

Table 1 Chronology of clinicopathological features in severe acute indeterminate hepatitis stratified by the interval between onset of jaundice and the time of liver biopsy.

Variables	≤2 weeks	>2 weeks	P value
Number of cases	21	22	
Age (years)	39.7 ± 11.2	47.4 ± 14.5	0.057
Male, n (%)	9 (42.9)	11 (50)	0.87
Diabetes, n (%)	2 (9.5)	1 (4.5)	0.607
Hypertension, n (%)	4 (19)	6 (27.3)	0.721
Hepatic encephalopathy, n (%)	1(4.8)	3(13.6)	0.513
Ascites, n (%)	2(9.5)	2(9.1)	1
BMI	27.7 ± 7.3	29.6 ± 5.5	0.35
MELD	26.0 ± 5.7	24.2 ± 6.1	0.319
MELD-Na	27.0 (26.2, 29.2)	25.9 (21.6, 27.1)	0.139
ALF-OFs	3.0 ± 0.5	2.9 ± 0.5	0.513
White blood cell (×10 <sup>9</sup> /L)	7.79 (6.3, 9.23)	8.26 (5.88, 9.84)	1
Platelet (×10 <sup>9</sup> /L)	225.19 ± 95.62	233.86 ± 101.64	0.775
Neutrophil (×10 <sup>9</sup> /L)	4.19 (3.35, 6.51)	4.94 (3.76, 7.31)	0.618
Lymphocyte (×10 <sup>9</sup> /L)	1.52 (0.84, 1.96)	1.35 (1.02, 1.71)	0.743
PT(second)	24.8 (17.9, 29.5)	19.3 (13.83, 23.27)	0.059
INR	2.2 (1.7, 2.6)	1.7 (1.25, 2.25)	0.074
APTT(second)	40.2 (35.27, 46.55)	43.45 (35.05, 55.55)	0.496
Sodium (mmol/L)	137 (135, 140)	137.5 (136.25, 139.75)	0.331
Creatinine (μmol/L)	84 (53, 98)	67.5 (57.25, 75.75)	0.224
Total bilirubin (μmol/L)	358.24 ± 206.91	366.05 ± 151.64	0.889
ALT (U/L)	1652.95 ± 1041.49	1144.27 ± 818.1	0.084
AST (U/L)	1688.86 ± 1458.94	940.64 ± 848.18	0.049
Albumin (g/L)	32.9 ± 6.79	35.14 ± 6.54	0.283
Hepatocyte <sup>#</sup> , n (%)			0.698
Absent	4 (19.1)	3 (13.6)	

Present	17 (81.0)	19 (86.4)	
Hepatocyte necrosis, n (%)			0.864
Confluent	12 (57.1)	12 (54.5)	
Multilobular	9 (42.9)	10 (45.4)	
Ductular reaction, n (%)			0.013
Absent	10 (47.6)	2 (9.1)	
Present	11 (52.4)	20 (90.9)	
Ductular cholestasis, n (%)			0.046
Absent	20 (95.2)	15 (68.2)	
Present	1 (4.8)	7 (31.8)	
Acidophilic body n (%)			0.255
Absent	6 (35.3)	3 (15.8)	
Present	11 (64.7)	16 (84.2)	
Ballooning, n (%)			0.939
Absent	11 (64.7)	11 (57.9)	
Present	6 (35.3)	8 (42.1)	
Multinucleation, n (%)			0.603
Absent	15 (88.2)	17 (94.4)	
Present	2 (11.8)	1 (5.6)	
Nuclear vacuolation, n (%)			0.182
Absent	16 (94.1)	14 (73.7)	
Present	1 (5.9)	5 (26.3)	
Anisokaryosis, n (%)			1
Absent	16 (94.1)	18 (94.7)	
Present	1 (5.9)	1 (5.3)	
Mitotic activity, n (%)			0.016
Occasional	10 (58.8)	18 (94.7)	
Frequent	7 (41.2)	1 (5.3)	
Steatosis, n (%)			0.650

Absent	14 (82.4)	17 (89.5)	
Present	3 (17.7)	2 (10.5)	
Canalicular cholestasis, n (%)			0.077
Mild	12 (70.6)	7 (36.8)	
Moderate	5 (29.4)	9 (47.4)	
Severe	0 (0)	3 (15.8)	
Lobular inflammation, n (%)			0.901
Mild	5 (29.4)	7 (36.8)	
Moderate	9 (52.9)	10 (52.6)	
Severe	3 (17.6)	2 (10.5)	
Portal inflammation, n (%)			0.831
Mild	8 (38.1)	7 (33.3)	
Moderate	10 (47.6)	12 (57.1)	
Severe	3 (14.3)	2 (9.5)	
Interface inflammation, n (%)			0.040
Absent	4 (23.5)	0 (0)	
Present	13 (76.5)	19(100)	
Lymphoid aggregate, n (%)			0.108
Absent	21 (100)	18 (81.8)	
Present	0 (0)	4 (18.2)	
Lymphoid follicle, n (%)			0.488
Absent	20 (95.2)	22 (100)	
Present	1 (4.8)	0 (0)	
Neutrophil, n (%)			0.705
Absent	3 (14.3)	4 (18.2)	
Rare	9 (42.9)	12 (54.5)	
Frequent	8 (38.1)	6 (27.3)	
Numerous	1 (4.8)	0 (0)	

