Role of Liver Enzymes in Patients with Blunt Abdominal Trauma to Diagnose Liver Injury

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Abstract

Background: The liver is the second most injured organ following blunt abdominal trauma (BAT) after spleen. Although the computed tomography (CT) scan is considered as the gold standard for diagnosing liver injury in BAT, it is not readily available in every hospital. This study was performed to evaluate the role of aspartate transaminase (AST) and alanine transaminase (ALT) in patients with BAT and its significance in predicting the diagnosis and severity of the liver injury.

Method: The study was conducted in Chitwan Medical College Teaching Hospital (CMCTH) from February 2019 to May 2020. During that period 96 patients with BAT presented to the emergency department(ED) of CMCTH.

Results: Among the 96 patients admitted with BAT, 38 patients had liver injury and 58 patients had no liver injury. The median length of the intensive care unit (ICU) stay of patients with liver injury was higher than without liver injury. There was a significant difference in the median level of AST and ALT (<0.001) between patients with liver injury and no liver injury. The median of AST and ALT of patients requiring blood transfusion was more than that of the patient not requiring blood transfusion($p<0.05$). The area under the ROC curve of AST was 0.89(95% Confidence Interval 0.86-0.98) and of ALT was 0.92(95% Confidence Interval 0.83-0.97). The area under the curve demonstrated that the test was a good predictor for the identification of liver injury and also the severity of liver enzymes. The cut-off values for the liver injury were 106 U/l and 80 U/l for AST and ALT respectively. Based on these values, AST ≥ 106 U/l had a sensitivity of 71.7 %, a specificity of 90 %, a positive predictive value of 86.8 %, and a negative predictive value of 77.6 %. The corresponding values for ALT ≥ 80 U/l were 77.8 %, 94.1%, 92.1% and 82.8 %, respectively.

Conclusion: In conclusion, we report the optimal cut-off value of AST and ALT for liver injury in BAT as ≥ 106 U/l and 80 U/l respectively. The elevated level of AST and ALT might assist the emergency physicians and surgeons to timely refer the suspected patients with the liver injury to a tertiary center.

Introduction

Blunt abdominal trauma (BAT) is one of the most common scenarios in the emergency department(ED). The prevalence of intra-abdominal injury in patients with blunt abdominal trauma is 13% [[1]]. Motor vehicle accident is one of the major causes of BAT. Other causes include fall injury, physical assault, sports, and crush injury [[2]]. The liver is the second most injured organ following BAT after spleen [[3]]. The clinical diagnosis of liver injury in BAT is a major challenge for emergency physicians and trauma surgeons.

Focus Assessment with Sonography for Trauma (FAST) scan is one of the useful radiological investigations of BAT but has low sensitivity in diagnosing the liver injury and is user-dependent. Therefore computed tomography (CT) scan is considered as the gold standard for diagnosing liver injury in BAT [[4],[5]]. CT scan helps to access not only the liver but also other associated organ injuries. Not all the health facilities will have access to the CT scan. In these centers, the elevation of liver enzymes i.e. aspartate transaminase (AST) and alanine transaminase (ALT) may provide valuable guidance to the emergency physician and surgeons to suspect liver trauma. Previous studies have shown that these parameters may assist in the prediction of liver trauma and their severity [6,7, 8, 9,10]. Patients will benefit greatly from timely referral to the tertiary trauma center.

So, the objective of this study was to evaluate the role of AST and ALT in patients with BAT and its significance in predicting the severity of the liver injury.

Methods And Material

The study was conducted in Chitwan Medical College Teaching Hospital (CMCTH) which was established in 2006. Since then CMCTH has developed as a multi-specialty tertiary care center in Nepal. The ED receives a huge number of trauma casualties from all over central Nepal. It was a prospective observational study from February 2019 to May 2020.

Inclusion criteria

- All the patients with blunt abdominal trauma who were admitted at CMCTH.

