Trajectory of liver function tests during the initial alcohol detoxification period: A preliminary analysis

Sir,

Liver enzyme levels in alcohol-dependent patients are not static and vary with the severity of alcohol-induced liver damage and may change with abstinence.\(^1,2\) Knowledge of short-term changes and the trajectory of change can help the treating clinicians in deciding which of these tests should be undertaken and when. The present study aimed to examine the trajectory of liver function test (LFT) in alcohol-dependent patients during the initial 10 days of detoxification period and compared it with healthy controls.

This case–control study was conducted at the National Drug Dependence Treatment Centre, All India Institute of Medical Sciences, New Delhi, India. Cases included male inpatients aged 18–65 years with a diagnosis of alcohol dependence as per the International Classification of Diseases-10, with regular drinking of alcohol for the last 15 days. Those who had dependence on any other psychoactive substance apart from alcohol or nicotine; had comorbid axis I psychiatric illness; or had severe medical illnesses/cerebrovascular accidents/seizure were excluded from the study. Controls included age- and gender-matched friends or nonbiological relatives of cases who accompanied them to the center. Controls with substance use apart from nicotine, or with any axis I psychiatric illness, or medical illness were excluded from the study. The study had institutional ethics approval.

Participants were assessed using a structured proforma on the day of admission which included demographic and clinical profile and clinical diagnoses. Two ml of blood sample was collected, and LFT parameters such as gamma glutamyl transferase (GGT), serum aspartate transaminase (AST)/serum alanine transaminase (ALT), alkaline phosphatase (ALP), total bilirubin, protein, and albumin were measured. Similarly, on days 5 and 10, the same tests were repeated. For controls, sample collection was carried out once at baseline. Patients were treated with appropriate benzodiazepines based on the severity of withdrawal symptoms.

All the 25 cases and 25 controls comprised males and did not differ in mean age (38.2 ± 8.5 years vs. 36.0 ± 11.6 years). Among the cases, the mean duration of regular alcohol use was 10.6 ± 8.5 years and the usual amount was 33.1 ± 19.3 units/day. The liver parameters among cases (on days 1, 5, and 10) and controls are presented in Table 1. Over the alcohol detoxification process (i.e., days 1, 5, and 10), GGT, AST, and ALT values of cases remained significantly higher than that of controls, which is in line with previous studies.\(^3,4\) The bilirubin levels remained higher in cases than controls only at day 1, but the differences were not significant at days 5 and 10. The serum albumin and total protein levels were lesser in cases as compared to controls, which is in line with some of the previous studies.\(^5,6\) Over the detoxification period of 10 days, only AST, ALT, and bilirubin levels significantly improved. In the present study, though serum bilirubin levels did not persistently differ between cases and controls, significant improvement in bilirubin levels occurred in patients with alcohol dependence within 10 days of alcohol detoxification, which is a noteworthy finding. Similarly, significant decrease in AST and ALT levels in the current study was consistent with that of the previous studies.\(^5,6\) Further supporting the evidence that they have been shown to be useful in monitoring known alcoholic patients for relapse.\(^6\) Monitoring AST and ALT may help in predicting the relapse at an earlier stage unlike GGT which, in the present study, showed nonsignificant improvement over the 10 days. Previous studies also reported that GGT levels in alcoholics return to normal within 2–3 weeks upon abstinence.\(^7\)

The receiver operator characteristic curves to differentiate individuals with alcohol dependence and those without such condition are shown in Table 1. GGT showed a sensitivity of 88% and a specificity of 96% at a cutoff value of 44 U/L in distinguishing alcohol dependence from control population, which is consistent with previous studies.\(^5,8\) However, GGT is not specific to alcoholism and is raised in many conditions.\(^5,9,10\) AST values in this study showed a sensitivity of 80% and a specificity of 100% at a cutoff value of 48 U/L in distinguishing alcohol dependence from control population. Area under the curve for AST (0.933, 95% confidence interval of 0.849–1.000) was nearly same as for GGT (0.934, 95% confidence interval of 0.849–1.000), suggesting that AST was almost as good a biomarker as GGT for differentiating alcohol-dependent individuals from healthy controls. The sensitivity and specificity of ALT were further less compared to those of GGT and AST. The area under the curve for serum albumin and total protein was low, and they may not be considered as good indicators for differentiating alcohol-dependent patients from that of healthy controls. Serum ALP levels did not differ significantly between cases and controls.

