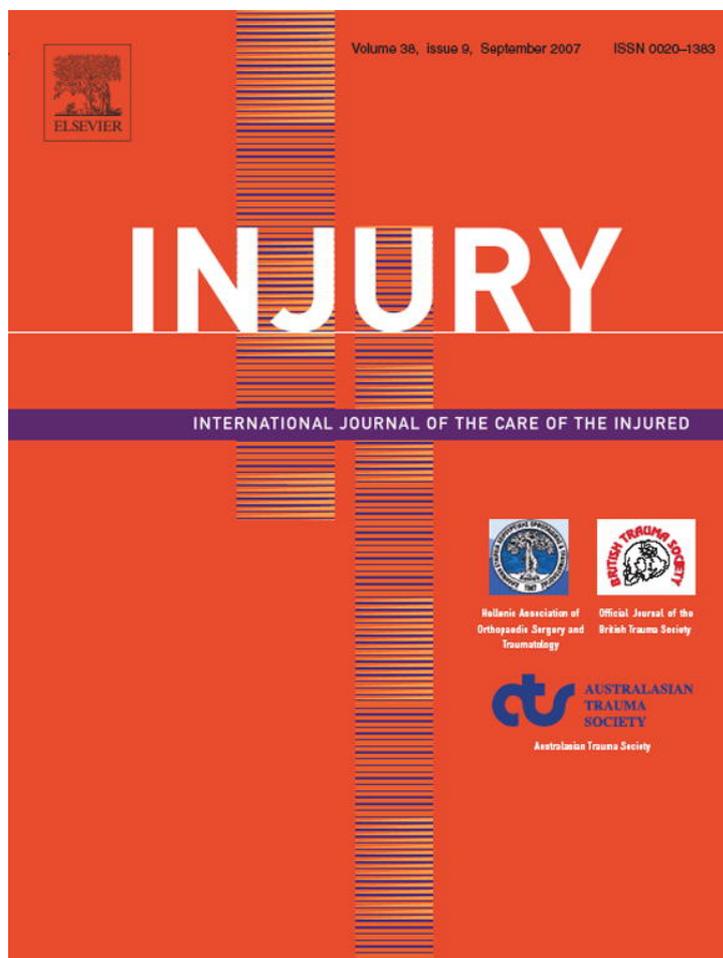


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# Blunt abdominal injury: Serum ALT—A marker of liver injury and a guide to assessment of its severity

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## KEYWORDS

Blunt hepatic injury;  
 Serum ALT;  
 Blunt liver injury

## Summary

**Background:** Elevated serum alanine aminotransferase (ALT) as a marker for diagnosis, and assessment of severity in patients with blunt hepatic injuries are hitherto un-described or casually mentioned in literature.

**Methods:** Prospective observational study of all patients admitted with blunt abdominal trauma accrued between May 2002 and December 2003. Upon admission, vital parameters were recorded and blood samples were drawn for haemogram and serum ALT (SGPT) levels. Patients were further evaluated with USG, CT scan or underwent a laparotomy.

**Results:** Of the 122 patients with blunt abdominal injury, 32 had raised ALT, among these 31 had liver injury. No patient with a normal ALT had hepatic injury. Five patients with a significantly raised ALT and negative USG had liver injury. Patients with modestly raised ALT, mostly resolved on non-operative treatment, whereas, patients with more marked rise had more serious hepatic injuries, more complications, greater transfusion requirement, and higher death rates.

**Conclusion:** This observational cohort study strongly suggests that raised serum ALT is a sensitive diagnostic marker for blunt liver injury and its levels may assist with prognosis and guide management.

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## Introduction

A rise in serum alanine aminotransferase (ALT) level reflects injury to viable hepatocytes. Our hypothesis

was that blunt hepatic trauma, similarly, would lead to a rise in serum level of this enzyme and the degree of rise may also correlate with the severity of hepatic injury.