Plasma cell, n (%)			0.169
Absent	8 (38.1)	3 (13.6)	
Rare	6 (28.6)	13 (59.1)	
Frequent	4 (19.1)	4 (18.2)	
Cluster	3 (14.3)	2 (9.1)	
Macrophages, n (%)			0.233
Absent	2 (9.5)	0 (0)	
Rare	2 (9.5)	2 (9.1)	
Frequent	7 (33.3)	13 (59.1)	
Numerous	10 (47.6)	7 (31.8)	
Eosinophil, n (%)			0.921
Absent	7 (33.3)	7 (31.8)	
Rare	10 (47.6)	9 (40.9)	
Frequent	3 (14.3)	5 (22.7)	
Numerous	1 (4.8)	1 (4.6)	
Perivenulitis, n (%)			0.287
Absent	11 (52.4)	16 (72.7)	
Present	10 (47.6)	6 (27.3)	
Fibrosis, n (%)			0.066
Mild	2(9.5)	7(31.8)	
Absence	19(90.5)	15(68.2)	
Death/transplantation, n (%)	15 (71.43)	9 (40.91)	0.088

# The characteristics of hepatocytes were only examined when enough liver parenchyma was present in the samples.

Categorical values are shown as n (%). Continuous variables are shown as mean ± standard deviation or median (interquartile range).

WBC, white blood cell count; PT, prothrombin time; INR, international normalised ratio; APTT, activated partial thromboplastin time; BUN, Blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; MELD score, model for end-stage liver disease score; MELD-Na score, end-stage liver disease-sodium score; ALF-OFs, Acute Liver Failure-Organ Failure Score.

Table 2 Comparison of biochemical indicators **at the time of biopsy** in patients with different pathological features

	No multilobular necrosis(n = 24)	Multilobular necrosis(n = 19)	<i>P</i> value	No ductular cholestasis (n=35)	Ductular cholestasis (n=8)	<i>P</i> value
Age(years)	40.4 ± 12.6	48.9 ± 12.9	0.019	42.1 ± 13.5	52 ± 10.2	0.007
Male, n (%)	13 (54.2)	9 (47.4)	0.186	17 (48.6)	5 (62.5)	0.6
Hepatic encephalopathy, n (%)	3(12.50)	1(5.26)	0.618	3(8.57)	1(12.50)	1
Ascites, n (%)	2(8.3)	2(19.5)	1	3(8.57)	1(12.50)	1
Jaundice duration (days)	25.3 ± 19.3	31.4±36.5	0.486	22.4 ±17.5	52.5±48.9	0.005
Hemoglobin (g/L)	130.7 ± 24.5	123.6 ± 20.9	0.310	130.3 ± 21.2	115.6 ± 27.9	0.194
White blood cell (×10 <sup>9</sup> /L)	6.5 (5.2, 9.0)	9.1 (6.4, 11.3)	0.038	7.1 (5.4, 9.4)	8.3 (6.0, 10.0)	0.795
Platelet (×10 <sup>9</sup> /L)	235.4 ±102.0	203.0 ± 97.5	0.296	235.2 ± 98.5	159.4 ± 87.6	0.053
Neutrophil (×10 <sup>9</sup> /L)	4.1 (2.9, 5.3)	4.9 (3.5, 8.0)	0.208	4.6 (3.4, 6.3)	3.7 (3.3, 5.9)	0.662
Lymphocyte (×10 <sup>9</sup> /L)	1.3 (0.9, 1.7)	1.44 (1.1, 2.6)	0.229	1.4 (1.1, 2.2)	1.3 (1.0, 1.5)	0.348
PT (second)	16.2 (13.4, 22.9)	28.2 (22, 30.9)	0.002	19.3 (13.9, 28.6)	22.6 (17.4, 29.0)	0.502
INR	1.4 (1.2, 2.0)	2.4 (1.9, 2.9)	0.001	1.7 (1.3, 2.6)	2.1 (1.6, 2.9)	0.235
APTT	36.5 (32.5, 42.7)	48.6 (40.3, 64.1)	0.018	41 (35.5, 47.7)	60.6 (31.3, 65.2)	0.386
Sodium (mmol/L)	138.2 ± 2.7	136.8 ± 2.7	0.120	137.4 ± 2.8	138.4 ± 2.4	0.337
Creatinine (μmol/L)	74.5 (61, 89.7)	74.5 (52, 98.7)	0.554	73 (59, 91)	80 (69.5, 83.5)	0.851

