Hepatic Dysfunction in Critically Ill Patients

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Abstract: Background and purpose: This study was conducted to evaluate abnormalities of liver functions in patients admitted to different ICU units and correlating these functions with the clinical situation predisposing the patient to this hepatic dysfunction. **Study design:** Case control study. **Subjects:** fifty patients admitted in different ICU units with hepatic dysfunction and ten control patients without hepatic dysfunction. **Place:** Kasr Al Ainy Hospital, Cairo University. **Method**: The fifty patients were subdivided into five groups, **Group I** 9 patients with hepatic dysfunction related to sepsis. **Group II** thirteen patients with hepatic dysfunction related to total parentral nutrition. **Group III** included eleven patients with ischemic hepatitis. **Group IV** five patients with drug induced hepatotoxicity. **Group V** included twelve patients with more than one of the previous causes. **Assessment:** The assessment was carried out by obtaining full patients history (personal, cause of admission to ICU, history of chronic diseases and drug history). Laboratory work was done in the form of CBC, bilirubin (total and direct), aminotransferases, alkaline phosphatase, gamma glutamyl transferase, serum albumin and coagulation profile. Abdominal ultrasound was done to exclude patients with liver cirrhosis, portal hypertension or hepatocellular carcinoma. The gained measures were analyzed by using SPSS program and ANOVA test was used to compare between groups. **Results:** The study showed that there was affection of synthetic and secretory functions of the liver. There were different patterns in hepatic dysfunction with dramatic elevation in liver enzymes (ALT & AST) in shocked hypoxic patients. Also elevated levels of (ALT & GGT) in group with hepatotoxicity and affection of albumin and coagulation profile in patients with sepsis. **Conclusion:** Ischemic hepatitis, parentral nutrition, sepsis and drug hepatotoxicity are predisposing factors to liver dysfunction in critically ill patients.
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Key words: liver dysfunction / Ischemic hepatitis/ total parentral nutrition.

1. Introduction

Hepatic dysfunction not only appears with chronic liver disease but also in critically ill patients. It appears with some conditions like ischemic hepatitis, congestive hepatopathy, total parenteral nutrition, sepsis and drug hepatotoxicity. Liver function affection is either presents as disturbed liver chemistry or as overt clinical manifestation of liver disease. This liver dysfunction was noticed in intensive care patients admitted for different causes [1]. This study tried to concentrate on the cause and predisposing factors of hepatic dysfunction in critically ill patients. In this study we tried to evaluate abnormalities of liver functions in patients admitted to different ICU units and correlating these functions with the clinical situation predisposing the patient to this hepatic dysfunction.

2. Patients and Methods

The study included fifty patients admitted in different ICU units with hepatic dysfunction and ten control patients without hepatic dysfunction.

The fifty patients were subdivided into five groups **Group I** 9 patients with hepatic dysfunction related to sepsis. **Group II** thirteen patients with hepatic dysfunction related to total parentral nutrition. **Group III** included eleven patients with ischemic hepatitis. **Group IV** five patients with drug induced hepatotoxicity. **Group V** included twelve patients with more than one of the previous causes.

Inclusion criteria included patients of both sexes if they have elevated liver enzymes, elevated bilirubin of more than 1.2mg/dl or elevated international normalized ratio of more than 1.4.

Exclusion criteria were patients who are less than 18 years old, had previously recognized liver disease by history or investigations in the form of: GIT bleeding, Ascites of hepatic origin, serum albumin less than 3 mg/dl with portal hypertension, history of hepatic encephalopathy and chronic viral hepatitis (HBV & HCV).

The assessment was carried out by obtaining full patients history (personal, present illness, cause of admission to ICU, history of chronic diseases and previous drug history). Laboratory work was done in the form of CBC, bilirubin (total and direct), aminotransferases, alkaline phosphatase, gamma glutamyl transferase, and serum albumin and

coagulation profile. Abdominal ultrasound was done to exclude patients with liver cirrhosis, portal hypertension or hepatocellular carcinoma. The gained measures were analyzed by using SPSS program and ANOVA test was used to compare between groups.

3. Results

Patients' demographic data of the five groups:

Our study showed no statistically significant difference in age and sex between the five groups and the control group as showed in figure (1).