Exclusion criteria

- Patients with penetrating abdominal trauma.
- Patients who died in emergency department during resuscitation.
- Patients who presented late after 24 hours of the trauma.
- Patients with a history of liver disease.
- Patients positive for Hepatitis B and Hepatitis C surface antigen

Study method

During 16 month, 96 patients with BAT presented to the emergency of CMCTH, Chitwan, Nepal. The patient was initially evaluated in the triage and necessary resuscitation was done according to Advanced Trauma Life Support (ATLS) protocol by the surgical residents from the Department of General Surgery. Appropriate history with age, gender, mode of injury, and time of trauma was obtained. Initial vital parameters with GCS at ED were recorded. Blood samples were sent for hemoglobin, hematocrit, white blood cell(WBC) count, serum AST and ALT. FAST scan was done and patients with hemodynamic instability were taken for laparotomy. CT scan was done in the rest of the stable patients. Based on the imaging and operative finding patients with liver injury and without liver injury were noted with the associated injury. The grade of liver injury was done according to the Organ injury Scale by the American Association of Surgery for Trauma (AAST) (2018 version) (Table 6) [11]. According to the trauma protocol of CMCTH all the patients with BAT are admitted in the hospital for minimum 24 hrs. All the data form was confirmed and completed by the first author on the same day of admission or within 24 hour of the admission. On discharge length of total hospital stay, length of ICU stay (if admitted in ICU), readmission in ICU, any blood transfusion, morbidity, and mortality were recorded and data were entered by the first author.

Data Analysis

All statistical analyses and graphics were performed with the IBM SPSS version 23.0 statistical package (International Business Machines Corp., New Orchard Road Armonk, New York 10,504 914–499-1900, USA) for Windows. For comparisons of clinical and grading characteristics between the two groups(liver injury and no liver injury), the Chi-squared test was used for categorical variables as appropriate, and Mann-Whitney U test used for quantitative variables(AST and ALT), whereas comparisons between more than two groups(grade of injury) were performed using Kruskal-Wallis test. Results were expressed as median (IQR). All p values are two-sided with p values < 0.05 considered statistically significant. The Receiver operating characteristic (ROC) was used to calculate the optimal cut-off value of AST and ALT and using the optimal cut-off value the sensitivity, specificity, positive predictive value, and negative predictive value were obtained [12].

Ethics Statement:

The institutional review committee of CMCTH approved this prospective observational study. Written consent was given by patients for the information to be used for the research.

Results

Patient's demographics

Among the 96 patients admitted with BAT, 38 patients had liver injury and 58 patients had no liver injury. The quantitative data were analyzed in the median because of the skewed distribution. The median age for liver injury was 27 years old. 78.9% of patients with liver injury were male and motor vehicle accident was the most common mode of injury with 71.1%. 5 patients with liver injury had a negative FAST scan. 8 patients with hemodynamic instability were taken directly to the operation room for emergency laparotomy and the rest of the patients underwent CT scan. Only 1 patient with liver injury was found during emergency laparotomy. The demographic profile of patients divided into two groups with liver injury and no liver injury is given in Table 1. There were no significant differences in ICU admission rate, days of hospital or ICU stay and mortality rate between the liver injury and no liver injury group.

Liver injuries

There were 4(10.5%) patients with grade I injuries and 11(28.9%) with grade II injuries, 18(47.4%) with grade III injuries, and 5(13.2%) with grade IV injuries. There was no grade V injury reported in our study. Out of 38 patients with liver injury, only 8(21.1%) patients had isolated liver injury while 30(78.9%) patients had a liver injury with combined injuries following BAT. Of the 30 patients with combined injuries with liver injury, 18 had chest injury, 24 had other abdominal injuries, 9 had head plus spine injury and 10 had pelvis plus extremities injury. The most common associated organ injured with liver injury was spleen with 37.5%. The patient with a liver injury with combined other associated injury tended to stay at ICU more days than with isolated liver injuries. 33(86.8%) patients out of 38 patients were treated conservatively. There was a significant difference in the median of hemoglobin ($p<0.05$), hematocrit ($p<0.05$), AST ($p<0.001$) and ALT ($p <0.001$) between different grades of liver injury (Table 2), while there was no difference in total ICU stay and hospital stay. The median of laboratory parameters and total ICU and hospital stay of each grade of liver injury is given in table 3.

