Original Article

Etiology of chronic liver disease in Iraqi children, with special emphasis on the role of liver biopsy

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ABSTRACT

Objectives: Pathology of liver diseases in children differ from that of the adult. In this study we reviewed data obtained from of liver biopsies, in addition to other supplementary investigations, to determine common causes of liver diseases in Iraqi children.

Methodology: Eighty liver biopsies were performed, between January 2009 – March 2010, for the diagnosis of various liver related diseases in children, at the Children's Welfare hospital, in addition to other complimentary tests, as required.

Results: Various types of congenital inborn errors of metabolism formed the major part of liver diseases in the studied sample (41%), followed by various types of congenital familial intarhepatic cholestasis. Autoimmune hepatitis accounted for 7.5% of the cases, and was the most frequent diagnosis in those older than two years.

Conclusion: Liver biopsy (with ultrasound guidance) was a safe procedure. Appropriate biopsy sample was obtained with the spring loaded needles. Heriditiry, familial causes of liver diseases were the most common, requiring efforts for the diagnosis and treatment of such diseases.

KEY WORDS: Liver diseases, Children, Liver biopsy.

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INTRODUCTION

Liver diseases in children are significant causes of morbidity and mortality in this age group. Pediatric hepatology continues to evolve as a critically important medical discipline. This vital transformation is the result of the extensive use of liver transplantation in children and of focused pediatric research.[1] Pediatric liver diseases have distinctive epidemiologic, clinical, and therapeutic aspects than those of adult diseases.

It is important to have the knowledge of the current spectrum of hepatobiliary disorders in Iraqi children. Various diagnostic tools including liver function tests, enzyme essays, or imaging techniques are available for the evaluation of liver disorders, but although liver biopsy is an invasive method, it is the corner stone for the precise diagnosis.[2-5]

The present study therefore relied on assessing the results of liver biopsies done for children (whom were referred to the GIt center), in correlation with

other investigations as required, in order to determine the existing pattern of hepatobiliary disorders in children presenting at this tertiary care center in Baghdad, as most of these cases fall into chronic complaints (in order to be subjected for liver biopsy), we regarded the work as a revision for the causes of chronic liver diseases in our society.

METHODOLOGY

Through the period from January 2009 to April 2010, eighty liver biopsies were done for the sake of the diagnosis of various problems suggestive of chronic liver disease (e.g. jaundice, unexplained hepatosplenomegaly, impaired liver function tests … etc). They were undertaken in the Children's welfare hospital in the Medical City teaching hospital, which is a tertiary care referral center, that receives patients from Baghdad and surrounding governorates. Actually the selection of patients to be submitted for liver biopsy was only when it was necessary to prove the diagnosis, or to assess the disease extent in a way that it affects the treatment to be applied, many other patients were exempted from this procedure despite being medically eligible for the reasons that will be mentioned later. Basic Lab investigations (including viral & immune markrs, alpha one antitrypsine level and copper profile, serum ferritin, serology for TORCHES infection, lipid profile and serum uric acid as indicated) and imaging procedures were done in all patients, endoscopic assessment was done when required, complementary investigations as chromatographic studies, with/without filter paper analysis for metabolic diseases were attempted (at St Joseph metabolic center/Beirut) when the suspicion of such disorders was strengthened.

Patients with viral hepatitis were exempted, also those with a diagnostic copper profile. Either the Menghini needle or the spring loaded disposable needles (when available) were used, under ultrasound guidance, with simple sedation by intravenous diazepam.

Samples initially preserved in 10% formalin, were analyzes in the Lab of the Gastroenterology center/Medical City hospital, using the standard Eosin & hematoxylin stain.

RESULTS

A total of eighty liver biopsies were done within a 13 month period. The male/female ratio was 1.4:1. The younger age group (<2 year old) formed more than 50% of evaluated cases. Table-I shows that various forms of congenital errors of metabolism formed the largest group. Glycogen storage diseases alone formed 24% of the total evaluated cases, all of them presenting with hepatomegaly. Remarkably in 16 out of the 19 cases their biopsies had advanced fibrosis and/or established cirrhosis. Lipid storage diseases were diagnosed by the specific histiocytes in the biopsy specimen. The rest of the inborn errors showed either intrahepatic cholestasis with variable degrees of liver cell degeneration, or a picture of fatty liver.

