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Pediatric Chronic Liver Diseases: A Clinicopathological Study from a Tertiary Care Center

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Abstract

Background

Chronic liver diseases (CLD) in children represent a growing health problem with significant morbidity and mortality. This study aimed to define the clinicopathological pattern of pediatric CLD in Sohag University Hospital, Sohag,Upper Egypt.

Materials and Methods

A total of 151children with CLD were included in a prospective hospital-based study from June 2014 to May 2018. Cases of acute liver illness or hepatic focal lesions were excluded. All patients were subjected to detailed history and thorough physical examination. Abdominal ultrasonography, CBC, liver function tests, viral serology, evaluation of autoantibodies for autoimmune hepatitis, and liver core biopsies were performed for all children.

Results

Pediatric CLD comprised 1.6% of total admissions in pediatric department. Neonatal cholestasis disorders (NCD), and metabolic liver disorders (MLD) were the leading causes of CLD (41.05% and 35.1%, respectively). NCD comprised neonatal hepatitis (25.1%), extrahepatic biliary atresia (13.2%), and paucity of interlobular bile ducts (2.7%). MLD included glycogen storage disease (26.5%), undetermined inborn error of metabolism (5.3%), Gaucher's disease (2.0%), and Niemann Pick disease (1.3%). Other causes of CLD comprised autoimmune hepatitis (8.6%), congenital hepatic fibrosis (5.9%), non-alcoholic fatty liver disease (4.0%), chronic hepatitis C infection (2.7%), and Budd Chiari disease (0.6%). On follow-up of 89 cases, stationary clinical course, clinical improvement, and clinical deterioration were seen in 52.8%, 34.8%, and 12.3% of them, respectively.

Conclusion

The rate of CLD is growing in Upper Egypt and is mainly caused by neonatal cholestasis and metabolic liver disorders. In general, the outcome of children is favorable and comparable to other countries.

Key Words: Children, Chronic liver diseases, Cholestasis, Egypt, Metabolic liver disorders.

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1- INTRODUCTION

Chronic liver diseases (CLD) in children represent a growing health problem with significant morbidity and mortality (1). The exact prevalence of pediatric CLD is unknown , though, in the United States, it has been reported that CLD is the cause of hospitalization of about 15,000 children every year (2). Pediatric liver diseases comprise a wide variety of disorders, including infections, developmental abnormalities, genetic, and metabolic disorders that ultimately result in progressive alterations in structure of liver and may end in cirrhosis and its consequences (3). Liver disorders which affect children are unique and different from those of adults and involve different groups of acute and chronic disorders.

The spectrum of pediatric liver diseases, especially those with genetic and metabolic etiologies, show variation according to geographical locations. This encourages studies on various features of pediatric liver diseases in different countries and communities (4). There is age dependent variation in causes of CLD. In the first years of life, biliary atresia, choledochal cysts, congenital hepatic fibrosis, galactosemia, Tyrosinemia, and alpha one antitrypsin deficiency are frequent causes of CLD. In older children etiologies of CLD include chronic viral hepatitis C and B, autoimmune hepatitis, Wilson's disease, cystic fibrosis and Primary sclerosing cholangitis (PSC) (5).

Recently, non-alcoholic fatty liver disease (NAFLD) has been described as a common cause of CLD with a pooled mean prevalence of 7.65 % in all children, and 34% in obese children (6). It is worth mentioning that the etiology of liver disease cannot be determined in 5-15 % of children with cirrhotic liver (7). The approach to the diagnosis and management of CLD has been revolutionized by the advent of better radiological diagnostic techniques, recent advances in the serodiagnosis of hepatotropic viruses, autoimmune markers and improved liver biopsy technique. Although being an invasive tool, histopathological evaluation of liver biopsy is still considered the cornerstone for diagnosis of CLD (8). Recently, non-invasive methods have been proposed for the assessment of CLD including transient liver elastography and biological markers that could help in assessment of liver fibrosis (5).

CLD in children are the precursors of adult liver disease. Knowledge of exact burden of CLD in children is important for health policy making by the government and its cost effective implementation, especially in developing countries (4). This study aimed to evaluate clinical pattern, pathological pattern and outcome of pediatric CLD in a tertiary care hospital in Upper Egypt.