Most liver injuries are traditionally diagnosed either by imaging studies (USG, CT scan) or exploratory laparotomy. Based on detection of free fluid, parenchymal injury or both, the overall sensitivity of emergency sonography for detection of blunt hepatic injury is 72%.<sup>8</sup>

In an autopsy study by Hodgsons et al. missed hepatic and splenic rupture accounted for the majority of emergency department deaths (37%)<sup>4</sup> and therefore even when an initial USG is negative for free fluid or liver lesion, clinically suspected injuries will require further diagnostic evaluation.

Computerised tomography has rapidly gained acceptance as a gold standard investigation for evaluation of trauma patients and provides an opportunity to identify specific solid organ injury. Despite the advantages of CT imaging, we believe that a CT scan suite, at times, may not provide a safe environment for resuscitation and additionally has limitations for patient who are too unstable for transportation. In addition, the high cost of a CT scan and its limited sensitivity to identify hollow viscus injury do not permit its widespread use to screen all patients with blunt abdominal trauma,

especially in a high turnover and resource limited trauma centre.

In brief, the preoperative diagnosis of blunt liver injury presently relies heavily on imaging studies that may not be consistently applicable to all patients. The role of serum enzymes as a diagnostic test for blunt liver injury has not been adequately explored, as yet. Therefore, in this prospective observational study of patients admitted with blunt abdominal trauma, we evaluate the significance of raised serum ALT for the diagnosis of hepatic injury and its severity.

## Patients and methods

### Study centre

Tertiary level trauma centre at the King Georges Medical University, Lucknow, India. The hospital is a busy academic and state level trauma referral centre<sup>2</sup> with almost 3000 annual admissions, resulting from the large number of trauma referrals alone.

### Study design

Prospective observational study (Fig. 1).

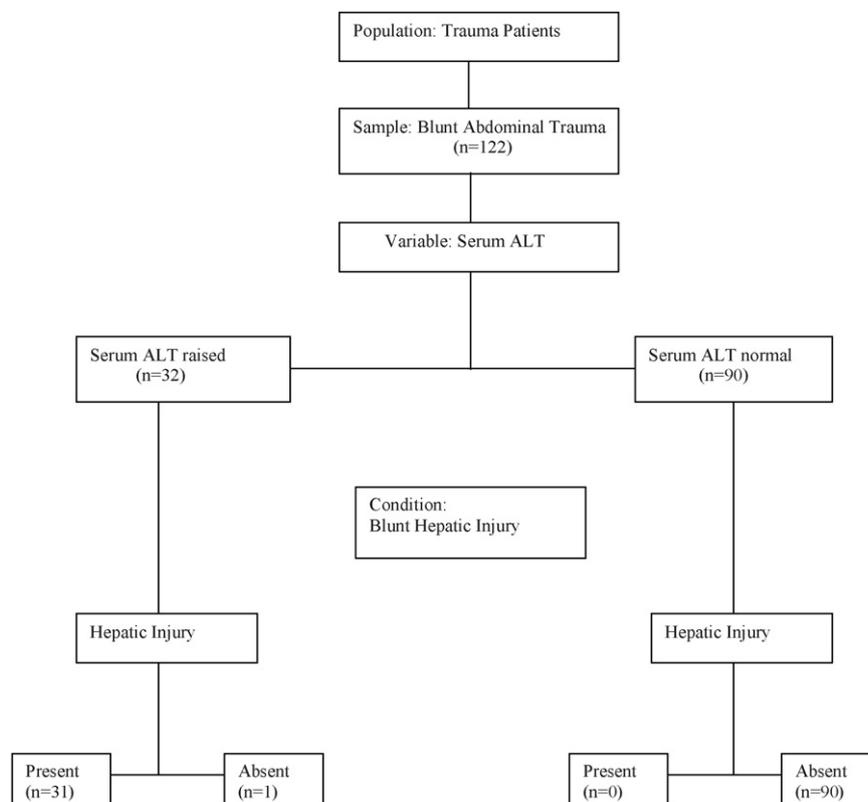


Figure 1 Study design (blunt hepatic injury and serum ALT).