The second most common diagnosis in the general sample was congenital intrahepatic cholestatic diseases (progressive familial intrahepatic cholestasis), followed by the neonatal hepatitis, of which 10 cases were diagnosed, with a male/female ratio of 1:1.5, and all were below two years except one three year old, with established cirrhosis. Two babies had positive serology for CMV, presenting with hemolytic anemia and hepatitis. Five cases of extra hepatic biliary atresia were diagnosed, forming 6.2% of the total, with the age ranging from 6 weeks – 4 months.

Autoimmune hepatitis formed 19% of the diagnosis above two years of age, second only to glycogen storage disease. One five year old boy had Sickle thalassemia, cholestasis, the liver histology showed a picture of chronic immune hepatitis. Two samples were as normal, one of a five year old child with unexplained hypoglycemia, the other was done for the evaluation of failure to thrive in a 20 month old girl.

DISCUSSION

Liver biopsy, being an invasive procedure, which carries a well recognized risks[5-7], is not easily practiced now a days in Iraq due to the security reasons in the country. Hence many patients with unstable medical conditions and those with severely shrunken, fibrosed livers, those in whom the diagnosis can be made by other lab tests, biopsy procedure is usually avoided. Many cases of Wilson's disease, those with viral hepatitis and very risky patients were exempted from this procedure, in addition patients with thalassemia are not routinely evaluated by liver biopsy as transplant procedures are not yet available. Liver biopsy was attempted only when it was thought to affect the diagnosis and the management of the patient.

However, in our evaluated sample, there was a preponderance of various errors of metabolism as a cause for chronic liver diseases, including storage disorders: glycogen and lipid storage disorders, in

addition to errors of aminoacids and fatty acid metabolism. The diagnosis of the latter was possible with the cooperation of St Joseph Center/Beirut, which provided the tandem mass spectrometry analysis, otherwise most of these disorders showed either unexplained fatty liver changes or a picture of unexplained cholestasis. The documented cases of liver diseases due to a metabolic error formed 41% of the total studied sample, Barakat et al[8] from Egypt found that 33% of chronic liver diseases in children ere due to metabolic disorders, while Monajemzadeh et al found it to form13.8% of liver diseases in Iranian children[9] and it formed no more than 4% in Muthuphei et al[10], Obafunwa et al[11]and Mackenjee et al.[12] Storage diseases alone formed 8.5% of such diseases in Ramakrishna et al review in India[13], while they accounted for 28.7% of our studied cases. The reasons why that metabolic diseases were so prevalent in our survey is that consanguinity is common among Iraqis and our clinic is in a referral tertiary care center, so there was clustering of chronic and familial diseases. In addition during the last years there has been increasing cooperation with the pathologists for better orientation towards picking certain pediatric liver problems. The lower incidence of these diseases in certain reviews probably refers to lower rate of diagnosis.

The second diagnosis in frequency was progressive familial intrahepatic cholestasis, both the syndromic and non syndromic forms, which accounted for 23,7% of the cases, while it was 9.25 in an Omani survey[14], and Monajemzadeh et al[9] found a 6.2% incidence of progressive familial intrahepatic cholestasis only, in some surveys the diagnosis was not mentioned at all as in Ramakrishna et al[13] and Muthuphei et al.[10] Actually our Gastroenterology center practices primarily adult Medicine in all it's sectors, and not until the later years that a better orientation have been created towards the diagnosis of certain pediatric problems. In one child the diagnosis of Allagile's syndrome was denied by the team of pathologists despite several revisions and it was only when the child received liver transplant that the diagnosis was documented on the removed diseased liver. On the other hand as it has been described previously that biopsy procedure was avoided in very sick and unstable patients, limiting actually the diagnostic range of diseases.

Table-I: Distribution of various liver diseases according to the age.

Liver disease	*Age groups*			*Total*
	<2yr No(%)	*>2-5yr No(%)*	*>5yr No(%)*	
Familial intrahepatic cholestasis	12	-	1	13(16.25%)
Allagile sy	3	-	3	6(7.5%)
EHBA	5	-	-	5((6.25%)
Neonatal hepatitis	9	1	-	10(12.5%)
AIH	1	4	1	6(7.5%)
GSD	9	6	4	19(23.75%)
Pneiman Pick	3	1	-	4(5%)
Tyrosinemia	3	-	-	3(3.75%)
FA oxidation disorders	3	1	-	4(2.5%)
Fatty liver (unexplained)	2	-	-	2(2.5%)
Galactosemia	1	-	-	1(1.25%)
Viral hepatitis	-	-	1	1(1.25%)
Kwashiorkor + pulmonary Tuberculosis	-	1	-	1(1.25%)
Dubin Jhonson sy	-	-	1	1(1.25%)
Normal histology		1	1	2(2.5%)
Non informative	2			2(2.5%)
Total	53(66.2%)	15(18.8%)	12(15%)	80(100%)

