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Epidemiology and Laboratory Investigations in Children with Chronic Liver Diseases in Sohag University Hospital

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ABSTRACT

Background: Chronic liver diseases encompasse metabolic, genetic, drug-induced and inflammatory diseases. The causes of liver disease in children vary with age. In countries where HBV is endemic, perinatal transmission remains the most important cause of chronic infection. The prevalence of hepatitis C infection was much higher in individuals receiving blood products for conditions such as thalassemia or haemophilia. Glycogen storage disorders may present with chronic liver disease.

Objectives: To study epidemiological features and laboratory investigations that may affect the incidence in children with chronic liver disease.

Patients and methods: Our study included 30 treatment-naïve patients with chronic liver disease of different aetiologies referred to the Department of Pediatrics, Sohag University Hospital. All patients were subjected to history taking, general and local examinations, laboratory investigations and measurement of serum ceruloplasmin.

Results: The mean age of children was 10.23 years in case group and 10.75 years in control group, ranging between 5.5 to 15 years. The majority of patients were females (53.3%) and the remained patients were males (46.7%). There was significant difference between patient and control groups as regard total leucocytic count. Also, there were significant differences between the two groups regarding ALT, AST, total bilirubin, direct bilirubin and concentration and high significant differences regarding serum albumin and prothrombin time.

Conclusion: Total leucocytic count, AST, ALT, bilirubin, and serum albumin concentration, and prothrombin time are significant investigations to rule out diagnosis and anticipate complications in patients with chronic liver diseases. ALT and PT are early sensitive markers that anticipate liver decompensation.

Keywords: Children, Chronic liver diseases, Epidemiology, Laboratory.

INTRODUCTION

Chronicity of liver disease is determined either by duration of liver disease (typically >3–6 months) or by evidence of either severe liver disease or physical stigmata of chronic liver disease (clubbing, spider telangiectasia and hepatosplenomegaly) [(1)].

The severity is variable; the affected child may have only biochemical evidence of liver dysfunction, may have stigmata of chronic liver disease, or may present in hepatic failure. Chronic liver disease may be caused commonly by persistent viral infections, metabolic diseases, drugs, autoimmune hepatitis, or unknown factors [(2)].

The causes of liver disease in paediatric patients vary with age. Some are associated with certain age groups, such as biliary atresia and idiopathic neonatal hepatitis, which are observed only at birth or shortly thereafter. Conversely, acetaminophen intoxication and Wilson disease are typical of older children, especially adolescents [(3)]. In countries where HBV is endemic, perinatal transmission remains the most important cause of chronic infection. Perinatal transmission also occurs in non-endemic countries, including the United States, mostly in children of HBV infected mothers who do not receive appropriate HBV immunoprophylaxis at birth [(4)].

The prevalence of Hepatitis C infection was much higher (50–95%) in individuals who received blood products for conditions such as thalassemia or haemophilia before 1990 (when a first-generation ELISA test became available and routine screening of the blood supply began) to as late as 1992 (when the second-generation ELISA test was introduced) [(5)]. Seroprevalence rates of 10–20% have been reported among children with a variety of other potential exposures such as malignancy, haemodialysis, extracorporeal membrane oxygenation, or surgery for congenital heart disease [(6)].

Glycogen storage disorders may present with chronic liver disease. Patients with the autosomal recessive liver-specific type may develop cirrhosis [(7)]. The hepatic injury in Wilson disease is believed to be caused by excess copper, which acts as a pro-oxidant and promotes the generation of free radicals [(8)].

The aim of this work was to study epidemiological features like age, gender and anthropometric measures that may affect incidence or prevalence in children with chronic liver disease and to laboratorily investigate children suspected to have chronic liver disease, which helps to diagnose and clarify aetiology, anticipate complications and compare it in cases and control.

PATIENTS AND METHODS

This hospital-based cross-sectional comparative study included 30 patients with chronic liver disease of different aetiologies, aged from 4 to 16 years.

In addition, 10 healthy subjects were included in the study as a control group.

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The study was carried out in the Department of Pediatrics, Sohag University Hospital in a study period of two years.

Inclusion criteria:

All patients suspected to have chronic liver disease aged 4-16 years at Pediatric Department Hepatology Clinic through comprehensive history taking, meticulous clinical examination and different laboratory investigations.

Exclusion criteria:

Patients or their caregivers who refused to give informed written consent to enroll in the study, and patients with decompensated liver or kidney diseases.