2- MATERIALS AND METHODS

2-1. Study design and population

This was a prospective hospital-based study conducted in Pediatric Department, Sohag University Hospital, a tertiary care hospital in Upper Egypt, in the period from June 2014 to May 2018. All children presented with diffuse chronic liver diseases were included in the study. Patients were recruited from pediatric gastroenterology clinic and pediatric department. Cases with acute liver disease and those with solitary or multiple hepatic focal lesions were excluded from the study.

2-2. Ethical Consideration

The protocol of the study was approved by Sohag Faculty of Medicine Ethics Committee in accordance with international agreements. Written informed consent was obtained from parents of all participants.

2-3. Inclusion and exclusion criteria

All children presented to pediatric department with manifestations of chronic liver diseases were included in the study. Patients with acute liver disease and those with solitary or multiple hepatic focal lesions were excluded from the study.

2-4. Methods

All patients were subjected to detailed history with emphasis on symptoms suggesting liver diseases and assessment of risk factors associated with hepatic disorders. A thorough physical examination was done to detect the manifestations of hepatobiliary diseases. Biochemical and hematological investigations were performed for all patients including complete blood count (CBC), liver function tests including serum level of bilirubin (total and fractionated), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase, gamm-glutamyl transpeptidase (GGT), prothrombin (PT) time, partial thromboplastin time (PTT), International Randomization Ratio (INR), urine analysis, reducing substance in urine, and thyroid function tests. Serological investigations like hepatitis B surface antigen (HBs Ag), hepatitis C virus (HCV) antibody, and hepatitis A virus IgM antibodies were done whenever necessary.

Gammaglobulin level, anti-smooth muscle antibody (ASMA), anti- liver kidney microsomal (Anti LKM) antibody levels were evaluated in children suspected of autoimmune hepatitis. Abdominal ultrasonography was done for all patients to assess liver size and echo pattern. In cases with cholestasis, 4 hours fasting is required before ultrasonography to detect abnormalities of gall bladder or presence of Choledochal cysts. Hepatobiliary scintigraphy (HBS) using hepatobiliary iminodiacetic acid (HIDA) was done when indicated. Liver core biopsies were obtained from all children after assurance of normal coagulation profile. Hematoxylin and Eosin (H & E) stained sections were prepared for pathological diagnosis of liver biopsies, and Gomori trichrome-stained sections were prepared for accurate assessment of hepatic fibrosis.

2-5. Statistical analysis

IBM-SPSS (22.0 for Windows) software version was used for data analysis and P-value <0.05 was considered significant. Categorical variables were demonstrated as number and percentages while continuous variables were summarized as mean (±standard deviation [SD]) and median. The frequency of observations among different categories was measured by Chi-Square test, difference among two continuous variables was evaluated by Mann-Whitney U test and difference among three or more continuous variables was evaluated by Kruskal-Wallis test.

3- RESULTS

This study included 151 children with diffuse liver diseases presented to Pediatric Department, Sohag University Hospitals, Upper Egypt between June 2014 and May 2018. Ninety-six (63.5 %) of the investigated children were boys and 55 (36.5 %) were girls. The age at diagnosis ranged between 0.5 and 144 months with mean (±SD), and median values of 20.4 (± 27.6), and 9.0 months, respectively. Two thirds of the children (n=100) fall in the age range of 1 to 24 months, 10 were neonates (28 days or younger), and 41 were older than 24 months.

The vast majority of children (n=147) had a full-term gestational age, and only four were preterm. Consanguinity among parents was reported in 47% (71/151) of the children. The clinical, sonographic and laboratory findings are summarized in **Table.1**. The main clinical presentation was abdominal distention and jaundice. History of failure to thrive, epistaxis, hematemesis, acholic stool, and itching was given in 6, 1, 1, 34, and 3 patients, respectively. Diabetes millets, pulmonary

stenosis, hydrocephalus, microcephaly, and purpura were reported in one patient each. Family history of glycogen storage disease and previous history of neonatal deaths were reported in 5 (3.3%), and 2 (1.3%) patients, respectively. Nearly 1/3 of the patients (31.8%, n=48) have microcytic hypochromic anemia with no other significant hematological abnormalities. Liver enzymes were raised in 124 (82.1%) of the cases, of which 6 and 8 patients had ALT, and AST values above 500 IU/L, respectively. Serum total bilirubin was raised in 71 (47%) children, of which 62 had direct hyperbilirubinemia and 9 children had combined direct, and indirect hyperbilirubinemia. Significant rise of serum total bilirubin above 10mg/dl was recorded in 20 (13.3%) of the children and the serum level of GGT was evaluated in 49 cases.

