Table 1. Hospitalization and laboratory parameters of the hepatitis E and A groups.

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| **Hepatitis (Group)** | | **E** | **A** | **Univariate statistics** | **Adjusted OR1** |
| **48 (24.0%)** | **152 (76.0%)** |  |  |
| Gender | M | 31 (64.6%) | 88 (57.9%) | ns. |  |
| F | 17 (35.4%) | 64 (42.1%) |  |  |
| Age at presentation (years) | μ ±DS | 50.62 ±15.6 | 39.06 ±15.0 | MW: p<0.001 |  |
| 50+ | 28 (58.3%) | 31 (20.4%) |  |  |
| [40,50) | 7 (14.6%) | 28 (18.4%) |  |  |
| [30,40) | 7 (14.6%) | 52 (34.2%) |  |  |
| [18,30) | 6 (12.5%) | 41 (27.0%) |  |  |
| Hospital stay duration (days) | Med (IQR) | 9 (7-14) | 11 (8-14) | MW: ns. | ns. |
| Direct bilirubin (mg/dL) | Med (IQR) | 1.24 (0.34-5.02) | 4.9 (2.66-6.99) | MW: p<0.001 | 0.194 (p<0.001) \* |
| Total bilirubin (mg/dL) | Med (IQR) | 1.73 (0.68-5.76) | 5.87 (3.38-8.2) | MW: p<0.001 | 0.182 (p<0.001) \* |
| ALP (IU/L) | Med (IQR) | 154.5 (119.25-192.75) | 205 (159.25-260.5) | MW: p<0.001 | 0.046 (p=0.003) \* |
| γ-GT (IU/L) | Med (IQR) | 229 (123.5-327) | 246 (154.75-355.5) | MW: ns. | 0.343 (p=0.048) \* |
| AST (IU/L) | Med (IQR) | 145.5 (69-676.75) | 870 (304.5-1666.75) | MW: p<0.001 | 0.112 (p<0.001) \* |
| > 350 | 17 (35.4%) | 99 (65.1%) | OR=0.29 [0.15, 0.58] (p<0.001) | 0.249 (p<0.001) |
| ALT (IU/L) | Med (IQR) | 401 (122.75-886.25) | 1817.5 (919.25-2801.75) | MW: p<0.001 | 0.045 (p<0.001) \* |
| > 350 | 26 (54.2%) | 132 (86.8%) | OR=0.18 [0.09, 0.37] (p<0.001) | 0.12 (p<0.001) |
| Prothrombin index (%) | Med (IQR) | 88.25 (75.2-100.38) | 72.7 (59.9-86.85) | T-test: p<0.001 | 1.039 (p<0.001) |
| < 70% | 9 (18.8%) | 60 (42.0%) | OR=0.32 [0.14, 0.71] (p=0.005) | 0.268 (p=0.002) |
| INR | Med (IQR) | 1.06 (0.99-1.13) | 1.16 (1.07-1.31) | MW: p<0.001 | 0.036 (p=0.002) |
| > 1.5 | 4 (8.3%) | 16 (11.2%) | ns. | ns. |
| 1: odds-ratio adjusted on age and gender; \*: data for the marked variables was transformed to its base 10 logarithm prior to logistic regression due to skewness therefore odds-ratios show tenfold increases/decreases in the respective laboratory parameters; μ ±DS: mean ±1 standard deviation; Med (IQR): median (inter-quartile range); MW: Mann-Whitney test; OR: odds-ratio [95% confidence interval] (p-value from Fisher test); ns.: not statistically significant at ɑ=0.05; ALP: Alkaline Phosphatase; γ-GT: Gamma-glutaryl Transferase; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase. | | | | | |

Table 2. Preexisting conditions and severity factors for hepatitis E and A patients.

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| **Hepatitis (Group)** | **E** | **A** | **OR (univariate)** | **Adjusted OR (univariate)1** | **OR (multivariate)2** |
| Chronic liver disease | 13 (27.1%) | 6 (3.9%) | 9.04 [3.21, 25.45] (p<0.001) | 7.194 (p<0.001) | 6.205 (p=0.002) |
| *\* Liver cirrhosis* | *6 (12.5%)* | *1 (0.7%)* | *21.57 [2.53, 184.16] (p<0.001)* | *12.5 (p=0.026)* |
| *\* Hepatitis B coinfection* | *6 (12.5%)* | *4 (2.6%)* | *5.29 [1.43, 19.60] (p=0.014)* | *6.711 (p=0.007)* |
| Neurologic disease | 6 (12.5%) | 2 (1.3%) | 10.71 [2.09, 55.04] (p=0.003) | 9.524 (p=0.011) | 4.758 (p=0.098) |
| Chronic kidney disease | 5 (10.4%) | 2 (1.3%) | 8.72 [1.63, 46.54] (p=0.009) | 5.181 (p=0.065) | 6.175 (p=0.056) |
| Diabetes mellitus | 10 (20.8%) | 9 (5.9%) | 4.18 [1.59, 11.02] (p=0.004) | 2.041 (p=0.190) | 3.386 (p=0.029) |
| Additional treatment need  (plasma: hep. A / ribavirin: hep. E) | 9 (18.8%) | 5 (3.3%) | 6.78 [2.15, 21.40] (p=0.001) | 4.926 (p=0.010) | 4.469 (p=0.025) |
| 1: odds-ratio adjusted for age and gender; 2: odds-ratio in multiple logistic regression with all listed covariates (liver cirrhosis and hepatitis B coinfection included under chronic liver disease). | | | | | |