Main Results

The clinical outcome of the patients with liver trauma is given in Table 4. The statical significance in AST and ALT level was seen only in the mortality rate of the patients whereas no significant difference was seen in ICU admission, surgical intervention for liver injury, and blood transfusion category. The receiver operating characteristic (ROC) curve analysis for AST and ALT is shown in Figures 1 and 2 respectively. The area under the ROC curve of AST was 0.89(95% Confidence Interval 0.86-0.98) and of ALT was 0.92(95% Confidence Interval 0.83-0.97). The area under the curve demonstrated that the test was a good predictor for the identification of liver injury. According to the ROC curve, the cut-off values for the liver injury were 106 U/l and 80 U/l for AST and ALT respectively. Using the cut-off value, sensitivity, specificity, positive predictive value, and negative predictive value were calculated (Table 5).

Discussion

Before CT scans were introduced, surgeons used to proceed for laparotomy when they suspected parenchymatous organ injury in BAT [13]. The availability of a modern multi-detector CT scan has helped today's surgeons tremendously in managing BAT with liver injury conservatively. It not only helps to establish the grade of injury but also helps to detect delayed complications of the high-grade liver injury [14 15]. The diagnosis of liver injury is challenging in peripheral centers all over the world where CT is not available. This even applies to developed countries like Japan. To establish the severity of the liver injury is beyond the reach of those emergency physicians and surgeons.

The development of the FAST scan is useful in diagnosing hemoperitoneum but because of its low sensitivity and specificity its role in BAT is limited [4,16]. The role of elevated liver enzymes in predicting the severity of liver injuries is still a matter of dispute. Liver enzymes AST and ALT are present in hepatocytes in high concentration and following BAT they leak into the blood circulation. Their main function is to catabolize amino acids, permitting them to enter the citric acid cycle. AST is typically found in the liver only but ALT is also found in heart, skeletal muscle, kidney, brain, and red blood cell [17]. The alteration of ALT and AST in chronic liver injury and drug-induced liver has been extensively studied [18]. Few studies have demonstrated their role as a marker in predicting the severity of liver injury [6,7,8,9,10].

In this prospective observational study, we investigate the role of AST and ALT in the diagnosis of liver injury and its severity. In the recent study, Koyoma et al reported the optimal cut-off value of AST and ALT was 109 U/l and 97U/l respectively for the patients with liver injury in blunt abdominal trauma. They suggested the optimal cut-off value as a predictor and also screening tool for CT scans for the presence of liver injury. Even in a developed country like Japan, they have pointed out the significance of AST and ALT levels for early CT scans and if not available, transfer to the patient to tertiary center [10]. Similar results were reported by Tian et al, Chang et al, Shrivastava et al and Lee et al [6,7,8,9]. Shrivastava et al only compared ALT level whereas other studies included both AST and ALT value.

Our study results also demonstrate that the increased level of AST and ALT predicts the underlying liver injury in patients with BAT. The median level of grade II liver injury was less than grade I liver injury. This may be because of very few patients with grade I liver injury. The median level of grade III and grade IV was much higher than grade I and II (Table 3). In countries like Nepal where there are few tertiary centers, patients with a high level of AST and ALT should be stabilized and immediately shifted to a tertiary care centers. The median of AST and ALT of patients requiring blood transfusion was more than that of the patient not requiring blood transfusion($p<0.05$). This shows that the AST and ALT level is not only important for the prediction of liver injury but also alerts the surgeons about the possible need for blood transfusion. Similarly, the median of AST and ALT in patients with mortality was significantly higher than patients without mortality ($p<0.05$). Since only 2 patients expired due to liver injury, the significance of AST and ALT in mortality cannot be suggested. One study reported elevated WBC counts together with elevated AST and ALT are strongly associated with liver injury[19]. But in our study, there was no association between WBC count and liver injury. Overall the sensitivity, specificity, positive and negative predictive value of AST and ALT for predicting liver injury was low, so we suggest not using these liver enzymes as a diagnostic tool but to use as a screening tool for possible liver injury.