Table-1: Clinical evaluation and biochemical parameters of investigated cases

Parameter	**Statistic**	
Presentation		
- Abdominal distention	Number (%)	71 (47.0)
- Jaundice	Number (%)	40 (26.5)
- Abdominal distention and jaundice	Number (%)	34(22.5)
- Acholic Stool	Number (%)	32 (21.2)
- Epileptic fits	Number (%)	5 (3.3)
- Dark urine	Number (%)	3 (2.0)
Clinical evaluation and US findings		
- Weight (kg)	Mean (±SD) and median	9.8 (±5.9) and 8.0
- Hepatomegaly	Number (%)	61 (40.4)
- Hepatosplenomegaly	Number (%)	49 (32.5)
- Ascites	Number (%)	5 (3.3)
- Dilated portal vein	Number (%)	1 (0.7)
- Liver coarse echo pattern	Number (%)	9 (5.9)
- Liver fibrosis / cirrhosis	Number (%)	3 (2.0)
- Non-visualized gall bladder	Number (%)	4 (2.6)
Laboratory investigations:		
- Serum ALT (n=151)	Mean (±SD) and median	208 (±179) and 185
- Serum AST (n=151)	Mean (±SD) and median	217 (±177) and 192
- Serum total bilirubin (n=151)	Mean (±SD) and median	4.2 (±3.9) and 1.2
- Serum direct bilirubin (n=151)	Mean (±SD) and median	3.2 (±3.6) and 0.2
- Serum GGT (n=57)	Mean (±SD) and median	185 (±163) and 90
- Positive anti-smooth muscle antibody	Number (%)	13 (8.6%)
- Cytomegalovirus positive	Number (%)	4 (2.6)
- Hepatitis C virus positive	Number (%)	3 (2%)

SD: Standard deviation; GGT: gamma-glutamyl transpeptidase; ALT: alanine transaminase; AST: aspartate transaminase.

Based on liver biopsy, chronic hepatitis was the most frequent cause of diffuse liver insult in this study, representing 37.1% followed by metabolic liver diseases, while Budd Chiari disease and end stage liver cirrhosis were reported in one case each (**Table.2)**. Among cases of hepatitis, idiopathic neonatal hepatitis tends to present clinically at a significantly younger age compared to autoimmune hepatitis (p<0001).

Table-2: Histopathological diagnosis of the investigated cases

Disease	Number (%)	Age (months)	Gender	
		Mean (±SD)/median	Male	Female
Chronic hepatitis:	**56 (37.1)**			
- Neonatal (idiopathic)	38 (25.1)	3.7 (±6.1)/2	25	13
- Autoimmune	13 (8.6)	39.7 (±26.5)/36	7	6
- Viral	4 (2.7)	56 (±33.8)/50	2	2
- Drug induced	1 (0.7)	NA	1	0
		P<0.0001	P=0.44	
Metabolic diseases:	**53 (35.1)**			
- Glycogen storage disease	40 (26.5)	29.4 (±26.5)/24	30	10
- Other metabolic diseases	13 (8.5)	17.8 (±11.3)/15	8	5
. Gaucher's disease	- 3(1.9)	P=0.22	P=0.35	
. Niemann Pick Disease	- 2(1.3)			
. Undetermined	- 8(5.3)			
Obstruction of bile pathway:	**24 (15.9)**			
- Major bile duct obstruction	20 (13.2)	3.87 (±2.7)/3	12	8
- Paucity of bile ductules	4 (2.7)	7.1 (±6.5)/6	2	2
		P=0.31	P=0.71	
Hepatic fibrosis:	**10 (6.6)**			
- Congenital hepatic fibrosis	9 (5.9)	46.4 (49.5)/15	4	5
- Parasitic portal tract fibrosis	1 (0.7)	NA	0	1
Hepatic steatosis	6 (4.0)	8.3 (±2.2)/8	4	2
Budd Chiari disease	1 (0.7)	NA	1	0
Biliary cirrhosis	1 (0.7)	NA	0	1

SD: standard deviation; NA: not applicable.