## Cohort definition

Patients presenting with blunt abdominal trauma (road traffic accident, fall, assault), over a period extending from May 2002 to December 2003, with no age exclusion.

## Data Collection

Proforma directed demographic profile (age, sex, address, mode of injury) and vital parameters (pulse, blood pressure, respiratory rate, and abdominal girth) of all patients at admission were recorded and blood samples were drawn for laboratory evaluation, which included haematocrit and serum ALT. The results of latter are available within 45–60 min from an auto-analyser within the hospitals 24 h emergency biochemistry laboratory. Additionally, when serum ALT levels are performed on a heparinised blood sample, on priority mode of an auto-analyser, the results can be made available in 30 min.

Haemodynamic status was defined in accordance to shock index<sup>9</sup>:

$$\left( \text{Shock index} = \frac{\text{Pulse rate}}{\text{Systolic blood pressure}} \right)$$

with shock being defined when this index is more than one.

Patients were assorted into groups and managed in accordance to our hospital practice, as follows:

- Group (A): Haemodynamically stable patients – defined as those with a shock index less than one, these patients were further evaluated with various imaging modalities.
- Group (B): All unstable patients (shock index more than one) that reached a stable haemodynamic status with less than 2000 mL of intra-venous fluids. These patients were further managed as warranted by their haemodynamic status and on the individual decision of their attending surgeon.
- Group (C): All unstable patients, not responding to resuscitation, were taken up for urgent exploration.

A CT scan was performed whenever permitted by the clinical status of the patient and when found necessary by the treating surgeon. Most patients however, were evaluated by USG performed by on duty residents of the department of radio-diagnosis, with at least one completed year of residency, as per the usual hospital postings. These ultrasound examinations were performed aiming for a detailed abdominal scan, to look for organ injury and free fluid.

## Follow up

All patients were followed up to death/discharge from hospital, and then up to a minimum of 6 weeks among all hospital survivors. Follow up after discharge included a clinical assessment by the attending surgeon, with radiological imaging (USG/CT Scan) being performed whenever considered necessary.

Findings of sonography, CT scan, laparotomy, laboratory tests and outcome were analysed.

## Statistical analysis

To estimate a sensitivity of 0.95 with a precision (half width of confidence interval) of 0.04, at  $\alpha = 0.05$ , a sample size of 115 patients was found to be necessary. Performance characteristics of at admission serum ALT as a test for hepatic injury were assessed in 122 patients with blunt abdominal injury. Additionally, serum ALT levels were compared among patients with various variables related to the severity of liver injury. These were: non-operative and operative management, survival and liver injury related deaths, blood transfusion requirement ( $\leq 2$  or  $> 2$  U), haemodynamic status at presentation (group A, B, C), liver injury grade<sup>7</sup> and complications on follow up.

Since the data were not normally distributed, comparisons were performed using non-parametric statistical test. Comparison among two groups was performed using Mann–Whitney–Wilcoxon Rank sum test, whereas comparisons between more than two groups were performed using Kruskal–Wallis test. Results were expressed as median (IQR), and  $P < 0.05$  was considered statistically significant.

Statistical calculations were performed using the statistical package for the social sciences software, version 7 (SPSS, Chicago, Illinois, USA).