All patients were subjected to: History taking. General and local examinations. Anthropometric measurements (weight, height and body mass index (BMI)). Laboratory investigations including complete blood count (CBC), complete liver function tests, coagulation profile and serology for hepatitis B (hepatitis B surface antigen, HBsAg and PCR) and hepatitis C (Hepatitis C antibody and PCR) serology for autoimmune diseases as anti liver-kidney microsomal antibodies, anti smooth muscle antibodies, total immunoglobulin and antinuclear antibodies when suspected, and serum ceruloplasmin.

Ethical consent:

The study was approved by the Ethical Committee of the Faculty of Medicine, Al-Azhar University. Informed written consent was obtained from parents of all participant children before recruitment in the study, after explaining the objectives of the work. Confidentiality was guaranteed on handling the data base. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) was used to calculate difference between groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation), and range. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data) and Mann-Whitney test was used when abnormally distributed (non-parametric).

P-value < 0.05 was considered significant and <0.001 was considered highly significant.

RESULTS

Table (1) shows the demographic data of our 40 studied children. As regard gender and age, the difference between the 2 groups was insignificant.

Table (1): Comparison between the studied group regarding demographic characteristics

Demographic characteristics	Groups		p
	Case group N=30 (%)	Control group N=10 (%)	
Gender:			
Male	14 (46.7)	5 (50)	0.855
Female	16 (53.3)	5 (50)	
Age (years):			
Mean ± SD	10.23 ± 2.87	10.75 ± 2.76	0.622
Range	5.5 - 15	5.5 - 15	

Table (2) shows the anthropometric measures of our 40 studied children. Body weight ranged between 22 and 56 kg in case group with mean body weight of 30.87 kg and between 24 and 50 kg in control group with mean of 37.7 kg. The weight of patient group was lower than in control group, with a statistically significant difference between the studied groups. Body mass index ranged between 12.82 and 21.88 kg/m^2 in case group with mean BMI of 16.8 kg/m^2 and between 14.27 and 22.96 kg/m^2 in control group with mean of 18.72 kg/m^2. BMI of patient group was lower than in control group, with a statistically significant difference between the studied groups.

Table (2): Comparison between the studied group regarding anthropometric measures

Anthropometri measures	Groups		p
	Case group N=30 (%)	Control group N=10 (%)	
Weight (kg): Mean ± SD	30.87 ± 9	37.7 ± 9.51	0.047*
Height (cm): Mean ± SD	134.27 ± 12.09	140.9 ± 12.23	0.142
BMI (kg/M^2) Mean ± SD	16.8 ± 2.12	18.72 ± 2.67	0.026*

*: Statistically significant

Statistically, there was non-significant difference between the studied groups regarding presence of hepatitis B or C (table 3).

Table (3): Comparison between the studied groups regarding serology

Demographic characteristics	Groups		p
	Case group N=30 (%)	Control group N=10 (%)	
Hepatitis B			
No	22 (73.4)	10 (100)	0.168
Yes	8 (26.4)	0 (0)	
Hepatitis C			
No	30 (100)	10 (100)	1
Yes	0 (0)	0 (0)	

Table (4) shows CBC findings of the studied cases. Statistically, there was significant difference between patient group and control group as regard total leucocytic count, while no significance was found as regard hemoglobin level or platelet count.

Table (4): Comparison between the studied group regarding CBC findings

CBC	Groups		p
	Case group N=30 (%)	Control group N=10 (%)	
TLC (10^3/mm^3): Mean ± SD	7.18 ± 1.93	8.85 ± 1.92	0.047*
Hemoglobin (g/dl): Mean ± SD	10.67 ± 1.24	12 ± 1	0.142
Platelet count (10^3/mm^3) Mean ± SD	197.67 ± 17.56	251.5 ± 7.65	0.381

*: Statistically significant

Table (5) shows liver function tests and coagulation parameters of the studied cases. Statistically, there were significant differences between the studied groups regarding ALT, AST, total bilirubin, direct bilirubin concentration and high significant differences regarding serum albumin and prothrombin time.

