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Risk factors and outcome of hepatic dysfunction in pediatric intensive care unit

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Abstract

Background: Hepatic failure is a commonly observed form of organ failure in people who are seriously ill. Liver damage and subsequent failure contribute significantly to a substantial rise in both mortality and morbidity rates. **The aim of the work** was To ascertain the risk factors, frequency, and prognosis of primary hepatic dysfunction in critically sick children hospitalized to the Pediatric Intensive Care Unit (PICU). **Subjects & methods;** this single-center cross sectional research was done at the PICU of Beni-Suef University Hospital. The study involved all cases admitted to the PICU from January to December 2022. Those were 400 patients admitted to PICU and 23 patients of them were primary hepatic dysfunction. **Result:** we observed significant associations between various health complications and hepatic dysfunction in patients, Only 5.7% of hospitalizations were attributed to primary hepatic dysfunction, and those with hypoxia were significantly more likely to experience hepatic dysfunction, where Hypoxia occurred in 11 (47.8%) of them and blood product transfusion in 11 (47.8%), which means that they are significant risk factors for primary hepatic dysfunction. Mechanical ventilation occurred in 3 (13 %) of primary hepatic patients, and

Sepsis in 5 (21.7%), Heart failure happened in 5 (21.7) %), Shock in 6 (26.1%) in primary hepatic patients. There are no patients with cardiac arrest in primary hepatic dysfunction and there are no patients who had surgery or abdominal surgery. So, they weren't risking factor of primary hepatic dysfunction. They had a high mortality rate at 73.9%. **Conclusion:** Hepatic dysfunction is a frequent finding in PICU. Consideration should be given to even a slight LFT rise in PICU. Primary hepatic dysfunction patients admitted to PICU have a significant death rate. The prevalence of primary hepatic dysfunction is strongly correlated with hypoxia, sepsis, cardiovascular events, and mechanical ventilation. Hepatic impairment is a significant predictor of PICU mortality and LOS.

1. Introduction:

Hepatic dysfunction in PICUis associated with or causes the acute disease that necessitates admission to the ICU. The liver is the maestro of several metabolic and inflammatory processes during critical illness. Therefore, hepatic dysfunction whether primary could hasten the worsening of the patient's condition leading to significant morbidity and mortality ***(1).***

Patients suffering from a primarily hepatic condition may require considerable medical attention owing to ALF or acute decompensation of CLD including ACLF. In these cases, the indication of ICU admission is usually bleeding, encephalopathy, or infection ***(2).***

Conversely, there are certain severely sick individuals who might be in critical condition without a confirmed liver illness yet show abnormal LFTs ***(3).***

The aim of this research was to ascertain the risk factors, frequency & prognosis of primary hepatic dysfunction in critically sick children hospitalized to the PICU.

2. Patients and Methods:

Study Design: This was a single center cross sectional research**.**

Patients and Setting: The participants were enlisted from the PICU at Beni-Suef University Hospital. All patients who were hospitalized to this PICU between January and December 2022 were included, except for those who matched the specified exclusion criteria: 1) Infants younger than 2 months old or 2) patients who have been in the PICU for

24 hours or less. Patients were monitored until their discharge or death at the PICU.

Ethical considerations:

The study received approval from the ethics committee of Beni-Suef University Hospital. The parents of all patients provided signed informed permission following receiving a simple explanation of the study's objective.

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Data collection: Data were gathered for the duration of the patients' hospitalization in the PICU. Here are the details for every patient:

1. Indication of admission to PICU: Indications of admission to PICU are a varied group of diseases and conditions, therefore these indications were categorized according to the main system affected; cardiovascular, respiratory, neurological, hepatic. or surgical (postoperative).

2. Demographic data: age and sex.

3. Vital signs: Blood pressure, temperature, heart rate & respiratory rate were documented on admission and at 7-days intervals (D1, D7, D14, etc.).

4. Clinical examination: Complete systemic examination for the presence of jaundice, hepatomegaly, splenomegaly, ascites, bleeding, or disturbed level of consciousness.

5. Abdominal ultrasonography when available.

6. Ventilation support and its duration.

7. Blood components transfusion and number of transfusions given.

8. Parenteral nutrition or Enteral nutrition.

9. Surgical procedures (if any).

10.Laboratory investigations.