Statistically, serum levels of ALT and AST were significantly higher in cases of chronic hepatitis compared to other diffuse liver diseases (**Figure 1 A and B**), and serum levels of total and direct bilirubin were significantly higher in cases of biliary obstruction and chronic hepatitis compared to metabolic liver diseases and hepatic fibrosis (**Figure 1 C and D**). Serum GGT showed a significant high level in cases of extra hepatic biliary atresia compared to cases of neonatal hepatitis (Mann-Whitney U, p<0.0001). The mean (±SD), and the median values of GGT in cases of extra hepatic biliary atresia were 352 IU (±151), and 384 IU compared to 80 IU (±25.5), and 79 IU in cases of neonatal hepatitis. In the current study, the main causes of diffuse liver disease were chronic hepatitis, metabolic disorders and biliary obstruction representing collectively 88.1% of the cases. Histological parameters that reflect degree of liver cell damage in these cases **(Figure.2)** was evaluated and compared **(Table.3)**. Piecemeal necrosis was detected in 11 cases; most of which had chronic hepatitis. Associated hepatic steatosis was identified in 19 tissue samples; 10 of which showed steatosis of more than 25% of hepatocytes. Moderate to severe hepatic inflammation was detected in 37 (24.5%) cases; while giant cell change of hepatocytes was observed in 25 tissue samples, and it was strongly associated with chronic hepatitis. Hepatic fibrosis and loss of liver architecture, both of which reflect irreversible liver damage are significantly more frequent in cases of biliary obstructive disease.

