# Comparison of albumin-bilirubin grade with Child-Pugh and Model for End Stage Liver Disease scores in chronic liver disease

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## ABSTRACT

Introduction: chronic liver diseases are characterized by injury to hepatocytes, chronic inflammation and progressive substitution of liver parenchyma by scar tissue or fibrosis. Albumin-bilirubin grade (ALBI) includes serum albumin and bilirubin levels, two most commonly performed and cost-effective parameters measured in the Clinical Laboratory. This study aims to establish an association between ALBI grade and Model for End stage Liver Disease (MELD) and Child-Pugh (CP) scores among chronic liver disease patients.
Methods: after ethical approval, information such as age, gender, provisional diagnosis, serum albumin and serum total bilirubin levels, prognostic scores of patients with liver disease were obtained from patient records. Albumin-bilirubin grading system was calculated as following: [$\log_{10}$ bilirubin (µmol/L) × 0.66] + [albumin (g/L) × −0.0852].
Results: this cross-sectional descriptive study recruited 100 patients with chronic liver disease and 100 healthy controls. Alcoholism was the common aetiology among the cases. ALBI was calculated; the mean (SD) grade among cases and controls were -0.94 (0.15) and -3.17 (0.23) respectively with a p-value of <0.001.There was statistically significant difference in ALBI grades between CP scores B and C (p value = 0.001). Pearson's correlation between MELD score and ALBI grade showed a statistically significant correlation (r = 0.723 with significance 0.001).
Discussion: our study demonstrated that there was a significant association between ALBI grade and the most commonly used prognostic scores such as CP and MELD.

## INTRODUCTION

Chronic liver diseases are characterized by injury to hepatocytes, chronic inflammation and progressive substitution of liver parenchyma by scar tissue or fibrosis. Chronic liver diseases arise from various causes; the most common being alcoholic and non-alcoholic fatty liver diseases (NAFLD). However, other relevant causes exist: infections, toxins, metabolic and autoimmune causes, malignancy.

The prognosis of chronic liver diseases is being assessed by scores like Child Pugh (CP) and Model for End stage Liver Disease (MELD). CP score calculation requires albumin, bilirubin, International Normalized Ratio, presence of hepatic encephalopathy and ascites. The presence of encephalopathy and ascites require a subjective evaluation; albumin serum concentration and ascites are related to each other leading to variations in grading. MELD score calculation requires serum creatinine, bilirubin and International Normalized Ratio; it is well known that serum creatinine values are influenced by factors like age, gender, muscle mass causing a large variation among individuals. A number of studies have shown that variability in creatinine and International Normalized Ratio determination in different laboratories have led to inconsistency in MELD scores (1,2). As CP and MELD scores show the mentioned limitations, there is an urgent need for other prognostic markers.

One novel indicator is the Albumin-Bilirubin (ALBI) grade utilized by Johnson et al. in 2015 for hepatocellular carcinoma (3). The ALBI grade includes serum albumin and bilirubin levels, the two most commonly performed and cost-effective parameters that are a part of routine liver function tests. Since the first paper, various studies have been carried on to verify its effectiveness and usefulness in hepatocellular cancer. Wang et al. conducted a study to compare ALBI grade with CP score and concluded that ALBI was better than CP in distinguishing patients into different groups based on prognosis of liver cancer; post-operative survival was also better defined in ALBI-classified patients than in CP-classified groups (4). A massive research had been done

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to support the usefulness of ALBI in the prognosis of liver cancer; however, studies that associate ALBI grade with liver diseases caused by different aetiologies are sparse (5, 6). ALBI grade has been studied to prognosticate 3-month outcome in patients with liver diseases induced by Hepatitis-B virus (7). A study by Chan AW et al. proved that ALBI is an independent marker for the prognosis of primary biliary cirrhosis (8).

A grading score to prognosticate liver diseases of any aetiology is essential for preventing its advancement to cirrhosis, malignancy or failure. This will aid clinicians and epidemiologists to provide treatment and prevention measures respectively and thereby decrease the morbidity and mortality due to liver diseases. Hitherto, ALBI grading has been studied in hepatocellular cancer survival and prognosis. Only few studies are available regarding the usage of ALBI grading in liver diseases other than cancer. This study is aimed to verify the usefulness in clinical practice of two simple, objective and commonly performed laboratory parameters to prognosticate liver diseases.