Neonatal hepatitis was diagnosed in a similar incidence as with Ahmed et al[2], and Monajemzadeh et al.[9] While the diagnosis of extra hepatic biliary atresia was lower in our series, 6.25%, in contrast to Ahmed et al 20%, and 11.8% in the Omani series[14], our people do not accept suggestions easily for surgical interventions in young babies, this is why they probably do not accept referrals for such reasons.
There were 6 cases with autoimmune hepatitis, forming 7.5%, which is close to Yachha et al in his Indian study, that found a 5% incidence in children[15], and a 4, 5 incidence in adults with chronic liver disease.[11] There was one child with pulmonary tuberculosis and features of Kwashiorkor disease, her liver biopsy showed fatty changes, with no evidence of granuloma.

Malignant liver diseases were dealt with by fine needle aspirate, rather than blind liver biopsy. In general congenital errors of metabolism, including storage disorders formed the largest proportion of pediatric chronic liver diseases, followed by familial intrahepatic cholestasis, those familial problems dominated the etiological list of pediatric chronic liver diseases, probably more than acquired problems, liver biopsy was a valuable aid in the diagnosis and improving expertise in the pediatric practice is mandatory.

REFERENCES

1. Delago-Borrego AD, Gonzalez-Peralta RP. Liver disease in children (Books and media reviews). JAMA 2008;299(9):1076-1077.
2. Ahmad M, Afzai S, Roshan E, Mubarik A, Bano S, Khan SA, et al. Usefulness of needle biopsy in the diagnosis of pediatric liver disorders. J Pak Med Assoc 2005;55:24-8.
3. Sherlock S. Diseases of the liver and biliary system: Needle biopsy of the liver. 8th ed. Boston, Melbourne: Blackwell Scientific Publications,1989:36-48
4. Valori R, Elias E. How to perform a percutaneous liver biopsy. Br J Hos Med 1989;42:408-409.
5. Gilmore IT, Burroughs A, Murray-Lyon IM, Williams R, Jenkins D, Hopkins A. Indication, methods, and outcomes of percutaneous liver biopsy in England and Wales: An audit by the British Society of Gastroenterology and the Royal College of Physicians of London. Gut 1995;36:437-441.
6. Lebensztejn DM, Kaczmarski M, Lotowska MS, Macha³a MB. Blind liver biopsy in children-diagnostic significance and complications in authors' own material. Med Sci Monit 2000;6(6):1155-1158.
7. Amaral JG, Swhartz J, Chait P, Temple M, John Ph, Smith Ch, et al. sonographically guided percutaneous liver biopsy in infants: A retrospective review. AJR 2006;187:W644-W649.
8. Barakat SH, El-Gendy W, Metwaly M, Mahfouz A. Chronic liver disease in children: An etiological study. Arch Dis of Child 2008;93:Pw565.
9. Monajemzadeh M, Tabriz HM, Mahjoub F, Fallahi G, Farahmand F. Liver needle biopsy in Iranian pediatric patients: Diagnostic significance and pattern of liver diseases. Indian J Path Micro 2009;52(1):10-13.
10. Muthuphei MN. Childhood liver disease in Ga-rankuwa hospital, South Africa. East Afri Med J 2000;77(9):508-509.
11. Obafunwa JO, Elesha SO. Childhood liver diseases in Jos, Nigeria: A retrospective histopathological study. Dept. of Pathology, University Teaching Hospital, Jos, Plateau State, Nigeria. East Afr Med J 1991;68(9):702-6.
12. Mackenjee MKR, Coovadia HM. Chronic liver disease in black children in Durban, South Africa. Ann Trop Paedi 2004;4:165-169.
13. Ramakrishna B, Date A, Kirubakaran C, Raghupathy P. The pattern of liver disease in Indian children: A review of 128 biopsied cases. Department of Pathology, Christian Medical College Hospital, Vellore, India. Ann Trop Paediatr 1993;13(2):159-63.
14. Akinbami FO, Venugopalan P, Nirmala V, Suresh J, Abiodun P. Pattern of chronic liver disease in Omani children- A clinicopathological review. West Afr J Med 2004;23(2):162-166.
15. Yachha SK, Sharma BC, Khanduri A, Srivastava A. Current spectrum of hepatobiliary disorders in Northern Indian. Pediatrics 1997;(34):885-890.
16. Monika J, Rawal KK, Sarin SK. Profile of autoimmune liver disease in India. Indian J Gastroenterol 1994;13(Suppl 1):A85.