- Liver function test LFTs to investigate liver dysfunction: ALT, AST, serum total and direct bilirubin, ALP, GGT, serum albumin, PT, prothrombin concentration & INR.
- Other routine labs recorded on 1st day of admission and repeated in intervals include serum creatinine, CBC with differential, blood gases (pH, PaCO2, PaO2, HCO3). PaO_2/FiO_2 ratio was measured.
- Other labs calculate mortality scores and record on 1st day of admission only, include serum calcium, blood urea nitrogen,serum potassium and random blood glucose.
- Laboratory tests were done to investigate primary liver dysfunction (when available) as: HAV IgM, HBsAg, HBcIgM, EBV IgM, CMV IgM.

11. Risk factor screening for primary hepatic dysfunction: In our study, possible risk factors for primary hepatic dysfunction were noticed as follows:

1- Sepsis and its grade

2-Hypoxia identified as PaO2/FiO2 < 300

3-Cardiovascular incidents (cardiac arrest, heart failure,or shock)

4-Mechanical ventilation and its duration

5-Surgery

6-Blood products transfusion (type and frequency)

7-Parenteral nutrition (duration)

12. Calculation of mortality Scores

From several mortality scores used in pediatrics, we chose to calculate:

Pediatric risk of mortality score (PRISM III).

Pediatric Sequential Organ Failure Assessment Score (pSOFA), as they are 'Pediatric Scores'. (Table 1)

frequently utilized in medical practice and, notably, they measure liver dysfunction utilizing variables such as PT and aspartate aminotransferase (AST) along with PT. The PRISM score was computed within the initial 24 hours following admission, whereas the pSOFA score was computed for each consecutive 24-hr duration. Both scores were calculated through the android application

Table (1): pSOFA Score **(4)**

Variables	pSOFA Score[a]				
	0	1	2	3	4
Respiratory $Pao_2:Fio_2$[b] OR $Spo_2:Fio_2$[c]	≥400	300-399	200-299	100-199 with respiratory support	<100 with respiratory support
	≥292	264-291	221-264	148-220 with respiratory support	<148 with respiratory support
Coagulation Platelet count, $\times 10^3/\mu L$	≥150	100-149	50-99	20-49	<20
Hepatic Bilirubin mg/dL	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	> 12.0
Cardiovascular MAP by age group or vasoactive infusion, mm Hg or µg/kg/min[d]					
< 1 mo	≥46	<46	Dopamine hydrochloride ≤5 or dobutamine	Dopamine hydrochloride >5 or epinephrine ≤0.1 or	Dopamine hydrochloride >15 or epinephrine >0.1 or
1-11 mo	≥55	<55			
12-23 mo	≥60	<60			
24-59 mo	≥62	<62			
60-143 mo	≥65	<65			

144-216 mo	≥67	<67	hydrochloride (any)	norepinephrine bitartrate ≤0.1	norepinephrine bitartrate >0.1
> 216 mo[e]	≥70hb	<70			
Neurologic Glasgow Coma Score[f]	15	13-14	10-12	6-9	< 6
Renal Creatinine by age group, mg/dL					
1-11 mo	<0.3	0.3-0.4	0.5-0.7	0.8-1.1	≥1.2
12-23 mo	<0.4	0.4-0.5	0.6-1.0	1.1-1.4	≥1.5
24-59 mo	<0.6	0.6-0.8	0.9-1.5	1.6-2.2	≥2.3
60-143 mo	<0.7	0.7-1.0	1.1-1.7	1.8-2.5	≥2.6
144-216 mo	<1.0	1.0-1.6	1.7-2.8	2.9-4.1	≥4.2
> 216 mo	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	≥5

13. Analysis of outcome: Two outcomes were analyzed: mortality and length of stay (LOS) in PICU. Long LOS > 7 days and brief LOS <= 7 days were distinguished by LOS.

Statistical analysis

Using the Microsoft Excel program, data was gathered throughout the course of the history, basic clinical examination, laboratory investigations, and outcome measurements. The data was then coded, entered, and analyzed. The data that was obtained was tabulated and analyzed utilizing SPSS version 25, which is a statistical tool for social research (Armonk, NY : IBM Corp). This was done on a computer that was compatible with IBM. The Kolmogorov–Smirnov test and the Shapiro–Wilk test were utilized to perform the normality test on the data. Statistics were performed in two different ways: Statistics that are descriptive: For qualitative data, the representation was a combination of numbers and percentages, while for quantitative data, the representation was the mean ± SD.

