Triple elevation of ALT is indicative of blunt hepatic trauma. Our local experience at rural district hospital

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Abstract

Objective: The aim of this study was to determine if the liver biomarkers such as Alanine Transaminase (ALT) and Aspartate Transaminase (AST) can be used as diagnostic markers in blunt Liver Injury (LI).

Methods: A retrospective review of all patients with blunt abdominal trauma from November 2013 until November 2014 was made. Patients with abnormally raised liver enzymes were identified and analyzed. Besides demographic data, other parameters investigated were Injury Severity Score (ISS), associated abdominal signs, grading of LI and its clinical management. A matched control was selected concurrently.

Results: A total of 34 patients were enrolled. Their mean ISS was 12 (range 4 – 41). Ten had mild to moderate LI, grade 2 and 3 (70% and 30% respectively). The mean age were 43.1 ± 15.7 years with most (90%) being males. Most of the patients (80%) were hemodynamically stable at presentation. Four patients (40%) demonstrated no abdominal signs suggestive of LI. The mean AST and ALT level were 406.8 ± 307.0 U/L and 377.7 ± 308.9 U/L respectively. CT scan was conducted in 60% of the patients. Raised liver enzymes consistently demonstrated high sensitivity of predicting LI (80 - 90%). A double elevation of AST and ALT are associated with 90% sensitivity, but has low specificity (62% and 66% respectively). Nevertheless elevation of ALT by three times was strongly related with LI (OR 34.2; 95% CI, 3.4 – 337.3) and improved specificity to 80%.

Conclusion: The use of liver enzymes in blunt hepatic trauma is very helpful with elevation of ALT by three times has high sensitivity (90%) and specificity (80%).

Introduction

Liver is the second most common organ prone to injury following blunt abdominal trauma [1]. Blunt liver injury (LI) can vary from minor contusion to avulsion and has been associated with morbidity and mortality [2]. Patients with unstable hemodynamics with hemoperitoneum do not pose a diagnostic challenge since the plan of care is clear [3]. However, difficulties still exists for further investigation in those with minimal clinical findings and stable clinically [1-3].

Focused Assessment of Sonography in Trauma (FAST) is a bedside ultrasound examination to identify presence of free intraperitoneal or pericardial fluids. It has limitations in blunt abdominal trauma with an overall sensitivity for detection of LI reported to be as low as 64% [3,4]. Its sensitivity is even lower when parenchymal injuries associated with no free fluid [5]. In contrast, CT scan has a well-established sensitivity (92-97%) and specificity (98.7%) in diagnosing LI and is therefore currently regarded as an imaging method of choice in stable blunt abdominal trauma [6]. Unfortunately not many medical institutions have a ready access to it.

Recently, raised liver enzymes such as Aspartate Transaminase (AST) and Alanine Transferase (ALT) have been shown to have both excellent diagnostic and prognostic values in blunt LI. In this study we aim to investigate if measurement of liver enzymes can be used in a local setting. If they can be applied locally, it will be a cheaper and easier but reliable method that can be used in institutions where CT scan is not readily available.

Material and methods

This is a retrospective 12-month study (November 2013-2014), which included all blunt abdominal trauma cases for patients ageing more than 12 years old who presented to the level II trauma centre in Hospital Kuala Krai, Kelantan, Malaysia. Our hospital is the only specialist hospital located in the southern part which provides health care services to approximately 320 000 people. The Emergency Department (ED) receives approximately 44,000 visits annually with 13% reported to be trauma related cases. The hospital covered an area of 11 000 km^2 with two non-specialist district hospitals.

Patients with abnormally raised liver enzymes (AST and ALT) were identified and enrolled. Apart from demographic data, other parameters interested were Injury Severity Score (ISS), associated abdominal signs, grading of liver injury and its clinical management were also recorded. Exclusion criteria were known chronic liver disease, delayed presentation (more than 24 hours), blood samples taken 12 hours following trauma and penetrating liver injury. Positive abdominal sign is defined as when two out of the three signs such as 1) external wound at right hypochondriac (RHC) or right lower chest, 2) RHC pain and 3) Tenderness at RHC during palpation. LI was graded based on the American Association for Surgery of Trauma (AAST), as assessed mostly by CT scan.

