Acute Liver Failure In Children: Etiology, Clinical Manifestation, Outcome

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ABSTRACT:

BACKGROUND:

Pediatric acute liver failure (PALF) is a complex, rapidly progressive clinical syndrome that is the final common pathway for many disparate conditions, some known and others yet to be identified. Acute liver failure was first defined by Trey and Davidson as a potentially reversible condition caused by severe liver damage accompanied by encephalopathy <8 weeks of symptom onset and in the absence of preexisting liver disease.

OBJECTIVE:

To assess the etiology, prognosis and outcome of FHF in a sample of Iraqi child patients

PATIENTS AND METHODS:

A prospective study was done on (50) patients diagnosed with acute hepatic failure admitted to the Gastroenterology and Hepatology unit in Children Welfare Teaching Hospital during the period from January 2015 to the December 2015**.** The patients referred to our center from all over Iraq**,** Detailed history, clinical examination, routine biochemical parameters, and relevant tests were carried out to all patients. Patients enrolled in this study with the age less than 16 years old with the exception of neonate (< 1 month). The acute hepatic failure was diagnosed with prolonged PT, PTT, elevated liver function test and the disturbance of level of consciousness.

RESULTS:

Hepatitis A was found to be the commonest cause of encephalopathy and was diagnosed in 18/50 (36.0%) of cases, 56% of cases presented with GIT bleeding, 32% of them presented with melena. The worst outcome (100% mortality) was associated with sepsis, CMV infection, and biliary atresia, and best outcome was associated with Wilson disease (20% mortality). The poor prognosis was found in grade 3 and 4 of encephalopathy and 68% of child died.

CONCLUSION:

Hepatitis A is the most common cause of the FHF with high mortality rate. Bad prognosis was found in grade 3 and 4 of encephalopathy, with GI bleeding, longer duration of illness before onset of encephalopathy.

KEYWORDS Liver failure, clinical manifestation and outcome.

INTRODUCTION:

Pediatric acute liver failure (PALF) is a complex, rapidly progressive clinical syndrome that is the final common pathway for many disparate conditions, some known and others yet identified [1]. The updated definition of (ALF) includes a series of clinical and biochemical indicators: Biochemical evidence of acute liver injury, no prior chronic liver disease, and coagulopathy of hepatic origin (prothrombin time PT>20 seconds; or INR ≥1.5 not corrected by vitamin K with clinical encephalopathy; or INR >2.0, with or without encephalopathy). [2]. Symptoms may persist for days or weeks before the child is brought to medical attention. Jaundice, encephalopathy, and hepatomegaly are common. In infants, jaundice may be mild or absent, and the predominant symptoms are hypoglycemia, vomiting, refusal to eat, irritability, changes in sleep patterns, and seizures [3]. Specific etiologies of pediatric acute liver failure (PALF) can be broadly categorized as infectious, immunologic, metabolic, and toxin or drug-related.

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In more than 50 percent of patients, a specific cause is not discovered, for this reason, the PALF is categorized as indeterminate [4].

Management of PALF requires admission to a highly skilled nursing environment with the initial treatment includes minimizing excess stimulation, head elevation up to 30 degrees, initial restriction of protein intake, treating suspected sepsis, and, if possible, removing sedative medications that might affect mental status [5].

Prognostic criteria include patient's age, etiology of liver disease, degree and onset of encephalopathy, serum bilirubin level, prothrombin time (PT) or international normalized ratio (INR), serum creatinine level, factor V level, and arterial pH level[6].

Acute liver failure in children is a potentially devastating disease. The mortality rate may reach 80-90% in the absence of liver transplantation [7].

AIMS OF THE STUDY:

To study the etiologies, patterns of presentation and the methods of diagnosis of all liver diseases cases in children less than 16 years referred to the Gastroenterology and Hepatology Unit in Children Welfare Teaching Hospital over six months period.

MATERIALS AND METHODS:

A prospective study was done on (50) patients diagnosed with acute hepatic failure admitted to the Gastroenterology and Hepatology unit in Children Welfare Teaching Hospital during the period from January 2015 to the January 2016. The patients were referred to this center from all over Iraq.

