# ALCOHOL-RELATED LIVER DISEASE PHENOTYPE IMPACTS SURVIVAL AFTER AN ACUTE VARICEAL BLEEDING EPISODE

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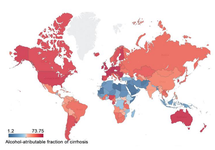
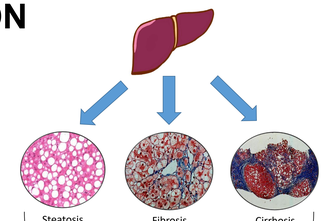
## INTRODUCTION




Alcohol-related liver disease (ALD) is a major cause of liver disease worldwide.




**Alcoholic hepatitis (AH)**
The prevalence of AH remains unknown and it is probably underdiagnosed, especially when AH concurs with liver-related complications

AH might be a concomitant event in cirrhotic patients with acute variceal bleeding (AVB). **We hypothesized that the presence of AH during an AVB event could be an important factor in both the clinical outcomes and the survival rates**

## AIM

We performed a nested study in the preemptive TIPS (p-TIPS) cohort by retrospectively analyzing this well characterized cohort of 2,138 patients with AVB. We aimed to **uncover the incidence and prognostic role of AH among patients admitted with an AVB episode:**

- Compare the clinical outcomes (transplant-free survival at 42 and 365 days, decompensations and infections) of AH patients to a) patients with alcoholic cirrhosis actively drinking without AH criteria, b) patients with alcoholic cirrhosis abstinent from alcohol, and c) patients with viral cirrhosis without alcohol intake.

## METHODS

This is a multicenter, international, observational study performed in 34 referral centers in Europe & Canada, between October 2011 and May 2015. All 34 centers collected data prospectively from all patients with cirrhosis admitted for AVB episode.

A total of 2138 patients were consecutively registered in the database. 916 patients were selected under the next categories: **patients with AH criteria** (n=99) according to the NIAAA criteria, **ALD cirrhosis actively drinking at the time of AVB (d-ALD)** (n=285), **ALD cirrhosis abstinent from alcohol (a-ALD)** (n=227) and **viral cirrhosis** (n=305). Survival was assessed by the Kaplan–Meier method and log-rank Mantel-Cox test.

## RESULTS

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**Patients with cirrhosis and AVB**
N = 2138

**Patients excluded**
N = 1410
-995 incomplete data
-117 sepsis
-233 shock
-287 CHC outside Milan or other neoplasia
-678 multiple etiology of cirrhosis

**Patients included**
N = 916

| AH | d-ALD | a-ALD | Viral |
|---|---|---|---|
| N = 99 | N = 285 | N = 227 | N = 305 |

**Prevalence of Alcoholic hepatitis:**
- 4.6% in the whole cohort (2138 patients)
  - 10.8% in the patients included (916)
  - 16% in the patients with ALD (611)

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**Table 1. Baseline caractheristics**

| | AH (N=99) | d-ALD (N=285) | a-ALD (N=227) | Viral (N=305) | *p* value |
|---|---|---|---|---|---|
| **Male, n (%)** | 84 (84.8) | 238 (83.5) | 195 (85.9) | 170 (55.7) | <0.001 |
| **Age, median (IQR)** | 51.9(44.7-58.7) | 56.99 (49.3-65.8) | 60.8 (53.7-66.1)Y ¥ | 61.7 (51.5-73.1)Y ab | <0.001 |
| **Time to cirrhosis diagnosis (months)** | 12 (0-36) | 23 (0-52) | 36 (12-72.5)Y ¥ | 49 (24-128.25)Y ab | <0.001 |
| **Previous decompensations, n (%)** | | | | | |
| Ascites | 41 (41.4) | 109 (38.2) | 152 (67)Y ¥ | 125 (41)b | <0.001 |
| Hepatic encefalopathy | 13 (13.1) | 30 (10.5) | 55 (24.2)Y ¥ | 35 (11.5)b | <0.001 |
| Gastrointestinal bleeding | 20 (20.2) | 101 (35.4) | 100 (44.1) | 93 (30.5) | <0.001 |
| **Liver function scores** | | | | | |
| **Child-Pugh, n (%)** | | | | | |
| A | 3 (3) | 75 (26.3)Y | 56 (24.7)Y | 86 (28.2)Y | <0.001 |
| B | 20 (20.2) | 172 (60.4)Y | 117 (51.5)Y ¥ | 184 (60.3)Y | <0.001 |
| C | 76 (76.8) | 38 (13.3)Y | 54 (23.8)Y ¥ | 35 (11.5)Yb | <0.001 |
| **MELD, median (IQR)** | 19.9 (17.2-22.7) | 13 (10.9-15.9)Y | 14.2 (11.2-17.96)Y ¥ | 11.9 (9.4-14.9)Y ab | <0.001 |
| **CLIF-AD, median (IQR)** | 54.1 (48.9-61.3) | 52.8 (46.9-57.7) | 54.5 (49.1-59.9)¥ | 50.4 (46.1-56.9)Y ab | <0.001 |