A matched control is selected concurrently as defined by having blunt abdominal trauma with no proven LI as confirmed by ultrasound or CT scan. An estimated sample size calculated for 90% power, α of 0.05, 1:2 for case:control to detect a minimum odds ratio (OR) of 30 yielded a total of 27 patients (9 cases and 18 controls). Statistical analysis was performed with SPSS version 18 using a Chi-squared test for discrete variables while unpaired t-test was used for continuous variables. The Level of significance was set at p<0.05. AST and ALT levels ≥35 U/L and 45 U/L respectively we considered abnormal.

Results

A total of 34 patients were enrolled. Their mean ISS was 12 (range 4 – 41). Ten had mild to moderate LI, grade 2 and 3 (70% and 30% respectively). The mean age were 43.1 ± 15.7 years with most (90%) being males. Most of the patients (80%) were hemodynamically stable at presentation. Two unstable patients were due to multiple long bone and pelvic fractures. Four patients (40%) demonstrated no positive signs suggestive of liver injury. Cases and controls were matched according to age, gender, mechanism of injury, hemodynamics at presentation and types of imaging conducted (table 1).

Interestingly, both groups had similar rates of positive abdominal signs (60% for cases and 54.2% for controls, p=0.7). Similarly, mean Total white counts (TWC) was also not statistically significant between the two groups (15.1 vs. 18.2, p= 0.175). As expected, the mean ISS was significantly higher among cases when compared to controls (18.8 vs. 10.0, p<0.05).The mean AST and ALT levels were significantly higher among cases when compared to control respectively (Table 1). Elevation of AST and ALT levels by two times is consistently associated with high sensitivity (90%) of detecting LI. However, the specificity is low (62% and 66% respectively). Surprisingly, elevation of AST by three times had lower sensitivity and specificity (80% and 71% respectively; OR=9.7). In contrast, elevation of ALT level by three times is the most reliable marker with 90% sensitivity and 80% specificity (OR=34.2: 95% CI, 3.4 – 337.3) (Table 2).

No liver related morbidity was observed with all cases successfully managed conservatively. There was a single mortality case which

Table 1. Investigated clinical parameters.

Parameters	Cases (n=10)	Control (n=24)	P value
Age (years) mean ± SD	43.1 ± 15.7	32.4 ± 13.5	0.05[a](NS)
Gender (M:F)	9:1	22:2	0.87 [b] (NS)
Mechanism of injury (MVA-related) n (%)	9 (90)	16 (66.7)	0.38 [b] (NS)
Hemodynamics (stable at presentation) n (%)	8 (80)	23 (95.8)	0.07 [b] (NS)
Positive abdominal signsn (%)	6 (60)	13 (54.2)	0.70[b] (NS)
Best imaging done (US:CT)	(6:4)	(11:13)	0.75 [b] (NS)
Mean AST U/L	406.8 ± 307.0	147.2 ± 195.4	0.006 [a]
Mean ALT U/L	377.7 ± 308.9	133.8 ± 217.9	0.01 [a]
Mean TWC X 10³/uL	15.1 ± 4.1	18.2 ± 6.0	0.18[a](NS)
Mean ISS	18.8 ± 11.0	10.0 ± 5.5	0.03 [a]

[a]t-test

[b]chi squared test

NS : Not significant.

ISS : Injury Severity Score

MVA: Motor vehicle accident

US: Ultrasound

CT: Computer tomography

TWC: Total white counts

Table 2. Estimated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the liver enzymes in predicting liver injury.