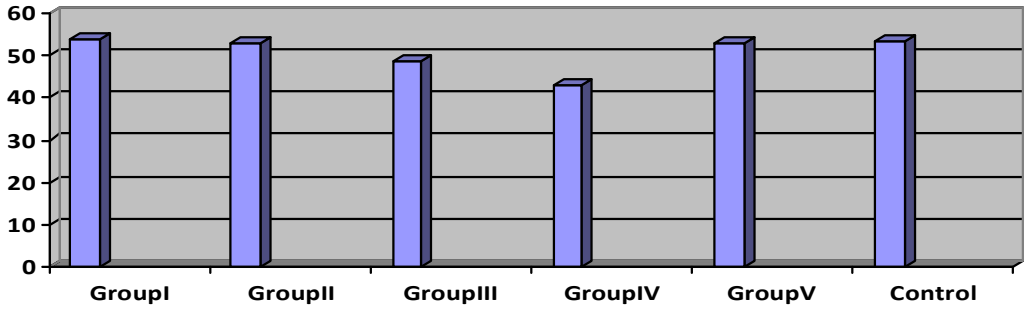

Figure (1): Mean difference of age in the studied groups and control group

The study showed difference in the mean value of the measured enzymes and laboratory results as in Group I (sepsis), the remarkable increase found in the elevation of mean level of GGT (X`=97.625), prolongation of prothrombin time (X`=17.9) and decrease in the HB level (X`=11.8). Group II (TPN) showed increase in ALP (X`=276.08), GGT (X`=148.2) and prolongation of PT (X`=17.10) also, ALP, ALT, AST increased markedly in Group III (Ischemic) and Group IV (Hepatotoxic) while in Group V (more than one cause) showed prolongation in PT (X`=21.98) and also elevation in TLC (X`=16.54) and decrease in HB concentration with mean value 9.25. **As regarding to transaminase level,** there was dramatic increase in the level of **AST** in the ischemic group (group III) and hepatotoxic group (group IV) with mean value (1109.36 & 1036) and showed statistically significant difference between the ischemic group and group I sepsis and group II TPN with p-value (0.02 & 0.01) and also, with control group with p-value 0.01. **ALT** showed marked increase in its level in the previous two groups with mean value (873.27 & 963) and also statistically significant difference between ischemic group and group I sepsis and group II TPN with p-value 0.04 & 0.03) and with control group with p-value 0.02.

Gamma –glutamyl transferase showed marked elevation in its level in all studied groups with mean value (97.625, 148.25, 82.57, 150.8 & 157.4) and increase in the level of **total bilirubin** in all groups as showed in figure (2).

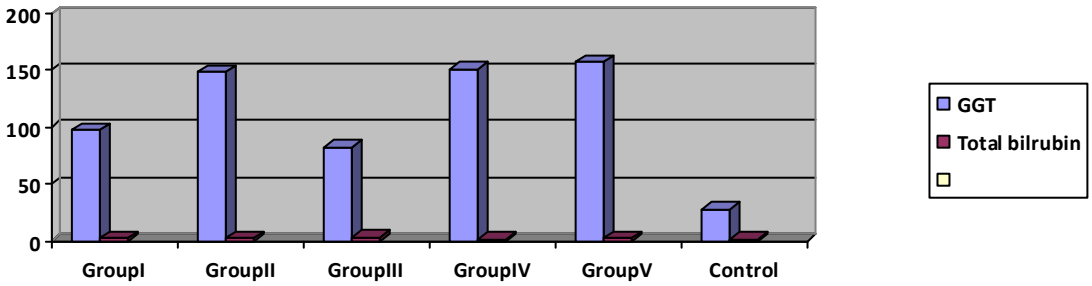

Figure (2): Frequency of GGT and total bilirubin in the studied groups and control group

Group I hepatic dysfunction related to sepsis: There is statistically significant difference in the level of **albumin** with the hepatotoxic group (IV) and control group with p-value (0.04 & 0.000) and also, high statistically significant difference with the control group in the level of **prothrombin** concentration with p-value (0.00).

Albumin level showed marked decrease in its level in group II (hepatic dysfunction related to total parenteral nutrition) and group V (group with more than one cause) with mean value (3.09 & 2.95) resulting in statistically significant difference between them and control group with p-value (0.04 & 0.01).

As regarding to Prothrombin Concentration there are statistically significant difference between the following groups (I, II, III, V) with control group with p-value (0.00,0.03,0.02 & 0.00).

Patient with hepatic dysfunction due to more than one cause, there were elevation in the mean level of transaminases, Alkaline phosphatase, GGT and bilirubin and there were deficiency in the level of albumin and prolongation in the PT as shown in table 1 and also, there were statistically significant difference in the level of prothrombin, prothrombin concentration, INR (international normalized ratio) and hemoglobin with the control group with p-value (0.00,0.02,0.00 & 0.00). Total leucocytic count (TLC) in this group there was statistically significant difference between it and hepatotoxic and TPN group with p-value (0.03 & 0.00).