## Results

Table 1 presents the demographic profile and mode of injury in the 122 consecutive patients with blunt

**Table 1** Demographic profile of Patients and Modes of injury

|                         |                          |
|-------------------------|--------------------------|
| Age (mean $\pm$ S.D.)   | 30.6 ( $\pm$ 11.9) years |
| Gender ratio (M:F)      | 108:14                   |
| Mechanism: <i>n</i> (%) |                          |
| Road traffic accidents  | 87 (71.3)                |
| Falls                   | 16 (13.1)                |
| Assault                 | 13 (10.7)                |
| Crush                   | 6 (4.9)                  |

**Table 2** Performance characteristics of serum ALT for blunt hepatic injury

|                    | Liver injury |    |
|--------------------|--------------|----|
|                    | Yes          | No |
| Elevated serum ALT |              |    |
| Yes                | 31           | 1  |
| No                 | 0            | 90 |

Sensitivity (CI\*): 100% (88.8–100%). Specificity (CI\*): 98.9% (94.0–100.0). Positive predictive value (CI\*): 96.9% (83.8–99.9%). Negative predictive value (CI\*): 100% (96.0–100%). \*Figures for confidence interval (CI) were obtained from the 7th edition of Geigy Scientific Tables.

abdominal trauma, admitted during the period of study. Out of these 122 patients, 96 patients underwent an abdominal ultrasound, whereas the remaining 26 patients underwent a laparotomy without a prior USG. In 47 patients, USG was followed by CT scan imaging. Hepatic injury was identified in 31 (25.4%) patients, by either sonography, CTscan or at laparotomy. Serum ALT levels were measured at admission in all 122 patients with a median time interval between injury and ALT estimation of 13 h (range 3–48 h).

Serum ALT levels were raised in 32 patients, which included all the 31 patients with liver injury (sensitivity 100%, Table 2). Only one patient with raised serum ALT did not have liver trauma (specificity 98.9%, Table 2) this patient was suffering with Hepatitis B. Moreover, liver injury was not identified in any of the remaining 90 patients with a normal serum ALT.

The median ALT level in patients who survived following blunt liver injury or died due to a cause unrelated to liver trauma was 690.0 U/L (911.5), in contrast, the median ALT levels among patients that died exclusively because of their liver injury was 1960 U/L (Table 3). This difference is statistically significant ( $P = 0.027$ ). More importantly, the median ALT level of 1442.5 U/L (884.5), in the 10 patients that required surgical intervention for their liver injury were also significantly higher when compared to the remaining 21 patients (median serum ALT = 480.0 U/L (581.0) ( $P < 0.001$ ), seventeen of which were managed non-operatively and four either underwent a non-therapeutic laparotomy or were explored for other associated injury.

Similarly, statistically significant and increasing ALT levels were observed among patients with

**Table 3** Clinical outcome in blunt hepatic trauma and serum ALT levels

| Outcome   |  | (n = 31) | Median | IQR   | Q <sub>1</sub> , Q <sub>3</sub> | Test statistics, P        |
|---|--|----------|--------|-------|---------------------------------|---------------------------|
| Death/Alive                                       | Deaths (due to liver injury)                         | 2        | 1960.0 | –     | –                               | 2.2, 0.027 <sup>a</sup>   |
|   | Alive + deaths unrelated to liver injury             | 29       | 690.0  | 911.5 | 306.5, 1218                     |                           |
| Management  | Operations (liver related)                           | 10       | 1442.5 | 884.5 | 967.5, 1852.0                   | 3.5, <0.001 <sup>a</sup>  |
|   | Non-operative + non-therapeutic/unrelated operations | 21       | 480.0  | 581.0 | 286.0, 867.0                    |                           |
| Clinical status                                   | Stable (group A)                                     | 15       | 341.0  | 298.0 | 280.0, 578.0                    | 18.3, <0.001 <sup>b</sup> |
|   | Unstable (group B)                                   | 11       | 928.0  | 460.0 | 770.0, 1230.0                   |                           |
|   | Critical (group C)                                   | 5        | 1780.0 | 481.5 | 1622.5, 2104.0                  |                           |
| Liver injury grade                                | 1  | 4        | 259.5  | 210.3 | 217.0, 427.3                    | 24.1, 0.001 <sup>b</sup>  |
|   | 2  | 11       | 341.0  | 246.0 | 292.0, 538.0                    |                           |
|   | 3  | 10       | 1067.2 | 470.5 | 789.5, 1260.0                   |                           |
|   | 4  | 6        | 1622.5 | 748.3 | 1337.8, 2086.0                  |                           |
| Blood transfusions                                | ≤2   | 16       | 378.8  | 467.0 | 283.0, 750.0                    | 3.8, <0.001 <sup>a</sup>  |
|   | >2   | 15       | 1230.0 | 675.0 | 1060.0, 1735.0                  |                           |
| Complications (liver injury related) on follow up | Present  | 6        | 1482.5 | 760.0 | 1092.0, 1852.0                  | 2.77, 0.006 <sup>a</sup>  |
|   | Absent   | 21       | 486.0  | 774.5 | 293.0, 1067.5                   |                           |