Liver enzymes	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
AST ≥ 2 x	90	62	50	93
ALT ≥ 2 x	90	66	52	94
AST ≥ 3 x	80	71	53	89
ALT ≥ 3 x	90	80	64	95

PPV = Positive predictive value
NPV = Negative predictive value

occurred due to severe poly-trauma with multi-organ failures.

Discussion

In blunt abdominal trauma, hemodynamically stable patient with minimal signs is often managed in general ward or sometimes discharged. Unfortunately, RHC pain is a fairly unreliable indicator of LI even if performed by skilled hands [1,2,7]. Forty percent of the patients admitted to our hospital showed no typical signs and symptoms of LI. Although conservative management is becoming a standard of care for hemodynamically stable patient, high grade (grade ≥III) LI requires intensive monitoring since nearly 30% tend to require adjunctive treatments including ERCP or percutaneous drainage of biliomas [8]. Therefore, in any cases of blunt abdominal trauma admitted especially to district hospitals, it is of paramount importance to correctly and promptly diagnose the LI which will allow patients to be properly triaged and referred urgently to specialist hospital. Other than CT scan, liver enzymes appear to have good sensitivity and specificity which surpasses that of ultrasound.

The levels of both enzyme (AST and ALT) are expected to rise following LI, as demonstrated by several studies [2-4]. Its diagnostic property is excellent despite of no consistent level concluded. In a previous study, Zhiqiang et al. [3] reported that ALT level of >57 U/l is most suitable in detecting LI when compared to other liver markers with sensitivity of 92.2%, specificity of 84.8%, PPV of 85.6% and NPV of 91.8% [3]. Similarly, Srivastava et al. [4] also reported that ALT is able to predict LI with higher sensitivity and specificity of 100% and 98.9% respectively [4]. Although AST was raised in all of the patients, ALT was significantly associated with it (OR 109.8), sensitivity, specificity, PPV and NPV of 94.5%, 86.4%, 89.7% and 92.7% respectively [6]. Comparable to other studies, in our series both AST and ALT levels were significantly increased with triple elevation of ALT (ALT >135 U/L) appeared to be the most reliable.

Many authors had demonstrated significant correlation between the level of liver enzymes (AST and ALT) and the grade of LI. Recently, Bilgic et al. [8] reported significantly higher AST, ALT and LDH levels in grade 3, 4, and 5 LI when compared to grade 1 and 2. Furthermore, the presence of other visceral injuries has been reported not to influence the level of liver enzymes [8]. Additionally, Stassen et al. [10] demonstrated that, probability of suffering from major injury (grade ≥ 3) was 44% in liver enzymes of >360 IU/L while a level of <360 IU/L is not associated with major LI despite a negative FAST [10]. Tan et al. [6] also concluded that more than double elevation of both enzymes correlated with major injury [6].

Many authors preferred ALT over AST due to its higher sensitivity and specificity [4, 6]. In this study, triple elevation of AST was inferior than ALT in predicting LI. In addition, Srivastava et al. [4] noticed that the median ALT in survivors of LI was significantly lower than those who died (690 U/L and 1960 U/L respectively). They concluded that

raised ALT successfully predicts LI with the higher degree suggesting high grade LI [4]. On the other hand, Zhiqiang *et al.* [3] noted that no correlation exist between the degree of elevated liver enzymes and the grade of injury [3]. However, based on our findings, we cannot make any conclusive suggestion on this matter since a complete spectrum of LI grade was not analysed. Furthermore, the study was not designed for this purpose. A lower prevalence of cases in the total number of investigated population (29%), may explain the low (64%) PPV for triple elevation of ALT in our findings. In contrast, the prevalence of LI cases in most series were approximately 50% - 60% [1,4,6,8].

Combining elevated enzymes and raised total white count or FAST have been shown able to improve its sensitivity and specificity. Lee *et al.* [1] suggested that a combination of raised enzymes (AST > 100 IU/L and ALT > 80 IU/L) and raised TWBC (> 10 000) can be used as an early warning system for possible LI with sensitivity of 90% and specificity of 92.3% respectively [1]. Similarly, incorporating FAST with elevated enzymes will improve the sensitivity and specificity to 88% and 98% respectively especially in children [9]. Unfortunately, we have not seen any significant difference in the degree of leucocytosis in both groups.

