clinical significance and outcome of nosocomial acquisition of spontaneous bacterial peritonitis in patients with liver cirrhosis. *Clin Infect Dis.* 2009;48:1230–6. [PubMed] [Google Scholar]
14. Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome—a liver-induced lung vascular disorder. *N Engl J Med.* 2008;358:2378–87. [PubMed] [Google Scholar]
15. Salerno F, Gerbes A, Ginès P, Wong F, Arroyo V. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. *Postgrad Med J.* 2008;84:662–70. [PubMed] [Google Scholar]
16. Giacchino R, Navone C, Ciravegna B, Viscoli C, Ferrea G, Facco F. Liver cirrhosis in childhood Considerations on 22 cases with different etiology. *Pediatr Med Chir.* 1990;12:147–52. [PubMed] [Google Scholar]
17. Ganji A, Malekzadeh F, Safavi M, Nassri-Moghaddam S, Nourie M, Merat S. et al. Digestive and Liver Disease Statistics in Iran. *Middle East J Dig Dis.* 2009;1:56–62. [Google Scholar]
18. Abedian S, Asl Soleimani H, Saberifiroozi M, Malekzadeh R. Common Digestive and Liver Diseases among 5880 Patients Admitted to Shariati Hospital, Tehran, Iran during 2000-2009. *Middle East J Dig Dis.* 2012;4:28–34. [PMC free article] [PubMed] [Google Scholar]
19. Hajiani E, Hashemi SJ, Masjedizadeh R, Ahmadzadeh S. Liver Cirrhosis seen in GI Clinics of Ahvaz, Iran. *Govaresh.* 2012;17:178–82. [Google Scholar]
20. Behroozian R, Bayazidchi M, Rasooli J. Systemic Inflammatory Response Syndrome and MELD Score in Hospital Outcome of Patients with Liver Cirrhosis. *Middle East J Dig Dis.* 2012;4:168–72. [PMC free article] [PubMed] [Google Scholar]
21. Chaabouni M, Bahloul S, Ben Romdhane W, Ben Saleh M, Ben Halima N, Chouchene C. et al. Epidemiological, etiological and evolutionary aspects of children cirrhosis in a developing country: experience of the pediatric department of SFAX University hospital, Tunisia. *Tunis Med.* 2007;85:738–43. [PubMed] [Google Scholar]
22. Bahador A, Salahi H, Nikeghbalian S, Dehghani SM, Dehghani M, Kakaei F, et al., editors. *Pediatric Liver Transplantation in Iran: A 9-Year Experience*. 2009: Elsevier. [PubMed]
23. Yachha SK, Sharma BC, Khanduri A, Srivastava A. Current spectrum of hepatobiliary disorders in northern India. *Indian Pediatr.* 1997;34:885–90. [PubMed] [Google Scholar]
24. Ferreira CT, da Silveira TR, Vieira SM, Taniguchi A, Pereira-Lima J. Immunogenicity and safety of hepatitis A vaccine in children with chronic liver disease. *J Pediatr Gastroenterol Nutr.* 2003;37:258–61. [PubMed] [Google Scholar]
25. Williams E, Questa H, Wacholder V, Rojas L, Cervio G, Bianco G. et al. Development of a pediatric liver transplantation program in Argentina. *Pediatr Surg Int.* 1998;13:319–22. [PubMed] [Google Scholar]
26. Al-Lawati TT, George M, Al-Lawati FA. Pattern of liver diseases in Oman. *Ann Trop Paediatr.* 2009;29:183–9. [PubMed] [Google Scholar]
27. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Yamamoto E. et al. Living related liver transplantation in children. *Am J Surg.* 1994;168:41–8. [PubMed] [Google Scholar]
28. Michitaka K, Nishiguchi S, Aoyagi Y, Hiasa Y, Tokumoto Y, Onji M. Etiology of liver cirrhosis in Japan: a nationwide survey. *J Gastroenterol.* 2010;45:86–94. [PubMed] [Google Scholar]
29. Saberifiroozi M, Serati AR, Malekhosseini SA, Salahi H, Bahador A, Lankarani KB. et al. Analysis of patients listed for liver transplantation in Shiraz, Iran. *Indian J Gastroenterol.* 2006;25:11–3. [PubMed] [Google Scholar].