There were some limitations during the study. This was a single institute study and the number of patients with liver injury was relatively small particularly grade I liver injury.

Conclusion

In conclusion, we report the optimal cut-off value of AST and ALT for liver injury in BAT as ≥ 106 U/l and 80 U/l respectively. In countries like Nepal, where CT scan is not available in every center, the elevated level of AST and ALT level might assist the emergency physicians and surgeons to timely refer the patients with suspected liver injury to a tertiary center.

Abbreviations

BAT= Blunt abdominal trauma, CT= Computed tomography, AST= Aspartate transaminase, ALT= alanine transaminase, ED= Emergency Department, CMCTH= Chitwan Medical College Teaching Hospital, ATLS= Advanced Trauma Life Support, GCS= Glasgow coma scale, FAST=Focus Assessment with Sonography for Trauma, WBC= white blood cell, ICU= Intensive care unit, ROC= Receiver operating characteristic

Declarations

Funding:

No funding was required for the study.

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Authors' contributions:

SA and NHC carried out the main manuscript writing. BA and SA collected and analyzed the data. TKK and KG assisted in drafting the manuscript and reviewed the article. All authors read and approved the final manuscript.

Availability of data and materials:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate:

Written consent was given by patients for the information to be stored in the hospital database and used for the research. This study was approved by our institutional review committee, Chitwan Medical College Teaching Hospital, Chitwan, Nepal

Consent for publication:

Written consent was given by the patients and their relatives to use their information in a research study and to be published.

Competing interests:

The authors declare that they have no competing interests.

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Tables

Table 1: Demographic features of liver injury and no-liver injury patients.

	Liver Injury (n=38)	Non-Liver Injury (n=58)	P value
Age, median (range) years	27.0(3-76)	31.50(6-83)	0.848
Gender, n(%)			0.236
Male	30(78.9)	51(87.9)	
Female	8(21.1)	7(12.1)	
Mechanism, n(%)			
Motor Vehicle Accident	27(71.1)	42(72.4)	0.654
Fall from height	7(18.4)	12(20.7)	
Physical Assault	4(10.5)	3(5.2)	
Crush injury	0	1(1.7)	
CT Scan n(%)			0.102
Performed	37(97.4)	51(87.9)	
Not performed	1(2.6)	7(12.1)	
ICU Admission, n(%)			0.338
Admitted	35(92.1)	56(96.6)	
Not admitted	3(7.9)	2(3.4)	
Re-admission in ICU, n(%)			0.854
Yes	3(7.9)	4(6.9)	
No	35(92.1)	54(93.1)	
Surgical intervention(all surgery),n(%)			0.494
Performed			
Not performed	15(39.5)	27(46.6)	
	23(60.5)	31(53.4)	
ICU stay, median, (range) days	3(0-22)	3(0-26)	0.721

Total Hospital, median (range) days	9(2-42)	9(1-60)	0.997
Mortality, n(%)			0.536
Yes	2(5.3)	5(8.6)	
No	36(94.7)	53(91.4)	

Table 2: Laboratory Parameters of patients with liver injury and no liver injury.