## METHODS

After obtaining approval from the Institutional Human Ethics Committee (IHEC), this descriptive cross-sectional study was conducted in a tertiary care centre.The study has been carried out according to the Helsinki Declaration of 1975 as revised in 2013.

The study participants were divided intwo groups – cases and controls. The cases included all patients diagnosed with liver disease who consulted medicine and gastroenterology department during the study period of one year. Information such as age, gender, provisional diagnosis, laboratory parameters like serum albumin and total bilirubin levels, CP and MELD scores were obtained from the medical records. Subsequently personal identifiers were removed. Since there was no direct contact between the investigator and participants, a waiver of consent was obtained from Ethics Committee.

The control group included healthy participants attending their routine health check-up screening and had no evidence of liver disease as per clinical and laboratory data. Patients with liver disease and without CP and MELD scores were excluded from the study. Patients with malignancy and renal diseases were excluded due to the impact on synthesis and excretion of albumin. Patients with anaemia, gall stones and those on drugs like sulphonamides, anti-psychotics, chemotherapy were excluded due to the influence of the therapy on bilirubin levels.

Based on the recently estimated serum albumin and total bilirubin levels, ALBI grade of each patient was calculated using the formula reported below.Using serum albumin (g/L) and serum total bilirubin (μmol/L), the ALBI grade was calculated as follows (3):

$$ALBI = 0.66 \times (\log_{10}\text{Total Bilirubin}) + \text{Serum albumin} \times (-0.085)$$

The ALBI grades were statistically compared among cases and controls. Serum albumin was estimated using Bromocresol Green method (end-point) and serum bilirubin was assayed using Diazo method (end-point) in auto-analyzer (Cobas 6000) using dedicated kits and reagents from the manufacturer (RocheDiagnostics, Mannheim, Germany).

### Statistical analysis

Student's t-test was used to compare continuous variables and Chi-square test for categorical variables. Pearson's correlation was employed to examine the relationship between clinical variables. ANOVA was done to compare significance between different groups. $p<0.05$ was considered as significant. Bonferroni's correction was used to compare the two groups when there was a statistically significant difference in group means revealed by one-way ANOVA. ROC curve analysis was done to predict the accuracy of the new grading with established scoring systems. Statistical Package for the Social Sciences version 24 was used for statistical analysis.

## RESULTS

This cross-sectional descriptive study recruited 100 cases with chronic liver disease and 100 healthy controls without liver disease. The mean (SD) age group of cases and controls were 50.36 (10.23) years and 50.51 (11.97) years respectively, with a p-value of 0.751. There were 12 females and 88 males among cases, and 20 females and 80 males among controls. Chi square test done to assess the significance of gender among the study groups revealed a p-value of 0.625. Hence, both the study groups were age and gender matched. The demographic characteristics of cases group are shown in Table 1.

**Table 1**
*Demographic characteristics of the cases*

| Characteristics | Cases |
|---|---|
| Age | 50.36 ± 10.23 years |
| Number of females | 12 (12%) |
| Number of males | 88 (88%) |
| Serum albumin,mean (SD) | 2.5 (0.4) |
| Serum bilirubin,mean (SD) | 6.9 (0.7) |
| Number of cases with CP-A | 2 |
| Number of cases with CP-B | 43 |
| Number of cases with CP-C | 55 |
| MELD score,mean (SD) | 21.83 (7.1) |

*CP-A, CP-B, CP-C, Child Plug groups A, B and C; MELD, Model for end stage liver disease score; SD, Standard deviation*

Alcohol stood as the major aetiology for 56% of the chronic liver disease patients; 13% had NAFLD. The

distribution of cases with other aetiologies was as follows: viral hepatitis 13%, cryptogenic 10%, autoimmune 4%, primary biliary cirrhosis 2%, Budd-Chiari syndrome 1%, and Wilson's disease 1%.