3. Result:

Table (2): Primary hepatic dysfunction group as regards demographic data

	Primary hepatic dysfunction (n = 23)	
	No.	**%**
Gender		
Male	17	73.9%
Female	6	26.1%
Age (month)		
(Min. – Max.)	(3–75)	
Mean ± SD.	26.30±25.74	
Weight (Kg.)		
(Min. – Max.)	(5–23)	
Mean ± SD.	12.15± 5.71	

This table shows that 17 (73.9%) were males. Their ages ranged between 3 months and 75 months.

Table (3): Risk factors and cause of admission for primary hepatic dysfunction groups.

Risk factors	**Primary hepatic dysfunction (n = 23)**	
	N	**%**
Cause of admission		
1ry liver disease	23	100%
Respiratory	0	0.0%
Neurological dysfunction	0	0.0%
Cardiovascular	0	0.0%
Postoperative	0	0.0%
Hypoxia	11	47.8%
Mechanical ventilation	3	13.0%
Sepsis	5	21.7%
Blood product transfusion	11	47.8%
Heart failure	5	21.7%
Cardiac arrest	0	0.0%
Shock	6	26.1%
Surgery	0	0.0%
Abdominal surgery	0	0.0%

This table shows that Patients experiencing hypoxia had a considerably greater likelihood of developing hepatic dysfunction, where Hypoxia occurred in 11 (47.8%) of primary hepatic patients and also blood product transfusion in 11 (47.8%), which means that they are significant risk factors

for primary hepatic dysfunction. Mechanical ventilation occurred in 3 (13 %) of primary hepatic patients, and Sepsis in 5 (21.7%), Heart failure happened in 5 (21.7) %), Shock in 6 (26.1%) in primary hepatic patients. There are no patients with cardiac arrest in primary hepatic dysfunction and there are no patients who had surgery or abdominal surgery. So, they weren't risking factor of primary hepatic dysfunction.

Table (4): LOS and mortality outcomes of critically ill children with primary hepatic dysfunction

Outcome	**Groups**	
	Primary hepatic dysfunction (n = 23)	
	N	**%**
LOS		
Short ≤ 7days	11	47.8%
Long >7days	12	52.2%
Mortality		
Died	17	73.9%
Discharged	6	26.1%

This table demonstrates how the impact of hepatic dysfunction on case outcome can be evaluated. We focused on two main parameters: PICU mortality rate and LOS. Long (>7 days) and brief (≤7 days) LOS were distinguished. 12 (52.2%) had an extended LOS. There was a significant correlation among primary hepatic dysfunction and an extended LOS in the PICU. 17 (73.9%) had passed away. There was a significant correlation among primary hepatic dysfunction and an overall rise in mortality.

Table (5): Critically ill children's outcomes with primary hepatic dysfunction as regards PRISM III and p SOFA scores

Outcome	Groups Primary hepatic dysfunction (n = 23)
PRISM III score	
Min. -Max.	1.00 - 23.00
Mean± SD	7.04 ± 7.14
p SOFA Score	
Min. -Max.	2.00 - 14.00
Mean± SD	5.39 ± 3.85

This table shows that cases with primary hepatic dysfunction had significantly high both PRISM III score, and p SOFA Score

4. Discussion:

In our study cases with primary hepatic dysfunction represented 23 patients so primary liver disease was present in 5.7 %

Kramer et al., (5) stated that intra-ICU admission was associated with an 11% prevalence of early hepatic dysfunction.

Hepatic dysfunction frequently manifests in the absence of observable alterations in the clinical profile of the patient. Therefore, the clinical suspicion of liver complications is predominately supported by atypical biochemical test results ***(6)***.

Our investigation found that individuals with primary hepatic dysfunction had a statistically significant decrease in Albumin levels contrasted with those without hepatic dysfunction (P<0.001).

Furthermore, our findings indicate that individuals with primary hepatic dysfunction had significantly elevated levels of Alt, AST, D. Bilirubin, T. Bilirubin, INR, and PT, in comparison to those without hepatic dysfunction.

Strassburg ***(7)*** concurred with our findings, stating that hyperbilirubinemia, elevated serum transaminases, , γ glutamyl-transferase (GGT) and alkaline phosphatase, as well as reduced serum albumin and coagulation factors levels, are the primary laboratory

indicators utilized to diagnose hepatic dysfunction.