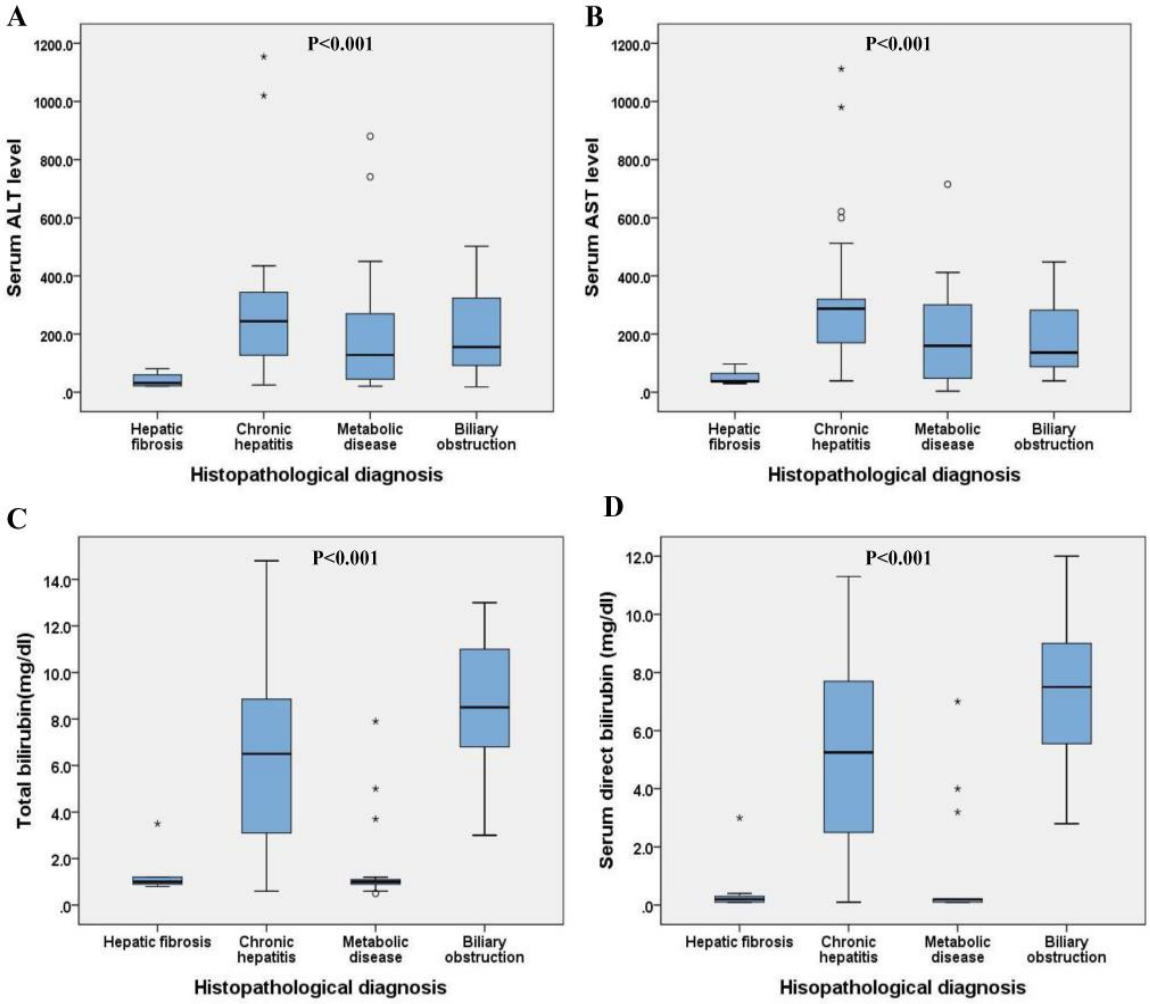

Fig.1: The main biochemical parameters in different patterns of CLD of investigated cases.

Table-3: Main pathological findings among frequent diffuse liver diseases of this study.

Disease	Chronic hepatitis Number (%)	Metabolic liver disease Number (%)	Biliary obstruction Number (%)	P- value
- **Hepatic necrosis**				
- Absent	47 (83.9)	52 (98.1)	23 (95.8)	0.02
- Detected	9 (16.1)	1 (1.9)	1 (94.2)	
- **Associated steatosis**				
- Absent	52 (92.8)	40 (75.4)	22 (91.6)	0.23
- Detected	4 (7.2)	13 (24.6)	2 (8.4)	
- **Hepatic inflammation**				
- No/mild	37 (66)	45 (84.9)	14 (58.3)	0.022
- Moderate/severe	19 (34)	8 (15.1)	10 (41.7)	
- **Giant cell change**				
- Absent	35 (62.5)	52 (98.1)	21(87.5)	0.0001
- Detected	21 (37.5)	1 (1.9)	3 (12.5)	
- **Hepatic fibrosis**				
- No/mild	48 (85.7)	48 (90.5)	8 (33.3)	0.0001
- Moderate/marked	8 (14.3)	5 (9.5)	16 (66.7)	
- **Liver architecture**				
- Preserved	50 (89.2)	50 (94.3)	14 (58.3)	0.001
- Distorted	6 (10.8)	3 (5.7)	10 (41.7)	