The mean (SD) ALBI grade among cases was -0.94 (0.15) and among controls was -3.17 (0.23). It was found to be significantly different among the two groups with p-value of <0.001.

Based on CP score, liver disease patients were classified into three groups namely CP-A (n=2), CP-B (n=30), CP-C (n=68). The mean (SD) of the ALBI scores among the three CP scores A, B, C are -1.48 (0.27), -1.42 (0.30) and -0.87 (0.19) respectively. The ALBI grade between these groups was compared using ANOVA showing a significant difference in the ALBI grade between CP-A, CP-B and CP-C patients (p value=0.001). Bonferroni test revealed a statistically significant difference in ALBI grades between CP B and C (p value = 0.001) (Table 2). ROC curve analysis was done to predict how accurately ALBI grading can be used to discriminate between patients with CP-B and CP-C. This provides an area under the curve of 0.786 with the 95% CI (0.669-0.867) (Figure 1).

**Table 2**
*Post hoc analysis of ALBI grade with Child Pugh scores of liver disease patients*

| CP score | Mean Difference (95% Confidence Interval) | Standard Error | p-value |
|---|---|---|---|
| CP-A *versus* CP-B | -0.245 (-1.084 – 0.593) | 0.344 | 1.000 |
| CP-B *versus* CP-C | -0.423* (-0.682 – (-0.164)) | 0.106 | 0.001* |
| CP-C *versus* CP-A | 0.668 (-0.152 – 1.489) | 0.337 | 0.150 |

*CP-A, CP-B, CP-C, Child Plug groups A, B and C; MELD, Model for end stage liver disease score; SD, Standard deviation*
**p value < 0.05 is considered significant*

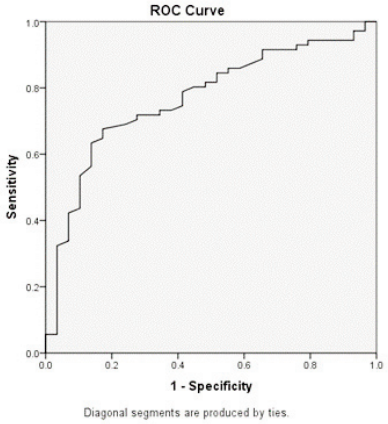


**Figure 1**
*ROC curve analysis of ALBI grading*
*AUC with 95% CI = 0.768*

CP-Apatients were excluded from the ROC curve calculation sincethere were only 2 participants in this group.

Pearson's correlation between MELD score and ALBI grade showed a statistically significant correlation (r = 0.723 with two-tailed significance 0.001). Scatter plot showing the correlation between MELD and ALBI is depicted in Figure 2. On the basis of aetiology, liver disease patients were divided into three categories as alcoholic liver disease, NAFLD and other aetiologies. The mean (SD) ALBI scores in the alcoholic liver disease, non-alcoholic fatty liver disease and other aetiologies groups were -0.79 (0.17), -1.03 (0.25) and -1.33 (0.25) respectively. The ALBI grade between these groups compared using ANOVA showed that there is a significant difference in the ALBI grade between the three categories (p value=0.001). Bonferroni test (post-hoc analysis) revealed a statistically significant difference in ALBI grades between alcoholic liver disease and other aetiologies (p - 0.001) while there was no statistically significant difference between alcoholic liver disease and NAFLD (Table 3).