Table 3. Hepatitis E patients who received ribavirin treatment. Summary of laboratory values (at admission / at discharge or transfer) and preexistent conditions

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age (years)** | **Gender** | **Direct bilirubin (mg/dL)** | **AST (IU/L)** | **ALT (IU/L)** | **INR** | **Recommendation for ribavirin treatment according to EASL guidelines** | **Evolution** | **MELD score**  **(3-months risk of death)** |
| 51 | F | 28.51 / 21.51 | 36 / 59 | 15 / 24 | 1.17 / 1.02 | Breast cancer, liver, lung and bone metastases | Transfer to gastroenterology dept. |  |
| 21 | M | 0.25 / 0.19 | 19 / 20 | 75 / 35 | 0.92 / 0.99 | Sagittal sinus thrombosis, bilateral facial palsy, one episode of seizures | Transfer to neurology dept. |  |
| 36 | M | 25.02 / 19.17 | 191 / 149 | 322 / 214 | 1.27 / 1.41 | Chronic hepatitis B with advanced fibrosis | Transfer to gastroenterology dept. | 23 (19.6%) |
| 38 | M | 1.67 / 1.98 | 1010 / 147 | 1750 / 607 | 1.12 / 1.02 | Hodgkin lymphoma with chemotherapy, bone marrow transplantation | Discharged at home. |  |
| 63 | M | 16.64 / 3.9 | 270 / 53 | 865 / 80 | 1.34 / 1.36 | Coagulation deficiency factors VIII & IX, autoimmune hepatitis | Discharged at home |  |
| 64 | M | 0.27 / 0.32 | 321 / 74 | 1014 / 332 | 0.99 / 0.96 | Retroperitoneal liposarcoma | Discharged at home |  |
| 69 | M | 1.31 / 0.81 | 570 / 85 | 436 / 141 | 1.12 / 1.01 | Newly diagnosed colon cancer, diabetes mellitus | Discharged at home |  |
| 74 | M | 0.67 / 1.16 | 460 / 37 | 1013 / 219 | 1.06 / 0.96 | Ethanolic liver cirrhosis, Alzheimer and vascular and dementia, diabetes mellitus | Discharged at home | 7 (1.9%) |
| 75 | M | 24.1 / 7.11 | 645 / 44 | 374 / 23 | 1.57 / 1.38 | Newly diagnosed ethanolic liver cirrhosis and hepatocarcinoma | Transfer to gastroenterology dept. | 24 (19.6%) |

Table 4. Summary of laboratory values (at admission / last before death) and preexisting conditions in patients who died with acute hepatitis E.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Age (years)** | **Gender** | **Direct bilirubin (mg/dL)** | **AST (IU/L)** | **ALT (IU/L)** | **INR** | **Preexisting conditions interpreted as causes of death** | **MELD score**  **(3-months risk of death)** |
| 59 | M | 18.99 / 28.3 | 618 / 73 | 262 / 16.6 | 1.8 / 4.15 | Hemorrhagic shock from esophageal varices, alcoholic liver cirrhosis (Child-Pugh C) | 35 (52.6%) |
| 61 | M | 12.8 / 23.71 | 1537 / 253 | 526 / 39.9 | 1.8 / 1.81 | Hemorrhagic shock from esophageal varices, alcoholic liver cirrhosis (Child-Pugh C) | 27 (19.6%) |
| 65 | M | 4.92 / 14.51 | 157 / 23 | 50 / 56.4 | 1.54 / 1.37 | Multiple system organ failure, alcoholic and hepatitis B viral cirrhosis (Child-Pugh B), endocarditis, cerebral embolism | 31 (52.6%) |

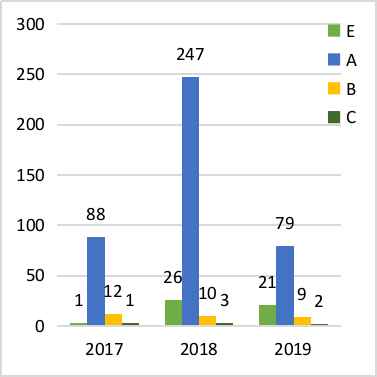


Figure 1. Distribution of acute viral hepatitis cases during the study period (2017 Jan 1 to 2019 Aug 30).

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Figure 2. Several patient parameters differ significantly between hepatitis A and E groups. Laboratory reference ranges have been marked by horizontal red lines where available. Means are marked by diamonds.