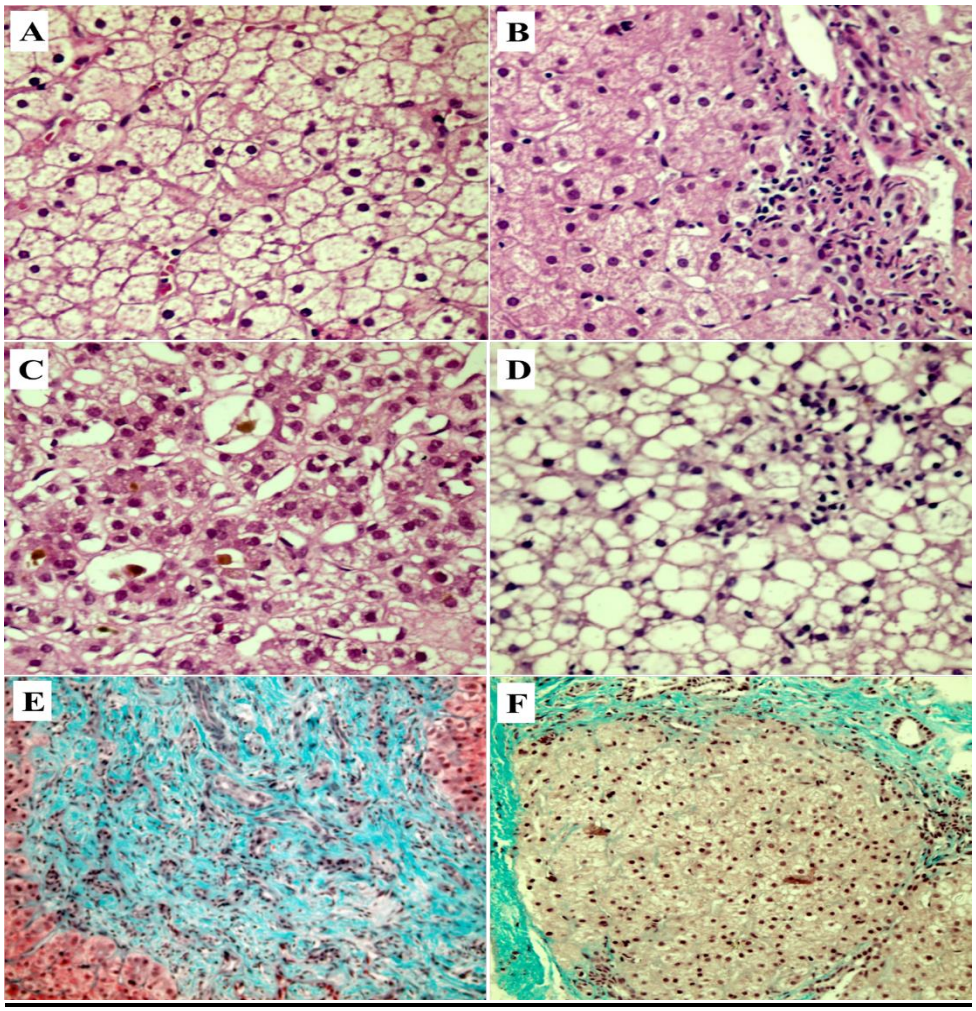

Fig.2: Histopathological patterns of investigated cases. Ballooning of hepatocytes, rarified cytoplasm and compressed sinusoids in glycogen storage disease (A), piecemeal necrosis and portal inflammation in chronic hepatitis (B), canalicular bile retention in biliary atresia (C), Macrovesicular hepatic steatosis (D), broad fibrous septum in congenital hepatic fibrosis (E) and regeneration nodules with distorted architecture in end stage biliary cirrhosis (F). H&E stained sections (A, B, C and D) and Gömöri trichrome stained sections (E and F); magnification is x400 for A, B, C and D and x200 for E and F.

All children included in this study had received supportive treatment in the form of vitamin A, D, E, and K. Additional individualized treatment based on clinical condition included: prednisolone, ursodeoxycholic acid, azathioprine, and Inderal in 5, 2, 1 and 1 patients, respectively. Children with glycogen storage disease received uncooked starch. Children with extrahepatic biliary atresia were re-evaluated for the benefit of surgical intervention, and only 8 of these cases underwent Kasi operation. Long term follow-up was available in 89 children with lost follow-up for the remaining cases. The mean (±SD) follow up duration was 14.2 (±11.5) months and the median was 12 months. Forty-seven children showed stationary clinical course while improvement and deterioration of clinical status were reported in 31 and 11 children, respectively **(Table.4)**.

Table-4: Outcome of diffuse hepatic liver diseases of investigated children

Disease	Patients` outcome, Number (%)			Total
	Improvement	Stationary	Deterioration	
- Chronic Hepatitis	23 (74.1)	7(22.5)	1(3.4)	31
- Metabolic diseases	5 (14.3)	28(80)	2(5.7)	35
- Biliary obstructive	3 (21.4)	4(28.6)	7(50)	14
- Congenital fibrosis	0	5(100)	0	5
- Hepatic Steatosis	0	2(100)	0	2
- Budd Chiari disease	0	1(100)	0	1
- Biliary cirrhosis	0	0(0)	1(100)	1
Total	31	47	11	89

4- DISCUSSION

The aim of this study was to define the clinicopathological pattern and the outcome of pediatric CLD in Sohag University Hospital, Upper Egypt. Neonatal cholestasis disorders (NCD), and metabolic liver disorders (MLD) were the leading causes of CLD (41.05% and 35.1%, respectively). In this 4-year study, 151 infants and children (aged from 15 days to 12 years) were diagnosed with CLD. They represent 1.6 % (151/9097) of total admissions in pediatric department during the same period. This finding was in agreement with Dhole et al., whereas they reported that CLD constitute 1.1 % of total admission (9). So, a very high index of suspicion is required for diagnosis of CLD. Male predominance (63.5%) in the current study was consistent with other studies that reported male predominance from 58% to 69 % in children with CLD (8-10). Contrary to our results, Dar et al. reported female predominance (55%) in children with CLD (11).