Total bilirubin (μmol/L)	327.8± 182.9	393.8± 156.0	0.209	349.3 ± 186.7	390.6 ± 90.3	0.366
ALT (U/L)	1272.5 (799.7, 2041.5)	538 (254, 1335.5)	0.023	1184 (686.5, 2012.5)	359.5 (202.7, 592.5)	0.011
AST (U/L)	1026.5 (648.25, 1502)	712 (357, 1017.5)	0.126	945 (702, 1505)	233.5 (149.7, 746.5)	0.012
ALP (U/L)	136 (114, 172.5)	189 (128, 221.5)	0.106	151 (118, 197.5)	148.5 (122.2, 191)	0.988
Albumin (g/L)	34.8 ± 7.9	30.1 ± 4.4	0.018	33.7 ± 7.0	28 ± 5.2	0.030
MELD	22.9 ± 7.4	27.7 ± 7.1	0.049	25.0 ± 8.2	25.0 ± 4.3	0.977
MELD-Na	24.1 ± 6.1	28.5 ± 6.6	0.042	26.4 ± 7.0	25.0 ± 4.9	0.546
ALF-OFs	3.4 ± 1.5	3.5 ± 0.5	0.729	3.4 ± 1.2	3.7 ± 0.5	0.600
Death/transplantation, n (%)	9(37.5)	15(78.9)	0.013	18(51.4)	6(75)	0.270

Categorical values are shown as n (%). Continuous variables are shown as mean ± standard deviation or median (interquartile range).

WBC, white blood cell count; PT, prothrombin time; INR, international normalised ratio; APTT, activated partial thromboplastin time; BUN, Blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; MELD score, model for end-stage liver disease score; MELD-Na score, end-stage liver disease-sodium score; ALF-OFs, Acute Liver Failure-Organ Failure Score.

Table 3 Baseline characteristics of patients with different outcomes

Variables	Survivor (n = 19)	Death or transplantation (n = 24)	P value
Age	43.4 ± 13.1	43.8 ± 13.9	0.929
Male, n (%)	9 (47.4)	11 (45.8)	0.920
Diabetes, n (%)	2 (10.5)	1 (4.2)	0.575
Hypertension, n (%)	5 (26.3)	5(20.8)	0.673
Hepatic encephalopathy, n (%)	2 (10.5)	2 (8.3)	1
Ascites, n (%)	1 (5.3)	3(12.5)	0.618
Duration of jaundice (days)	28 (14-49)	14(11-26)	0.002
Duration of jaundice <2 weeks , n (%)	6(31.6)	15(62.5)	0.044
BMI	31.3 ± 6.7	26.6 ± 5.5	0.018
MELD	21.5 ± 6.1	27.7 ± 4.2	<0.001
MELD-Na	23.2 ± 6.2	28.5 ± 4.1	0.002
ALF-OFs	2.7 ± 0.5	3.2 ± 0.4	0.010
White blood cell (×10 <sup>9</sup> /L)	7.0 (5.5, 8.9)	8.6 (6.4, 9.8)	0.226
Platelet (×10 <sup>9</sup> /L)	248.9 ± 101.6	214.3 ± 93.7	0.258
Neutrophil (×10 <sup>9</sup> /L)	4.6 (3.7, 6.0)	4.7 (3.4, 7.9)	0.723
Lymphocyte (×10 <sup>9</sup> /L)	1.4 (1.0, 1.9)	1.5 (0.9, 1.9)	0.961
INR	1.6 ± 0.8	2.6 ± 1.1	<0.001
APTT(second)	36.2 (32.7, 41.4)	46.3 (37.6, 49.9)	0.026
Sodium (mmol/L)	137 (135.5, 138.5)	137.5 (136.5, 140)	0.436
Creatinine (µmol/L)	74 (66.5, 85)	63.5 (49, 108.5)	0.334
Total bilirubin (µmol/L)	309.2 ± 185.6	404.2 ± 164.7	0.088
ALT (U/L)	1415.4 ± 1007.0	1374.7 ± 938.5	0.893
AST (U/L)	1371.5 ± 1435.1	1254.2 ± 1072.9	0.903
ALP (U/L)	149 (123, 176)	139 (112.5, 196.5)	0.633
Albumin (g/L)	35.7 ± 7.5	32.6 ± 5.6	0.145

Categorical values are shown as n (%). Continuous variables are shown as mean ± standard deviation or median (interquartile range).

BMI, body mass index; INR, international normalised ratio; APTT, activated partial thromboplastin time; ALT, alanine aminotransferase; AST, aspartate aminotransferase;

ALP, alkaline phosphatase; MELD score, model for end-stage liver disease score; MELD-Na score, end-stage liver disease-sodium score; ALF-OFs, Acute Liver Failure-Organ Failure Score.