Q<sub>1</sub>: 1st Quartile, Q<sub>3</sub>: 3rd Quartile.

<sup>a</sup> Mann–Whitney–Wilcoxon Rank sum test.

<sup>b</sup> Kruskal–Wallis test.

increasing grade of liver injury<sup>7</sup> (grade 1, 2, 3, 4) and also among patients in the various study groups stratified on the basis of their haemodynamic status (group A, B, C) (Table 2). However, no patients with grade 5 and 6 liver trauma, which includes extremely serious and vascular injuries, reported to this hospital, during the period of study.

For blood transfusions, the median ALT in patients requiring more than 2 U was 1230.0 U/L (675.0), whereas median ALT in patients needing 2 U or less was only 378.8 U/L (467.0) ( $P < 0.001$ ) (Table 3).

Six patients, in this series, suffered hepatic injury related complications. Three had intra-peritoneal biloma formation, whereas haemobilia, delayed bleeding and thoraco-biliary fistula formation occurred in one patient each. The median serum ALT in patients with such liver injury related complications was 1482.5 U/L (760.0), whereas median serum ALT in the remaining (complication free) survivors of blunt hepatic injury was 486.0 U/L (774.5). ( $P = 0.006$ ) (Table 3).

## Discussion

Raised hepatic enzymes in patients with blunt hepatic trauma are considered a mundane laboratory finding and the diagnostic utility of this parameter has not been studied in detail as a predictor of liver trauma and to assess its severity. Additionally, raised hepatic enzymes in patients with blunt trauma are often casually attributed to ischaemic hepatitis (shock liver), believed to result from shock. Seeto et al.<sup>10</sup> investigated this phenomenon and compared 31 patients (case group) who met the definitions of ischaemic hepatitis with a control group of 31 previously healthy patients sustaining major non-hepatic trauma. Both groups had documented systolic blood pressure  $< 75$  mmHg for at least 15 min. Despite the marked reduction in blood pressure, no patient in the control group developed ischaemic hepatitis. The mean ( $\pm$ S.D.) peak serum AST level in the control group was  $78 \pm 72$  IU; in contrast the mean peak AST level in the case group was  $2088 \pm 2165$  IU. All patients with ischaemic hepatitis had evidence of underlying heart disease. Systemic hypotension or shock alone did not lead to ischaemic hepatitis in any patient. In our study too, the absence of rise in serum ALT in haemodynamically unstable patients without liver injury and an increase in serum ALT in haemodynamically stable patients with hepatic injury, corroborate with the findings of Seeto et al.

An important strength of a cohort study lies in its ability to demonstrate that 'cause preceded the effect',<sup>5</sup> and is therefore an appropriate study design to evaluate the usefulness of a diagnostic

test. The findings from our study strongly suggest a cause and effect relationship between blunt hepatic trauma and raised serum ALT, in this subset of patients and therefore highlight the diagnostic utility of this investigation.