The main clinical presentations in this study were jaundice, abdominal distension (47%), jaundice (26.5%), acholic stool (21.2%), hepatomegaly (40.4%), and hepatosplenomegaly (32.5%). These findings were similar to what has been reported by other studies (9-12). The etiological spectrum of CLD varies according to patients' age, geographical location of the study, prevalence of the disease, availability of diagnostic tools, experience of the physicians and referral pattern (12). In this series, neonatal cholestasis disorders (41.05%), and metabolic liver disorders (35.1%) were the leading causes of pediatric CLD. Similar pattern was reported by Akinbami et al. (13) in a study of CLD in Omani children whereas they demonstrated that neonatal cholestasis constituted 50% of CLD. Also, metabolic liver disease accounted for 36%, and 36.5% of CLD in 2 studies from Pakistan (8, 14). In addition, Sathe (15), in a study from Western India, reported that metabolic liver disease constituted 41.2 % of CLD cases. Contrary to our results, Rajeshwari and Gogia (12) reported that cryptogenic cirrhosis was the main cause of CLD in children referred to a tertiary care hospital in New Delhi, India.

Authors explained this high incidence of cryptogenic cirrhosis by referral of undiagnosed cases from other hospitals and by the presence of unrecognized infective agent or metabolic causes. Also, Hanif et al, in a study from Karachi in Pakistan, reported that the main cause of chronic liver disease in children was chronic Hepatitis B. In addition, in a study from Nigeria, Obafunwa and Elesha reported that hepatic schistosomaias (37.5%) was the commonest etiology of childhood CLD in tropical countries due to high prevelance of infection by schistosoma (16). In the present study, neonatal cholestasis disorders comprised neonatal hepatitis (25.1% of CLD), extrahepatic biliary atresia (13.2% of CLD), and paucity of interlobular bile

ducts (2.7% of CLD). These results were in agreement with Akinbami et al. (13) as they demonstrated that neonatal hepatitis was found in 28.9% of children with CLD followed by EHBA in 11.8 % of cases then paucity of interlobular bile ducts in 9.2% of cases. Similar incidence of EHBA was reported by Cheema et al. (14) (13.4%) of cases, Narayan et al. (12.8%) of cases (4), and Sathe (10.3%) of cases (15). However, lower incidence of EHBA was reported by other studies ranging from 1.1% to 8.1% of CLD cases (8, 9, 12, 17-19). Also, other studies reported lower prevalence of NH ranging from 7.1% to 10% among causes of CLD (4, 9, 17). This variation can be explained by difference in the age of study groups.

Cases with neonatal hepatitis are managed medically, while in extrahepatic biliary atresia (EHBA) early surgical intervention by Kasai portoenterostomy (KPE) is required to improve the outcome of these cases (20). In this study almost all cases of NH received medical treatment in the form of vitamin A, D, E, and K, and responded well to treatment. Nine out of 20 (45%) cases of EHBA underwent KPE. Two of the operated infants (22.2%) had successful Kasi with establishment of bile flow, colored stool, and absent jaundice for one year after operation. Out of 7 (77.7%) infants with failed Kasi operation, 5 developed progressive liver disease, one died 2 months after operation, and one lost follow-up. Eleven cases with EHBA (55%) lost the chance for KPE due to late presentation, 6 of them had progressive liver disease and 5 lost follow- up. The outcome of Kasi operation for EHBA was compatible with the previously established records which show that a small proportion of infants with EHBA benefit from early Kasi operation, and approximately 60% of cases develop progressive liver disease (21). In the current study, metabolic liver disorders were diagnosed in 35.1% of CLD cases with glycogen storage disease as the commonest disorder, constituting 26.5% of CLD causes. Other metabolic liver diseases accounted for 8.65% of CLD cases and comprised Gaucher's disease (n=3), Niemann Pick disease (n=2), and 8 cases with undetermined inborn error of metabolism. These findings were in agreement with Hashmi et al. (8) who reported that metabolic disorders were found in 36.5% of pediatric liver disease patients, and glycogen storage disease was the most common metabolic disorder in (16.2%) of patients. Also, Cheema et al. (14) reported that metabolic disorders constituted 36 % of histological diagnosis of pediatric liver disease with glycogen storage disorder disease accounting for 13.7% of cases. In the study done by Sathe (15), metabolic liver disease constituted 41.2 % of CLD cases, with the most common being Wilson disease (n=15, 15.4%) followed by Gaucher's disease (n=10, 10.3%), and glycogen storage disorder (n =4, 4.1%), and Niemann Pick disease in one patient.