Laboratory Parameters	Patients with liver injury	Patients with no liver injury	p-value
WBC, median (range) mm^{-3}	10450 (4650-20800)	10000 (1990-25010)	0.943
Hb% median (range) g/dl	11.4 (6.8-15.6)	12.8(5.6-17.2)	0.067
PCV median (range) %	34.5 (21.20-45.50)	36.35(17.40- 48)	0.232
AST median (range) U/l	379(26- 6080)	46(17-339)	< 0.001
ALT median (range) U/l	290.5(27-2681)	39 (12-415)	< 0.001

Table 3: Laboratory parameters and outcome of each grade of liver injury.(The Kruskal-Wallis test)

	Grade I(n=4)	Grade II(n=11)	Grade III(n=18)	Grade IV (n=5)	p value
WBC,median(range) mm^{-3}	12945(10300-14480)	8990(4650-20800)	8700(4900-14900)	12150(6900-18800)	0.541
Hb% median (range) g/dl	14.1 (6.8-15.6)	11.4(9.0-14.8)	11.55(7.5-14.8)	9(7.7-9.9)	0.028*
PCV median (range) %	40.75(23-45.30)	39.10(28.60-45)	34.80(21.30-44.10)	23.50(21.20-29.60)	0.027*
AST median (range) U/l	173(26-317)	134(47-888)	341(38-6080)	619(432-1800)	< 0.001
ALT median (range) U/l	144(27-332)	118(33-787)	263(48-2681)	559(324-2300)	< 0.001
Total hospital stay, median(range) days	6.5(4-10)	9(4-30)	8(2-25)	11(5-40)	0.662
Total ICU stay, median (range) days	1(0-3)	2(0-22)	2.5(1-13)	5(3-10)	0.161

*p<0.05

Table 4: Clinical out-come of the patients with liver injury and their AST and ALT levels.

Outcome	n(%)	Median AST (range) U/l	P value	Median ALT (range) U/l	P value
ICU admission			0.685		0.978
Yes	35(92.1)	323(38-6080)		256(33-2681)	
No	3(7.9)	317(26-604)		332(27-638)	
Surgical intervention (liver injury related)			0.110		0.088
Yes	5(13.2)	619(323-1800)		569(324-2300)	
No	33(86.8)	314(26-6080)		241(27-2681)	
Mortality			0.022		0.019*
Yes	2(5.3)	3940(1800-6080)		2490.5(2300-2681)	
No	36(94.7)	314(26-1993)		248.5(27-787)	
Blood transfusion done			0.381		0.154*
Yes	9(23.7)	359(47-6080)		569(93-2681)	
No	29(76.3)	314(26-1993)		241(27-667)	

* $p < 0.05$

Table 5: Sensitivity and specificity of AST and ALT for liver injury

	AST>= 106 U/l	ALT >= 80 U/l
Sensitivity	71.7%	77.8%
Specificity	90%	94.1%
Positive Predictive Value	86.8%	92.1%
Negative Predictive Value	77.6%	82.8%

Table 6: Liver injury Scale by AAST(American Association for the Surgery of Trauma) 2018

AAST Grade	Imaging Criteria (CT finding)	Operative Finding
I	– Subcapsular hematoma <10% surface area – Parenchymal laceration <1 cm in depth	– Subcapsular hematoma <10% surface area – Parenchymal laceration <1 cm in depth Capsular tear
II	– Subcapsular hematoma 10–50% surface area; intraparenchymal hematoma <10 cm in diameter – Laceration 1–3 cmin depth and ≤ 10 cm length	– Subcapsular hematoma 10–50% surface area; intraparenchymal hematoma <10 cm in diameter – Laceration 1–3 cm in depth and ≤ 10 cm length
III	– Subcapsular hematoma >50% surface area; ruptured subcapsular or parenchymal hematoma – Intraparenchymal hematoma >10 cm – Laceration >3 cm depth – Any injury in the presence of a liver vascular injury or active bleeding contained within liver parenchyma	– Subcapsular hematoma >50% surface area or expanding; ruptured subcapsular or parenchymal hematoma – Intraparenchymal hematoma >10 cm – Laceration >3 cm in depth
IV	– Parenchymal disruption involving 25–75% of a hepatic lobe – Active bleeding extending beyond the liver parenchyma into the peritoneum	– Parenchymal disruption involving 25–75% of a hepatic lobe
V	– Parenchymal disruption >75% of hepatic lobe –Juxtahepatic venous injury to include retrohepatic vena cava and central major hepatic veins	– Parenchymal disruption >75% of hepatic lobe – Juxtahepatic venous injury to include retrohepatic vena cava and central major hepatic veins