There are some limitations to our study. It was retrospective in nature with relatively small sample size as compared to others. Therefore, the possibility of committing type 1 error (false positive) is high since approximately 50% of the control group had only ultrasound rather than CT scan. Moreover, 20% of the control had triple elevation of both enzymes. Future prospective study with larger sample size encompassing entire spectrum of LI and control group taken only from those who had CT scan is very much needed.

Conclusion

The level of liver enzymes particularly triple elevation of ALT is useful in predicting blunt hepatic trauma and provides good sensitivity (90%) and specificity (80%). Patients with stable hemodynamics with no obvious signs of LI but has raised liver enzymes should alert a local trauma physician about a possibility of LI in which they can be transferred to the specialist hospital for further imaging and management.

Authors' contribution

Asri che Jusoh involved in designing, compiling and writing the paper.

Faiz Najmuddin Ghazi participated in doing literature search and organizing the reviewed paper.

Afiq Muizz Rasidi involved in acquisition of data and prepares the case history.

Conflict of interest

Asri Che Jusoh, Ahmad Faiz Najmuddin Ghazi and Afiq Muiz Rasidi declare that we have no conflict of interest and no fund involved.

References

1. Lee WC, Kuo LC, Cheng YC, Chen CW, Lin YK, et al. (2010) Combination of white blood cell count with liver enzymes in the diagnosis of blunt liver laceration. *Am J Emerg Med* 28: 1024-1029. [Crossref]

2. Ritchie AH, Williscroft DM (2006) Elevated liver enzymes as a predictor of liver injury in stable blunt abdominal trauma patients: case report and systematic review of the literature. *Can J Rural Med* 11: 283-287. [Crossref]

3. ZHIQIANG TIAN, HONG LIU, XIAOFANG SU, ZHENG FANG, ZHITAO DONG, et al. (2012) Role of elevated liver transaminase levels in the diagnosis of liver injury after blunt abdominal trauma. *ExpTher Med* 4: 255-260. [Crossref]

4. Srivastava AR, Kumar S, Agarwal GG, Ranjan P (2007) Blunt abdominal injury: serum ALT-A marker of liver injury and a guide to assessment of its severity. *Injury* 38: 1069-1074. [Crossref]

5. Richards JR, McGahan JP, Pali MJ, Bohnen PA (1999) Sonographic detection of blunt hepatic trauma: hemoperitoneum and parenchymal patterns of injury. *J Trauma* 47: 1092-1097. [Crossref]

6. Tan KK, Bang SL, Vijayan A, Chiu MT (2009) Hepatic enzymes have a role in the diagnosis of hepatic injury after blunt abdominal trauma. *Injruy* 40: 978-983. [Crossref]

7. Schurink GW, Bode PJ, van Luijt PA, van Vugt AB (1997) The value of physical examination in the diagnosis of patients with blunt abdominal trauma: a retrospective study. *Injury* 28: 261-265. [Crossref]

8. Bilgic I, Gelecek S, Akgun AE, Ozmen MM (2014) Predictive value of liver transaminases levels in abdominal trauma. *Am J Emerg Med* 32: 705-708. [Crossref]

9. Sola JE, Cheung MC, Yang R, Koslow S, Lanuti E, et al. (2009) Pediatric FAST and elevated liver transaminases: An effective screening tool in blunt abdominal trauma. *J Surg Res* 157: 103-107. [Crossref]

10. Stassen NA, Lukan JK, Carrillo EH, Spain DA, Norfleet LA, et al. (2002) Examination of the role of abdominal computed tomography in the evaluation of victims of trauma with increased aspartate aminotransferase in the era of focused abdominal sonography for trauma. *Surgery* 132: 642-646. [Crossref]