In this study, patients with glycogen storage disease received treatment with uncooked starch and showed a stationary course on follow-up. Autoimmune hepatitis was encountered in 13 (8.6%) of our cases. All of them were type I autoimmune hepatitis (had positive anti smooth muscle antibodies [ASMA] and negative liver kidney microsomal [LKM] antibodies). This is in agreement with Dhole et al. (9) who reported that the incidence of autoimmune hepatitis among patients with CLD was 10.9%, and Zhange et al. who demonstrated that autoimmune hepatitis was found in 7.1% of children with CLD (19). A higher incidence of autoimmune disease (16%) was reported by Hanif et al. (10), and a lower incidence (4%) was reported by Rajeshwari and Gogia (12). In the present study, out of 13 cases with autoimmune hepatitis, 7 cases improved on treatment with prednisolone,

one patient had a stationary course on treatment with prednisolone and azathioprine, and 5 cases lost follow-up with unrecognized outcome. Congenital hepatic fibrosis was diagnosed in 5.9% of our cases. This was in agreement with the study on Omani children whereas congenital hepatic fibrosis constituted 6.5% of CLD cases (13). However, Sobhan et al. (22) reported congenital hepatic fibrosis in 3.3% of CLD cases and in a Chinese study the frequency was 3.1% of cases (19). Out of 9 cases with congenital hepatic fibrosis, 5 had stationary course and 4 lost follow-up with unrecognized outcome.

Several recent studies have demonstrated the rising frequency of NAFLD in children (23-25).In the current study, NAFLD was diagnosed in 4% of cases. These cases had bright liver echo pattern by ultrasonography and elevated liver enzymes. Liver biopsy in these cases showed hepatic steatosis. Sobhan et al., reported that NAFLD was diagnosed in 16.5% of children with CLD (22). The difference in incidence may be explained by difference in age of the patients as most of our patients were below 2 years.

It has been estimated that chronic hepatitis C infection was found in 3% of children under 19 years of age in upper Egypt and 9% in lower Egypt (26). In this study hepatitis C infection was the cause of CLD in 4 (2.7%) patients. Rajeshwari and Gogia reported only one patient with chronic hepatitis C (12), and Hanif et al. reported no case with hepatitis C infection (10). This incidence was lower than what has been reported by Tahir et al (31.66%) (18), and (6.4%) reported by Dar et al. (3). Again, the difference may be explained by difference in age group, prevalence of the diseases and referral pattern. In this study, Budd Chiari disease was diagnosed in one patient who was lost to follow-up with unrecognized outcome. There are no reported cases of Wilson disease in our cases perhaps due to the young age of our cases, as the majority of cases were younger than 2 years of age and Wilson disease is a rare disease and usually manifests in older children (5, 15).

4-1. Limitation

This study has some limitations as it was a single center study, and many patients may be managed in other centers. Lack of investigations for metabolic and genetic diseases in our center is another limitation factor.

5- CONCLUSION

The rate of CLD is growing in Upper Egypt, in this 4-year study, 151 infants and children were diagnosed with CLD, representing 1.6 % of total admissions in pediatric department. The most common presentations were jaundice and abdominal distension. Neonatal cholestasis disorders and metabolic liver disorders were the leading causes of pediatric CLD. Other etiologies included autoimmune hepatitis, congenital hepatic fibrosis, NAFLD, and chronic hepatitis C infection. Budd Chiari disease was the least common etiology in this series. In general, the outcome of children is favorable and comparable to other countries.

6- CONFLICT OF INTEREST: None.

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