Figures

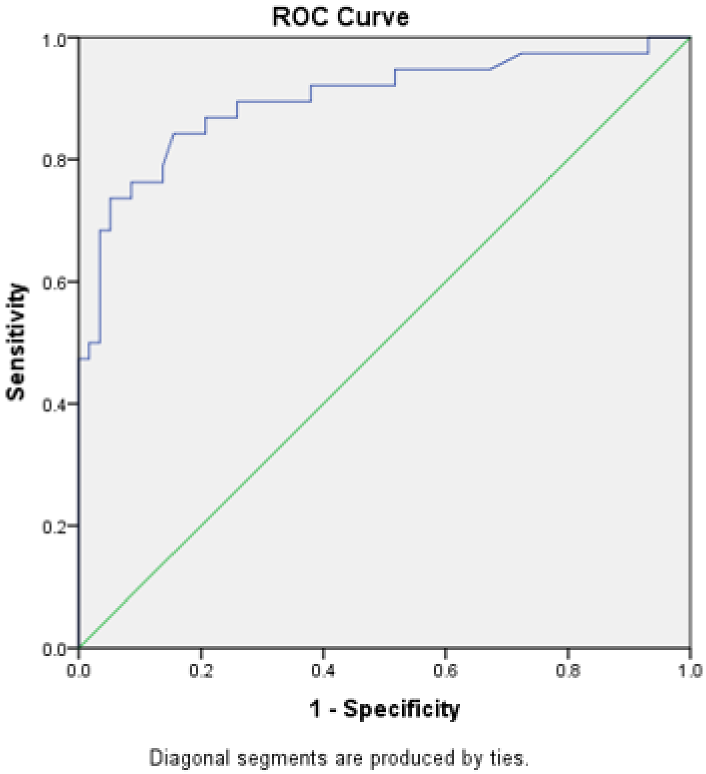

Figure 1

ROC curve of AST. ROC- receiver operating characteristic, AST- aspartate aminotransferase

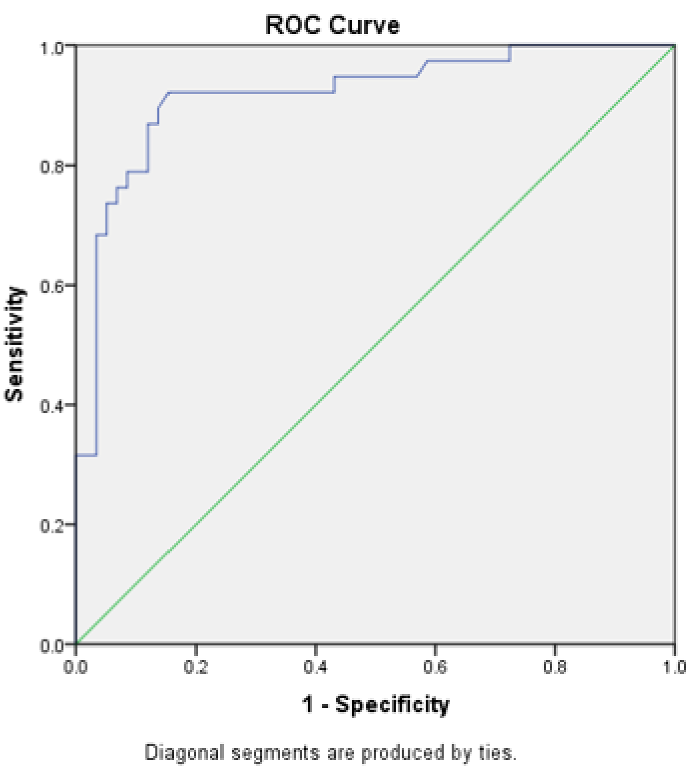

Figure 2

ROC curve of ALT. ROC- receiver operating characteristic, ALT- alanine aminotransferase