Despite their poor sensitivity and specificity, these signs frequently suggest hepatocellular or biliary damage and are thus commonly employed for detection liver disease ***(Kortgen et al., 8).***

Our study found that 21.7% of septic patients had primary hepatic impairment. Sepsis was found to be strongly associated with hepatic dysfunction, with people with sepsis having a 5-fold greater risk of developing hepatic dysfunction than those without sepsis.The liver is essential in the body's fight against sepsis, but it is also vulnerable to harm ***(9).***

A pre-existing liver failure raises the risk of an infection escalating to sepsis. In contrast, liver damage during sepsis is a separate risk factor for both multiple organ failure and sepsis-related mortality ***(10).***

The extended LOS in the PICU raises the risk of infection and sepsis.

This is due to the fact that patients were subjected to various procedures and numerous skin pricks for sample throughout their extended LOS, which might have increased their vulnerability to sepsis ***(11).***

According to a research conducted by Porto et al. in ***(12)***, the existence of an invasive medical device & a longer LOS in the PICU are significant hazard factors for acquiring nosocomial infections in PICU cases.

In our research, among the patients who encountered cardiovascular events, 5 individuals (2.7%) developed heart failure, whereas 6 individuals (26.1%) received shock in primary hepatic patients.

In such circumstances, the liver experiences a negative impact as a result of reduced blood flow, which therefore hampers the supply of oxygen. This effect is more pronounced when sepsis is present, as it raises the demand for oxygen and affects its extraction by the liver cells (hepatocytes) ***(13).***

Likewise, the liver is impacted in instances of hypoxia. Out of the patients with hypoxia, 11 individuals (47.8%) had primary hepatic impairment in our research.

Fuhrmann et al. (14) have observed that HLI is the primary factor leading to significantly elevated aminotransferase levels in hospitals. It is present in a maximum of 10% of patients who are seriously unwell in the medical ICU.

In our study, Mechanical ventilation occurred in 3(13%) of primary hepatic patients. In agreement with us, ***Mogahed et al., (11)*** reported that (65.1%) of secondary hepatic patients mechanically ventilated.

In our study: There are no patients with cardiac arrest in primary hepatic dysfunction and there are no patients who had surgery or abdominal surgery. So, they weren't risking factor of primary hepatic dysfunction.

In our study twenty-three patients were admitted to the PICU with primary liver

disease representing 5.7% of the total number of admissions in our study. Yet, cases with primary hepatic dysfunction had the highest mortality rate of 73.9 % among other causes of admission. So primary hepatic patients had the lowest rate of admission to PICU with the highest rate of mortality.

In agreement with us, *Mogahed et al., (11),* noticed that Ten patients with primary liver illness were admitted to the PICU, accounting for 6.6% of all admissions in our research. Among the other causes of hospitalization, individuals with primary hepatic dysfunction had the highest fatality rate of 70%.

Also, in a study of ***Grama et al., (15)*** noticed that acute liver failure (ALF) is a rare disease, correlated with great mortality.

In our study, 12 patients (52.2%) had long LOS and 17 patients (73.9%) had died. Primary hepatic dysfunction was correlated with a significant elevation in the LOS in the PICU. and increase in the mortality.

Consistent with our findings, *Harbrecht et al., (16)* reported that Hepatic dysfunction exhibited a significant relationship with elevated duration of stay in an ICU, as well as mortality. The introduction of hepatic failure led to a significant rise in the LOS for patients who did not have any other organ dysfunction as well as for those with renal dysfunction and respiratory dysfunction.

In our study, Patients with primary hepatic dysfunction had high both PRISM III score, and p SOFA Score

Le Gall et al., (17) stated that, Literature on liver failure has centered on bilirubin since it was identified as a significant indicator of liver dysfunction in ICU critical illness scoring systems, such as the Simplified Sequential Organ Failure Assessment (SOFA) score and the Simplified Acute Physiology Score (SAPS) score.

5. Conclusion:

Hepatic dysfunction is a frequent finding in PICU. Consideration should be given to even a slight LFT rise in PICU. Primary hepatic dysfunction patients admitted to PICU have a significant death rate. The prevalence of primary hepatic dysfunction is strongly correlated with hypoxia and blood product transfusion. Hepatic impairment is a significant predictor of PICU mortality and LOS.

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