This study has some important clinical implications. Measuring baseline GGT, AST, and ALT levels might
Table 1: Liver function test parameters of cases and controls

| Parameter       | Case day 1 (I) | Case day 5 (II) | Case day 10 (III) | Control baseline (C) | Comparison of cases and controls | Change in cases from day 1 to 10; \(F (P^*), \text{partial } \eta^2\) |
|-----------------|---------------|----------------|-------------------|----------------------|----------------------------------|----------------------------------|
| Total bilirubin (mg/dL) | 1.06 (0.52)   | 0.62 (0.35)    | 0.48 (0.25)       | 0.57 (0.30)           | I > C                            | 18.814 (<0.001)*, 0.621          |
| AST (U/L)       | 109.72 (75.82)| 101.32 (59.47) | 73.56 (51.83)     | 31.36 (8.11)         | I, II, III > C                   | 10.649 (0.001)*, 0.481           |
| ALT (U/L)       | 83.92 (72.98) | 96.24 (75.32)  | 91.72 (61.10)     | 39.44 (17.40)        | I, II, III > C                   | 0.576 (0.570), 0.048             |
| GGT (U/L)       | 348.32 (633.32)| 261.48 (472.64)| 202.88 (341.28)   | 25.4 (11.28)         | I, II, III > C                   | 2.614 (0.095), 0.185             |
| ALP (U/L)       | 272.16 (106.88)| 227.64 (82.81) | 210.04 (91.59)    | 228.48 (40.92)       | NS                               | 7.083 (0.004)*, 0.381            |
| Total protein (g/dL) | 7.09 (0.72) | 7.01 (0.52) | 6.98 (0.45) | 7.56 (0.48) | I, II, III < C | 0.589 (0.563), 0.049 |
| Albumin (g/dL)  | 3.98 (0.71)   | 3.84 (0.52)    | 3.82 (0.48)       | 4.66 (0.41)          | I, II, III < C                   | 1.519 (0.240), 0.117            |

\*P<0.05, only significant differences shown in comparison of cases and controls, change in cases in LFT parameters shown in terms of Pillai’s Trace \(F (P^*)\) with effect sizes. AST – Aspartate aminotransferase; ALT – Alanine aminotransferase; GGT – Gamma glutamyl transferase; ALP – Alkaline phosphatase; NS – Not significant; LFT – Liver function test

strengthen the objective evidence for establishing chronic alcohol use. These are simple tests which can be administered at primary and secondary care settings where more sophisticated investigations are not available. Further, monitoring some of these simple LFT parameters (AST, ALT, and bilirubin levels) could be useful for clinicians in providing feedback to the patient, which may help in motivating the patient with alcohol dependence to maintain abstinence. Further, it could also help in monitoring relapse.

The study has some limitations such as not being able to control for confounding factors such as obesity, coffee intake, medications for withdrawal symptoms, stress due to inpatient management, single-center experience, small sample size, and inclusion of only male participants. Further prospective well-designed studies are needed for addressing these limitations. Yet, the findings suggest that some parameters such as GGT, AST, and ALT can help distinguish alcohol-dependent and healthy individuals. Some parameters such as AST, ALP, and total bilirubin may change over the detoxification period of about 10 days, which can be used in giving feedback, thus might be useful for clinicians who have some LFT parameters for monitoring during the course of treatment.

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Conflicts of interest
There are no conflicts of interest.

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REFERENCES

1. Torruellas C, French SW, Medici V. Diagnosis of alcoholic liver disease. World J Gastroenterol 2014;20(1):1684-99.
2. Campbell S, Timms PM, Maxwell PR, Doherty EM, Rahman MZ, Lean ME, et al. Effect of alcohol withdrawal on liver transaminase levels and markers of liver fibrosis. J Gastroenterol Hepatol 2001;16:1254-9.
3. Alatalo P, Koivisto H, Puukka K, Hietala J, Anttila P, Bloigu R, et al. Biomarkers of liver status in heavy drinkers, moderate drinkers and abstainers. Alcohol Alcohol 2009;44:199-203.
4. Torkadi PP, Apte IC, Bhute AK. Biochemical evaluation of patients of alcoholic liver disease and non-alcoholic liver disease. Indian J Clin Biochem 2014;29:79-83.
5. Das AK, Chandra P, Gupta A, Ahmad N. Obesity and the levels of liver enzymes (ALT, AST & GGT) in East Medinipur, India. Asian J Med Sci 2015;6:40-2.
6. Tavakoli HR, Hull M, Michael Okasinski L. Review of current clinical biomarkers for the detection of alcohol dependence. Innov Clin Neurosci 2011;8:26-33.
7. Niemelä O. Biomarker-based approaches for assessing alcohol use disorders. Int J Environ Res Public Health 2016;13:166.
8. Miller PM, Anton RF. Biochemical alcohol screening in primary health care. Addict Behav 2004;29:1427-37.
9. Conigrave KM, Degenhardt LJ, Whitley JB, Saunders JB, Helander A, Tabakoff B, et al. CDT, GGT, and AST as markers of alcohol use: The WHO/ISBRA collaborative project. Alcohol Clin Exp Res 2002;26:332-9.
10. Helander A. Biological markers in alcoholism. In: Fleschhacker W.W., Brooks D.J., editor. Addiction Mechanisms, Phenomenology and Treatment, 1st edn. Vienna: Springer; 2003. p. 15-32..

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