Patients enrolled in this study were younger than 16 years old with the exception of neonate (< 1 month). And the acute hepatic failure was diagnosed as the summation of clinical and biochemical parameters, as follows:

- The acute onset of liver disease with no known evidence of chronic liver disease.
- Biochemical and/or clinical evidence of severe liver dysfunction:
  - hepatic-based coagulopathy, with a prothrombin time (PT) ≥20 s or international normalized ratio (INR) ≥2.0, that is not corrected by parenteral vitamin K
  - And/or hepatic encephalopathy (must be present if the PT is 15.0–19.9 s or INR 1.5–1.9, but not if PT ≥20 s or INR ≥2.0) with prolonged PT, PTT, elevated liver function test and disturbed of consciousness. [3]

All patients were evaluated with a detailed history and clinical examination on admission and the following investigations were done: CBP, Blood film, LFT, PT, PTT, total serum protein and S. albumin, RFT, RBS and CRP.

MS/MS metabolic screen, LSD (Lysosomal storage disease), hepatitis screen, IFAT for kala-azar, TORCH assay, immunoglobulin assay and autoimmune markers for AIH, 24 hour urine collection for copper, and serum ceruloplasmin were done on a selected group of patients according to their age group and clinical suspicion.

Radiological investigations included (chest X ray, ultrasound, CT or MRI) was done accordingly, liver biopsy could not be done because of the critical situation of all patients in the study group.

Statistical analysis:

Analysis of data was carried out using (Statistical Packages for Social Sciences- version 20). Standard Chi-square test was used to determine the associations between two categorical variables. Yates correction formula and fishers exact test were applied for chi-square test whenever it was needed. *P* value of less than 0.05 was considered as statistically significant.

RESULTS:

Hepatitis A was diagnosed in 18/50 (36%) of the studied group, undiagnosed patient 12(24%), Wilson disease in 5(10%), Sepsis 4 (8%), Kalaazar 4 (8%), CMV 3(6%), and Autoimmune hepatitis 2 (4%). Other diagnosis was reported in only one patient for each, these included (Hepatitis B, Herpes) 2(4%). (Table -1).

Regarding clinical presentation, melena was reported in 16 cases (32%) while hematemesis in only 4 cases (8%). On the other hand 8 cases (16%) had both hematemesis and melena. The remaining 22 cases (44%) had no GIT bleeding. (Table -2). Hepatitis A infection and sepsis were significantly associated with higher mortalities. Out of the 18 patients with hepatitis A infection only 5 (27.8%) had good prognosis and survived while 13 died (72.2%).

On the other hand none of the children with sepsis survived, mortality rate was 100% among those with sepsis. Higher mortality rates were also reported among cases with CMV and undiagnosed cases however, the differences didn't reach the statistical significance (P>0.05).
Fifty percent mortality rate was recorded in Kalaazar, Autoimmune hepatitis and other diseases (Hepatitis B, Herpes infection) showed fifty percent mortality rate with no statistical significance.

From other point of view, the best result was obtained in Wilson's disease, 4 cases (80%) survived compared to only one died(20%) (Table -3).
It had been significantly found that grade 3 and 4 encephalopathy had the poorest prognosis compared to grade 1 and 2, where all cases with grade 3 and 4 died while all cases with grade 1 and 2 had good prognosis (P<0.05) (table -4).

Table -1: Frequency distribution of the diagnoses

	Number (No.)	Percentage (%)
Hepatitis A	18	36.0
Wilson disease	5	10.0
Sepsis	4	8.0
Kalaazar	4	8.0
CMV	3	6.0
Autoimmune hepatitis	2	4.0
Others *	2	4.0
Undiagnosed	12	24.0
Total	**50**	**100.0**

Others* : Hepatitis B, Herpes infection

Table -2 Distribution of types of GIT bleeding among the cases

Type	Number (No.)	Percentage (%)
Melena	16	32.0
Hematemesis	4	8.0
Hematemesis & Melena	8	16.0
None	22	44.0
Total	**50**	**100.0**

Table -3: Relationship between prognosis and the etiology of the FHF.

	Number	Survived(n = 16)		Died (n = 34)		P.value
		No.	%	No.	%	
Hepatitis A	18	5	27.8	13	72.2	**0.019**sig
Sepsis	4	0	0.0	4	100.0	**0.016**sig
Wilson disease	5	4	80.0	1	20.0	0.11ns
Kalaazar	4	2	50.0	2	50.0	0.40ns
CMV	3	0	0.0	3	100.0	0.27ns
Autoimmune hepatitis	2	1	50.0	1	50.0	0.82 ns
Others (HBV, Herpes,)	2	1	50.0	1	50.0	0.82 ns
Undiagnosed	12	3	25.0	9	75.0	0.67 ns

Table -4: prognosis and grading of the disease.