**Table 2. Caractheristics during admission**

| | AH (N=99) | d-ALD (N=285) | a-ALD (N= 227) | Viral (N= 305) | *p* value |
|---|---|---|---|---|---|
| **Early TIPS, n (%)** | 11 (11.1) | 12 (4.2)Y | 9 (4)Y | 6 (2)Y | 0.001 |
| **Failure to initial therapy, n (%)** | 13 (13.1) | 34 (11.9) | 27 (11.9) | 23 (7.5) | 0.2 |
| **Need for rescue therapy, n (%)** | 11 (11.1) | 33 (11.5) | 23 (10.1) | 19 (6.2) | 0.2 |
| **Days of hospitalisation, n (%)** | 12 (8.75-19) | 8 (6-12)Y | 10 (7-15)Y ¥ | 9 (7-13)Y | <0.001 |
| **Decompensations during hospitalisation, n (%)** | | | | | |
| AKI (including HRS) | 10 (10.1) | 15 (5.2) | 21 (9.2) | 24 (7.8) | 0.3 |
| Infections (including SBP) | 34 (34.3) | 77 (27) | 67 (29.5) | 59 (19.3)Y b | 0.009 |
| Ascites | 30 (36.1) | 62 (24) | 55 (31.1) | 78 (29.3) | 0.2 |
| Hepatic encefalopathy | 23 (23.2) | 30 (10.5)Y | 39 (17.2) | 33(10.8)Y | 0.02 |

Alcoholic hepatitis, AH; ALD cirrhosis actively drinking at the time of AVB, d-ALD; ALD cirrhosis abstinent from alcohol at the time of AVB, a-ALD, and viral cirrhosis. Ψ *p* value <0.05 between AH and any other group (d-ALD, a-ALD and viral). ¥ *p* value <0.05 between d-ALD and a-ALD , α *p value* <0.05 between d-ALD and viral cirrhosis β *p value* <0.05 between a-ALD and viral cirrhosis

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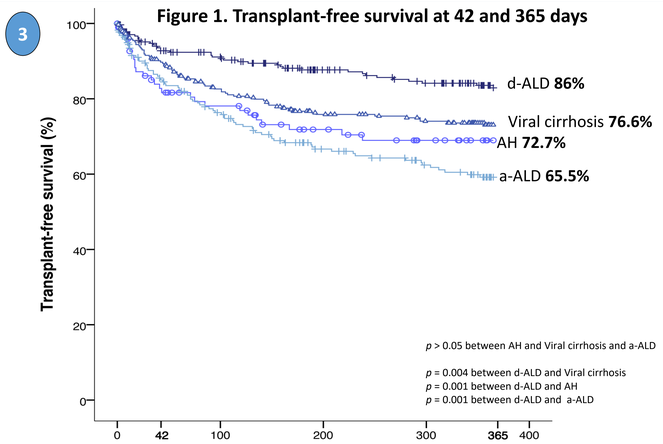
**Figure 1. Transplant-free survival at 42 and 365 days**




Number at risk (events)

| | Baseline | | 42 days | | 365 days |
|---|---|---|---|---|---|
| AH | 99 | (25) | 74 | (40) | 34 |
| d-ALD | 285 | (50) | 235 | (105) | 130 |
| a-ALD | 226* | (57) | 169 | (89) | 80 |
| Viral | 303* | (47) | 256 | (125) | 131 |

Alcoholic hepatitis, AH; ALD cirrhosis actively drinking at the time of AVB, d-ALD; ALD cirrhosis abstinent from alcohol at the time of AVB, a-ALD, and viral cirrhosis. * a-ALD: Assessable 226 out of 227. * Viral: assessable 303 out of 305.