Table (1): Frequency of different hormones in group V (hepatic dysfunction due to more than one cause)

Group V	*Mean X`*	*Minimum*	*Maximum*
AST	549.8	33	1427
ALT	494	33	1365
ALP	271.9	198	400
GGT	157.4	100	270
Bilirubin	2.11	0.4	5
Albumin	2.95	1.3	4.8
PT	21.98	12	43

As regarding to platelet level there was dramatic decrease in its level in the first group (sepsis) and second group (TPN) with mean value (120.22 & 147.91) and there is statistically significant difference between these studied groups and control group with p-value (0.00 & 0.01).

These results showed correlations between the pattern of hepatic dysfunction and cause however, unfortunately we cannot depend on these patterns as specific pattern for each group but we can depend on its as an indicator for the cause. In a different way each pattern cannot prove any of mentioned causes or even exclude one of it, this is due to small number of sample and some causes like drugs.

4. Discussion

This is a retrospective study of 50 critically ill patients admitted in ICU of different conditions who had hepatic dysfunction in the form of abnormalities in transaminases, Albumin, bilirubin, PC, INR, alkaline phosphatase, GGT. The study was designed to search for the precipitating factor of these conditions and to assess the pattern of this liver dysfunction and comparing these patterns with previous studies.

Our results showed that there were elevations of AST, alkaline phosphatase, bilirubin levels in the patients who received TPN and this agree with the results of a study done by **Naini and Lassman [2]** who reported elevation in the same enzymes in patient receiving TPN. Also there was elevation in the level of bilirubin 66%, alkaline phosphatase in 74% and transaminase levels in 81% of patients.

Regarding hypoxic hepatitis group there was a dramatic elevation in transaminases to levels more than 1000 IU/L in the first 2 days. Also, there was affection of albumin, bilirubin, and alkaline phosphatase levels. Our study found that there were different underlying causes of hypoxic hepatitis mainly cardiogenic shock in 7 patients, respiratory failure in 2 patients and hypovolemic shock in 2 patients and that means that heart failure is not the only cause of ischemic hepatitis but also, hypoxic states can cause the severe pattern of liver injury hence the name hypoxic hepatitis. This was agreed by **Yukihiro S. [3]** who reported that patients usually show rapid (within 24-48 h) and dramatic transient increases in serum aminotransferase, lactate dehydrogenase (LDH) levels and bilirubin following periods of hemodynamic instability or hypoxia. He reported three features that can distinguish ischemic hepatitis from acute viral hepatitis: LDH elevation is more marked in ischemic than in viral hepatitis; serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations rapidly return to normal in ischemic hepatitis, usually within 7-10 d; and ischemic hepatitis is more often complicated by renal damage.

Regarding our study which showed hepatic injury associated with only drugs as a precipitating factor to it. Patients with amiodarone and respridone both were accidentally discovered with routine labs for the patients by taking history of drugs used in the past there were positive history to use of these drugs for a long period 5 years for amiodarone and more than one year for respridone. In contrast to that patient with paracetamol toxicity admitted with acute hepatic

injury and patients who started fluconazole at hospital then liver dysfunction was noticed by follow up of liver functions. Liver enzymes were markedly elevated with paracetamol toxicity. This agreed with **Farrellet al, [4]** who also reported marked elevation of liver enzymes in acute paracetamol toxicity.

Our results showed fluconazole as a risk factor to hepatic dysfunction after usage for 10 to 14 days and this require following liver function before and after initiation of treatment with this antifungal drug. This agreed with Moseley [5] who reported that asymptomatic elevations in liver enzymes occur in less than 7% of patients treated with fluconazole, but the rate may be higher in patients with HIV infection, and that at least 3 deaths from acute hepatocellular injury.

Sepsis also induces liver damage through hemodynamic alterations or through direct or indirect assault on the hepatocytes or through both. Accordingly, liver dysfunction induced by sepsis is recognized as one of the components that contribute to the severity of the disease. In septic group of patients there were affection of Albumin, prothrombin time and elevation of levels of bilirubin. Also, there was mild elevation in levels of transaminases. This agreed with a cohort of 1,342 episodes of sepsis syndrome, liver failure was present in 12% within 28 days of the onset of disease with affection of nearly all liver enzymes **[6].**

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