Elevated Liver Fatty Acid Binding Protein (FABP1) serum levels improve prognostic discrimination of King’s College Criteria and the ALFSG index in acetaminophen-induced acute liver failure: a nested case control study.

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Body Of Abstract

Background: Acetaminophen (APAP)-induced acute liver failure (ALF) is associated with significant mortality. To date, traditional prognostic scores lack discrimination in identifying patients with APAP-ALF who will die without liver transplant (LT), and those who will survive with medical management alone. Failure to identify those in need of LT results in a potentially preventable death while wrongly classifying prospective survivors as in need of LT subjects the patient to unnecessary LT. Liver-type fatty acid binding protein (FABP1) is a small (15 kDa) cytoplasmic protein abundantly expressed in hepatocytes. The prognostic value of serum FABP1 levels in APAP-ALF patients has not been reported. Aim: To determine whether serial samples (early; day 1 or late; day 3-5) of serum FABP1 levels are associated with 21-day mortality in the absence of LT. Methods: Nested case control study 198 APAP-ALF patients (99 survivors, 99 non-survivors) from the US Acute Liver Failure Study Group (ALFSG) Registry. Patient samples were analyzed for FABP1 using solid-phase enzyme-linked immunosorbent assay (ELISA) and assessed with clinical data. In addition, 51 healthy controls (University of Alberta) were included. Results: APAP-ALF survivors had significantly lower serum FABP1 levels on admission (238.6 vs. 690.8 ng/ml, P<0.0001) and late (148.4 vs. 612.3 ng/ml, P<0.0001) compared with non-survivors (Figure 1). Using multivariable logistic regression, increased serum FABP1 early (Log FABP1 Odds Ratio (OR) 1.31, P=0.03) and late (Log L-FABP OR 1.50, P=0.005) were associated with significantly increased 21-day mortality after adjusting for significant covariates (MELD, vasopressor use). Area under the receiver operating curve (AUROC) for early and late multivariable models were 0.778 and 0.907 respectively. The addition of FABP1 (Table 1) significantly improved the AUROC of the King’s College Criteria (KCC) (Early: 0.552 alone, 0.711 with L-FABP; Late: 0.604 alone, 0.797 with FABP1, respectively) as well as the ALFSG prognostic index (Early: 0.686 alone, 0.766 with FABP1; Late: 0.711 alone, 0.815 with FABP1, respectively). Summary: Serum levels of FABP1 in APAP-ALF patients were significantly associated with 21-day mortality measured at early and late time points after adjusting for significant covariates (MELD, vasopressor use). Area under the receiver operating curve (AUROC) for early and late multivariable models were 0.778 and 0.907 respectively. The addition of FABP1 (Table 1) significantly improved the AUROC of the King’s College Criteria (KCC) (Early: 0.552 alone, 0.711 with L-FABP; Late: 0.604 alone, 0.797 with FABP1, respectively) as well as the ALFSG prognostic index (Early: 0.686 alone, 0.766 with FABP1; Late: 0.711 alone, 0.815 with FABP1, respectively). Summary: Serum levels of FABP1 in APAP-ALF patients were significantly associated with 21-day mortality measured at early and late time points after adjusting for significant covariates. FABP1 improved performance (AUROC) when combined with existing prognostic scores at serial time points. Conclusions: In patients with APAP-ALF, FABP1 showed good potential to discriminate survivors from non-survivors at multiple time-points and significantly improved models currently used in clinical practice. Validation of FABP1 as a clinical prediction tool in APAP-ALF merits further investigation. The study was sponsored by NIH grant U-01 58369 (from NIDDK) and a
grant from the University of Alberta Hospital Foundation (UHF).

**Table 1. Comparison of Model Performance (Early and Late) for 198 APAP-ALF patients.**

<table>
<thead>
<tr>
<th>MODELS</th>
<th>EARLY (Admission)</th>
<th>LATE (Day 3-5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>KCC</td>
<td>174</td>
<td>110</td>
</tr>
<tr>
<td>KCC+FABP1</td>
<td>174</td>
<td>110</td>
</tr>
<tr>
<td>ALFSG Index</td>
<td>192</td>
<td>124</td>
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<tr>
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<td>192</td>
<td>124</td>
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<tr>
<td>Variable</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>KCC</td>
<td>0.552 (0.502,0.602)</td>
<td>0.604 (0.555,0.654)</td>
</tr>
<tr>
<td>KCC+FABP1</td>
<td>0.711 (0.635,0.787)</td>
<td>0.797 (0.712,0.882)</td>
</tr>
<tr>
<td>ALFSG Index</td>
<td>0.686 (0.624,0.747)</td>
<td>0.711 (0.635,0.788)</td>
</tr>
<tr>
<td>ALFSG Index+FABP1</td>
<td>0.766 (0.699,0.833)</td>
<td>0.815 (0.736,0.894)</td>
</tr>
</tbody>
</table>

**Figure: Figure 1: Serum levels of FABP1 (ng/ml) in healthy controls, non-survivors (early ~ admission), survivors (early), non-survivors (late ~ day 3-5), survivors (late).**
Disclosure/Financial Association

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