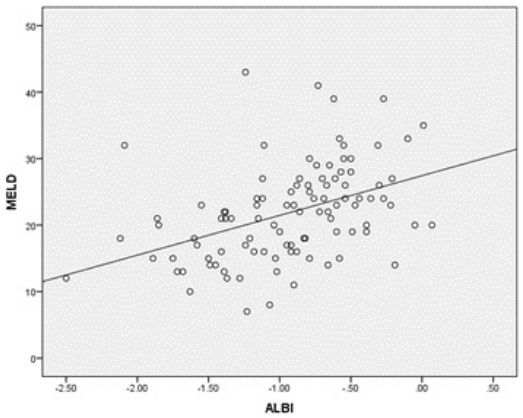


**Figure 2**
*Scatter-plot showing correlation between MELD and ALBI*

**Table 3**
*Comparison of ALBI grade among alcoholic liver disease, NAFLD and other aetiologies of liver disease*

| Aetiology | Mean Difference (95% Confidence Interval) | Standard Error | p-value |
|---|---|---|---|
| Alcohol *versus* NAFLD | 0.534 (-0.079 – 1.149) | 0.254 | 0.111 |
| NAFLD *versus*Other aetiologies | 1.350* (0.770-1.929) | 0.240 | 0.001* |
| Other aetiologies *versus* Alcohol | -1.884* [-2.202 – (-1.567)] | 0.131 | 0.001* |

*CP-A, CP-B, CP-C, Child Plug groups A, B and C; MELD, Model for end stage liver disease score; SD, Standard deviation*
**p value < 0.05 is considered significant*

## DISCUSSION

This paper was aimed to study the ALBI grades in chronic liver disease patients of aetiologies other than hepatocellular cancer. Most of the liver disease patients in the study population were around the age of fifty and males outweighed in all aetiologies of liver disease.

The etiological profile of the patients with liver disease revealed alcoholism as the foremost among all causes. There is a rise in alcohol related liver disease in the developing countries; this can be attributed to the increasing income *per capitas* as well trends of increasing consumption as part of urbanization, migration and embracing western lifestyle in these countries.

ALBI grade was introduced by Johnson et al (3); the different grades of the score are: ≤−2.60 (ALBI grade 1), >−2.60 to ≤−1.39 (ALBI grade 2), and >−1.39 (ALBI grade 3). This simple and objective score demonstrated its usefulness in the evaluation of prognosis in patients with liver cancer (3).This study demonstrated that liver disease patients belong to grade 3 [-3.17(0.23)] as compared to participants without liver disease who belong to grade 1 [-0.94(0.15)]. The rationale of the marker is that in liver disease, albumin synthesis is decreased due to the destruction of hepatocytes and bilirubin levels are raised due to the impaired metabolism of bilirubin.

The study also analysed the association between CP score and ALBI grading and revealed that ALBI was significantly different in the patients with CP-B and C scores. This finding was consistent with the results of the study by Fragakiet al and Chen et al. CP-C indicates worse prognosis and this study shows that these patients are correctly identified by using ALBI grading- a more cost-effective tool (7, 9). However the association of ALBI grading with significant difference only among CP-B and -C is due to the under representation of CP-A category among the cases. The findings of this study were in contradiction to those by Johnson et al. who showed that within the CP-A class there were two distinct patient groups showing significant differences in survival outcomes that ALBI grading was able to discriminate (3).

Furthermore, this study depicts a good correlation between MELD scores and ALBI grading with an r value of 0.723. This was consistent with findings in a retrospective study conducted by Deli Zou et al. where it was demonstrated that ALBI grade was comparable with CP and MELD to prognosticate acute upper gastrointestinal bleeding due to liver cirrhosis (10). We found that ALBI grade had a moderate to high prognostic performance.

This study verified that ALBI grading was significantly different in liver disease due to alcoholism and other causes such as autoimmune or viral infections. However, there was no difference in ALBI between alcoholic liver disease and NAFLD. This might be because of the presence of a greater number of cases with alcoholism and very few cases with other causes. However large-scale studies are required to establish a significant association. Our study concluded that there was significant association between ALBI and the commonly used severity and prognostic scores such as CP and MELD.

The limitations of this study are twofold: first, it was conducted in a single tertiary care centre with a relatively small number of cases; second, a follow-up of patients to assess the prognostic implications and their overall survival in relation to their ALBI grading is required.

This study has expanded the usage of ALBI in multiple aetiologies of chronic liver disease. It will be useful in the future to analyse each etiological category separately with an adequate number of patients for different diagnosis.

It can be concluded that ALBI grade is economically and technically feasible and could thus become one of the biomarkers to be used in many clinical services from primary health care centre to a tertiary care multispecialty centre. ALBI grading could be used as a cost-effective tool to measure disease severity in liver disease patients as a surrogate marker to existing scores.

## CONFLICT OF INTEREST

None.

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