Table (5): Comparison between the studied group regarding liver function test and coagulation parameters

Parameters	Groups		p
	Case group N=30 (%)	Control group N=10 (%)	
ALT (U/L): Mean ± SD	76.4 ± 9.14	21.5 ± 5.24	0.036*
AST (U/L): Mean ± SD	90.53 ± 19.22	18.7 ± 4.36	0.005*
Total bilirubin (mg/dl) Mean ± SD	1.001 ± 0.67	0.5 ± 0.07	0.003*
Direct bilirubin (mg/dl) Mean ± SD	0.29 ± 0.04	0.12 ± 0.06	0.003*
Serum albumin: Mean ± SD	3.51 ± 0.58	4.36 ± 0.5	<0.001**
Prothrombin time (sec) Mean ± SD	12.44 ± 0.78	11 ± 0.87	<0.001**
Prothrombin concentration Mean ± SD	85.34 ± 10.7	91.4 ± 5.62	0.029*

*: Statistically significant, **: Statistically highly significant

DISCUSSION

Chronic liver disease encompasses a wide spectrum of disorders, including infectious, metabolic, genetic, drug induced, idiopathic, structural, and autoimmune diseases. The initial clinical presentation and laboratory workup in many of these diseases may be similar, and a definitive diagnosis is often made by specialized laboratory investigations and histologic examination of liver tissue where indicated [(1)]. The etiology of liver fibrosis in children differs from the adult population. Pediatric patients more often suffer from rare congenital liver diseases, genetically defined disorders or metabolic diseases than from chronic viral hepatitis [(1)].

In our study, we aimed at studying epidemiological features like age, gender, anthropometric measures that may affect incidence or prevalence in children with chronic liver disease and to laboratorily investigate children suspected to have chronic liver disease, which helps to diagnose and clarify aetiology, anticipate complications and compare cases and control.

Our study included 30 patients with chronic liver disease of different aetiologies and 10 healthy subjects as a control group.

Our study showed that there was non-statistically significant difference between the studied groups as regarding either age or gender. Mean age was 10.23 ± 2.87 years in case group (14 males and 16 females) and 10.75 ± 2.76 years in control group (5 males and 5 females). **Schenk *et al.* [(9)]** determined the value of sonoelastography in pediatric liver diseases in comparison with liver biopsy in 34 children (17 females and 17 males, mean age, 10.53 ± 5.66 years). Similar results were presented by **Sönmez *et al.* [(10)]** who studied the role of share-wave elastography (SWE) in terms of diagnostic value in children diagnosed with chronic liver disease. Their study included 81 patients with chronic liver disease and 26 healthy cases. The maximum age of the patients who participated in the study was 17 years.

Our study showed the anthropometric measures of our 40 studied children. The weight of patient group was significantly lower than in control group. The mean of body mass index in case group was 16.8 kg/m^2 and in control group was 18.72 kg/ m^2. BMI of patient group was significantly lower than in control group. **Moran-Lev *et al.* [(11)]** found that mean body mass index [BMI] was 38.8±9.7 in obese children and adolescents with NAFLD and revealed that a higher BMI carries a greater risk for advanced liver fibrosis in pediatrics.

In our study, six patients within case group had hepatitis B infection (positive HbsAg) while no one of them had hepatitis C, all participants within control group had neither positive HbsAg nor HCV antibodies. Statistically, there was non-significant difference between the studied groups regarding presence of hepatitis B or C. **Bellentancil *et al.* [(12)]** found that among the 1,473 patients who were classified as having liver disease, 167 (2.4%) were positive for HBsAg or HCV antibody positive (healthy carriers).

In our study, there was significant difference between patient group and control group as regard total leucocytic count, while no significance was found as regard hemoglobin level or platelet count.

Also, there were significant differences between the studied groups regarding ALT, AST, total bilirubin, direct bilirubin concentration and high significant differences regarding serum albumin and prothrombin time.

Ventureira *et al.* [(13)] analyzed the follow-up of patients with hypertransaminasaemia and without apparent liver disease. The follow-up of most children with elevation of ALT in the absence of apparent liver disease was inadequate, especially in those with mild elevation. This constitutes a missed opportunity for the early diagnosis and treatment of potential liver disease in a large number of children. All children with unexplained hypertransaminasaemia should undergo evaluation with application of consensus based thresholds and with a standardised approach.

CONCLUSION

Total leucocytic count, AST, ALT, total and direct bilirubin, serum albumin and prothrombin time and concentration are significant and important investigations to rule out diagnosis and anticipate complications in patients with chronic liver diseases. ALT and PT are early sensitive markers that anticipate liver decompensation.

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