**Figure 2. Transplant-free survival according to CLIF-C AD score**

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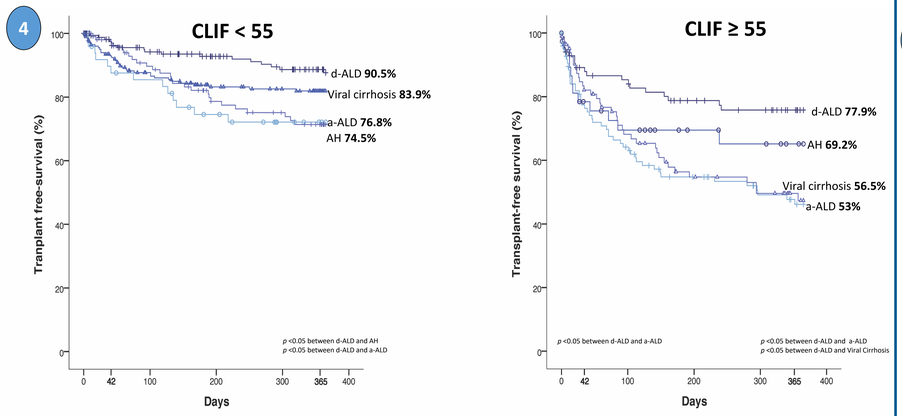


Number at risk (events)

| | Baseline | | 42 days | | 365 days |
|---|---|---|---|---|---|
| AH | 51 | (9) | 42 | (21) | 21 |
| d-ALD | 179 | (28) | 151 | (65) | 86 |
| a-ALD | 112* | (17) | 95 | (48) | 47 |
| Viral | 211* | (32) | 179 | (73) | 106 |

Number at risk (events)

| | Baseline | | 42 days | | 365 days |
|---|---|---|---|---|---|
| AH | 39 | (12) | 27 | (16) | 11 |
| d-ALD | 86 | (18) | 68 | (29) | 39 |
| a-ALD | 100 | (33) | 67 | (38) | 29 |
| Viral | 85 | (23) | 62 | (42) | 20 |

Alcoholic hepatitis, AH; ALD cirrhosis actively drinking at the time of AVB, d-ALD; ALD cirrhosis abstinent from alcohol at the time of AVB, a-ALD, and viral cirrhosis. *a-ALD: assessable 112 out of 113. Viral: assessable 211 out of 212.

**Figure 3. Transplant-free Survival. Among Abstainers at 6 months**

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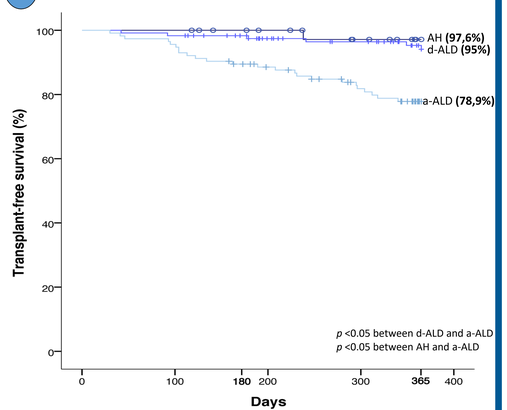


Number at risk (events)

| | | | |
|---|---|---|---|
| AH | 42 | (1) | 41 |
| d-ALD | 119 | (6) | 113 |
| a-ALD | 114 | (24) | 90 |

Alcoholic hepatitis, AH; ALD cirrhosis actively drinking at the time of AVB, d-ALD; ALD cirrhosis abstinent from alcohol at the time of AVB, a-ALD, and viral cirrhosis

## CONCLUSIONS

The prevalence of AH was 4.6% in the whole cohort, 10.8% within the patients included and 16% within ALD patients.

AH patients presented with higher percentages of complications during hospitalization

The underlying etiology and ALD phenotype might have an impact on survival after an AVB:

- Patients with AH presented better survival at 365 days than expected
- ALD cirrhosis actively drinking at the time of AVB (d-ALD) had the best survival at all-time points
- **ALD cirrhosis abstinent from alcohol (a-ALD)** patients had the worst long-term survival

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