Data from 43 children with blunt abdominal trauma, report that elevated serum transaminases have a sensitivity of 100% and a specificity of 92.3% for identifying hepatic injury.<sup>3</sup> In the present study, the sensitivity and specificity of raised serum ALT in prediction of blunt hepatic injury was 100 and 98.9%, respectively, which is in agreement to the above findings. As already mentioned, missed hepatic injuries contribute significantly to the emergency department deaths. In our study, elevated ALT successfully predicted liver injury in five patients (16%) that had a negative abdominal sonography, strongly suggesting a role for identification of such patients. This view is further strengthened by findings that raised serum ALT among children suffering physical abuse can successfully predict liver lacerations.<sup>1</sup>

Our study further demonstrates that median serum ALT levels are significantly higher among patients with higher grades of liver injury; patients treated non-operatively had a lower median serum ALT as compared to patients requiring operative intervention for their liver injury. Additionally, the transfusion requirements were also higher among patients with a higher serum ALT. Patients that died because of their hepatic trauma and those with an unstable haemodynamic status at presentation also had significantly higher median serum ALT levels (Table 2). Similar relationships have been demonstrated by other studies. One such study suggests a higher serum AST and ALT levels in grade 3 and 4 injuries as opposed to raised but lower levels in grade 1 and 2 injuries.<sup>6</sup> Another study identifies a 14% chance of minor and no chance of a major hepatic injury in patients with serum AST (SGOT) level  $< 360$  U/L, opposed to an overall 88% chance of a liver injury and 44% chance of a grade 3 injury in patients with serum AST  $> 360$  U/L.<sup>11</sup>

Complications inherent to hepatic trauma are bilomas, haemobilia, delayed bleeding and thoraco-biliary fistula formation. Complications of these kind are uncommon for low grade injuries and in our study, such complications occurred more often among patients with a more marked rise in serum ALT following trauma.

This study supports the hypothesis that raised serum ALT levels; successfully predict hepatic injury in patients of blunt abdominal trauma. Higher serum ALT levels, following blunt trauma, may also suggest a higher grade liver injury. In addition, potential benefits like easy availability, low cost, and quick results may make screening by serum ALT an extremely

valuable tool in the work up of patients with blunt abdominal trauma, especially at remote centres of developing countries that do not have easy access to expensive/expert radiological evaluation.

### Study limitations

Although, we attempted to control many important confounders in our study, we were unable to account for a few. These factors are therefore potentially important limitations of the study.

First, the time interval between injury and ALT estimation could not be standardised in this study. This was predominantly due to delayed referrals from less specialised centres and late presentations from accidents occurring at remote areas. The influence of very early and very late ALT measurements, on our findings is therefore unknown and will have to be investigated at centres with shorter prehospital transport time. However, in spite of this limitation, cause and effect relationship between blunt hepatic trauma and raised serum ALT has been established by the present study. Additionally, in the 122 patients assessed 3–48 h after injury, no patient with liver trauma was missed on this account.

The second limitation of this study is the unavailability of a uniform radiological imaging in all patients. In the absence of a uniformly applicable gold standard investigation, to compare with, there remains a possibility of certain injuries being missed in the normal serum ALT group. However, we have considered an overall assessment by imaging, progress in hospital, laparotomy findings and satisfactory discharge from hospital, as a reasonably good marker of the presence or absence of liver injury, to permit comparison with a single value of ALT at admission. In addition, liver injury grade reported in this study is also an admixture of CT scan, USG and operative findings. Of the 31 patients with liver injury, five patients underwent immediate laparotomy, with diagnosis being reached in the operating room. Seven patients were evaluated only by a USG performed by residents from the department of radio-diagnosis. Both CT scan and USG were available for only 19 patients. However, we feel that once the diagnosis of liver injury has been reached by either tool, estimating the grade of liver injury is

not difficult and the impact of this bias is likely minimal.

Third, the low absolute number of deaths exclusively due to liver injury ( $n = 2$ ), preclude reliable subgroup analysis with this variable. Nonetheless, comparisons using surrogates for the severity of injury (clinical status, modality of management, injury grade, transfusion requirement and complications) validate and strengthen our conclusions.

### Conflict of interest

None.

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