Grade	Survived (n = 16)		Died (n = 34)	
Grade 1	10	100.0%	0	0.0%
Grade 2	6	100.0%	0	0.0%
Grade 3	0	0.0%	3	100.0%
Grade 4	0	0.0%	31	100.0%
P.value< **0.001**				

DISCUSSION:

In the present study the most common cause was the viral hepatitis type A (36%), which is similar to that concluded byAl-AzzawiS.et al., in Iraq 2011[8] where 15(48.4%) of cases were due to viral hepatitis and the majority of cases were HAV (32.3%), Latif N. et al.(2010) [9] revealed that HAV was found to cause the disease in (56%) of children and (58%) in Kaur S. et al in India (2013)[10], (31%)by Kumar KJ et al [11], but it is inconsistent with that registered by Williams R (1996) [12] and Shapiro CN (2000)[13] in which the hepatitis B was predominant in the Far East and hepatitis C in Japan. Also it is inconsistent with Squire et al. [1] in which only 1% of the patient's children had hepatitis A, this may be attributed to a high prevalence of the hepatitis A virus in our community in addition to the low socioeconomic status and no HAV vaccination program.

Autoimmune hepatitis was found in (4%) of cases which is nearly similar to Suchy F J[14] in which Autoimmune hepatitis comprised (5%), the undiagnosed cases present in (20%) of patient which is not consistent with what was found in Suchy F J[14] in which it accounts for 40-50% and this is may be explained by small sample size. Wilson disease was present in (10%) of cases which was slightly more than what was found by Al-Azzawi S. (6.5%) [8], but less than what was found by Dehghani S M. (20.7%) of the patients [15], Septic shock with liver failure was observed in 4(8%) nearly similar to was found by Al-Azzawi S (6.5%). [8]

Visceral Leishmaniasis (Kalaazar) was present in 4(8%) of patients who developed FHF but it was not a common cause of FHF and was not reported within the important factors for the initiation of the condition, although it was reported in a study done in in India by Arun K et al [16] who found patients with visceral Leishmaniasis developed FHF, this finding may be due to ignorance of the disease and delay in seeking medical advice and services.

In this study CMV was found in 3 (6 %) similar to 2(6.5%) by Al- Azzawi S. in Iraq 2011[8]

In this study about 16(32%) of child had melena more than that reported by Ranganathan S. et al. [17] in which it was present in 3 (12%) of the children, and hematemesis 4(8%) less than reported by Ranganathan, S. 11 (44%) and this may be explained by small size sample . [17]

In the current study all patients (100%) with sepsis are died, this may be due to the parents seeking late medical treatment High mortality rate was found in hepatitis A virus 13 (72.2%) which agreed with Al-Azzawi S. [8] in which hepatitis A virus carries high mortality rate 7(22%). The highest mortality rate associated with sepsis, cytomegalovirus infection and biliary atresia.

In the current study, the poor outcomes were observed in children with grade 3 and 4 in which all of them died as compared with those in grade 1 and 2 amongst whom no deaths were recorded. In Al-Azzawi S. et al [8] the mortality with grade III was (84.6%), and (100%) with grade IV which was more than that found by Poddar et al in which all patients with grade I or II and (53%) with grade III or IV recovered while (47%) with grade III or IV died [18].

Squires et al observed that only (25%) of grade III or IV had spontaneous recovery [1]. Other studies also reported higher mortality in higher grade of encephalopathy such as Bendre et al who showed (85.7%) with grade III and grade IV and (9%) with grade I &II [19].

Intensive care unit was not available for all patient as we do not have the facilities of hepatic transplantation and methods of artificial liver support. Adding these facilities will significantly improve patient care in our country.

CONCLUSION:

Hepatitis A is the most common cause of FHF with high mortality rate. The highest mortality rate was associated with sepsis, cytomegalovirus infection and biliary atresia. The poor prognosis was found in grade 3 and 4 of encephalopathy, patients with GI bleeding and longer duration of illness before onset of encephalopathy.

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