Supplementary Table 1 Features used to establish diagnosis of Wilson disease in 41 Wilson disease with acute liver failure patients, with Leipzig Wilson disease scores

Patient No.	K-F rings	Cp	24-h urine copper	Typical brain MRI	CNHA	*ATP7B* variant	WD score	ALP/T B < 4	AST/ALT > 2.2	Outcome
1	2	2	2	0	1	4	11	Y	Y	Liver transplant[1]
2	0	2	2	0	1	4	9	0	0	Liver transplant[1]
3	2	2	2	0	0	4	10	0	0	Survival
4	2	2	2	0	0	4	10	0	0	Survival
5	2	2	2	0	1	4	11	Y	Y	Survival
6	2	2	2	2	0	4	12	0	0	Survival
7	2	2	2	0	0	4	10	0	0	Survival
8	2	2	2	2	1	4	13	0	0	Survival
9	2	2	2	2	1	4	13	0	Y	Death
10	2	2	2	0	1	NA	7	0	0	Survival
11	2	2	2	0	1	4	11	Y	0	Survival
12	2	2	NA	2	1	4	11	0	Y	Death

13	0	2	2	0	0	4	8	0	0	Survival
14	2	1	2	0	1	4	10	0	0	Survival
15	2	2	2	2	1	4	13	Y	Y	Liver transplant[1]
16	2	2	2	2	0	4	12	0	0	Survival
17	2	2	2	0	1	4	11	0	Y	Survival
18	2	2	2	0	1	4	11	0	Y	Survival
19	2	2	2	0	1	NA	7	0	0	Survival
20	0	2	2	0	0	4	8	0	0	Survival
21	2	2	2	NA	0	4	10	0	0	Survival
22	2	1	2	0	0	4	9	0	Y	Survival
23	0	2	2	0	0	4	8	0	Y	Survival
24	2	2	2	0	1	4	11	0	0	Survival
25	2	2	2	0	0	4	10	0	0	Survival
26	2	2	2	2	0	4	12	0	0	Survival
27	2	2	2	0	0	4	10	Y	0	Survival
28	2	2	2	2	0	4	12	0	0	Survival
29	2	1	2	2	1	4	12	0	Y	Survival

	K-F rings	Cp	Urinary copper	CNHA	Brain MRI	ATP7B variant	Score			Outcome
30	2	2	2	0	0	4	10	0	0	Survival
31	2	2	2	0	1	4	11	0	0	Survival
32	2	2	2	0	0	4	10	0	Y	Survival
33	2	2	2	2	1	NA	9	0	0	Survival
34	2	2	2	0	1	4	11	Y	Y	Survival
35	2	2	2	2	0	4	12	0	0	Survival
36	2	2	2	0	1	NA	7	0	0	Survival
37	2	2	NA	NA	1	NA	5	Y	0	Death
38	0	2	2	2	1	4	11	Y	Y	Survival
39	2	2	2	0	0	4	10	0	Y	Survival
40	2	2	2	2	0	4	12	0	0	Survival
41	2	2	2	0	0	4	10	0	Y	Survival

Scoring system, Leipzig[19], Kayser-Fleischer rings: 0 = absent, 2 = present; serum ceruloplasmin: 0 = > 0.2 g/L, 1 = 0.1-0.2 g/L, 2 = < 0.1 g/L; 24-h urinary copper: 0 = normal, 1 = > 40 µg/24 h, 2 = > 80 µg/24 h; Coombs-negative hemolytic anemia: 0 = absent, 1 = present; typical brain magnetic resonance imaging: 0 = absent, 2 = present; *ATP7B* variant: 0 = no disease-causing variant detected, 2 = 1 disease-causing variant detected, 4 = 2 disease-causing variants detected. Diagnostic score of Wilson disease = sum of the assigned scores. [1]All 3 patients who came to liver transplant survived. K-F rings: Kayser-Fleischer rings; Cp: Ceruloplasmin; CNHA: Coombs-negative hemolytic anemia; NA: not available; WD: Wilson disease; Y: Yes; ALP/TB:

Ratio of alkaline phosphatase (IU/L) to total bilirubin (mg/dL); AST/ALT: Ratio of aspartate aminotransferase (IU/L) to alanine aminotransferase (IU/L).

Supplementary Table 2 Formulas and treatments proposed in different scoring systems

Scoring system	Disease originally studied	Parameters	Algorithms	Score categories and indicated treatment
KCHC	WD	Serum bilirubin (µmol/L), AST (IU/L), albumin (g/L), INR, leukocytes ($10^{9/L}$)	Each parameter classified into 5 levels and scored as 0 to 4 score. Total score, sum of scores of 5 parameters.	Cutoff value for predicting mortality of 11; ≥ 11 suggests urgent listing for LT
MELD		Age ≥ 12 years old, serum bilirubin (mg/dL), INR, serum creatinine (mg/dL)	$3.78 \times \ln[\text{serum bilirubin}] + 11.2 \times \ln[\text{INR}] + 9.57 \times \ln[\text{serum creatinine}] + 6.43$	Scores stratified into 5 levels predicting mortality risk.
MELD-Na	Chronic liver disease	MELD-Na replaces the standard MELD if MELD > 11, Na (mmol/L)	$[0.025 \times \text{MELD} \times (140 - \text{Na})] + 140$; Na < 125 calculated at 125, Na > 140 calculated at 140	Higher scores signal greater priority for LT.
PELD		Age < 12 year old, serum bilirubin (mg/dL), INR, albumin (g/dL), gender,	$4.80 \times \ln[\text{serum bilirubin}] + 18.57 \times \ln[\text{INR}] - 6.87 \times \ln[\text{albumin}] + 4.36 \ (< 1 \text{ yr}) + 6.67$ (growth failure*)	Score ≥ 30 predicts over 50%

		height, weight		mortality.
LIU-PT		Peak values of serum bilirubin (mg/dL), PT(s) or INR, and ammonia (µmol/L) during hospital sta	$3.584 \times$ serum bilirubin $+ 1.809 \times$ PT $+ 0.307 \times$ ammonia	Quartiles based on scores represent risk of death. Lower two quartiles represent low risk of death, upper two quartiles represent moderate and high risks of death or need for LT. Median scores for the LIU-PT, LIU-INR, aLIU-PTt, and aLIU-INR are
LIU-INR			$3.507 \times$ serum bilirubin $+ 54.51 \times$ INR $+ 0.254 \times$ ammonia	
aLIU-PT			$6.9 \times$ admission serum bilirubin $+ 4.0 \times$ admission PT	
	PALF			
aLIU-INR		Serum bilirubin (mg/dL), PT(s) or INR at admission	$8.4 \times$ admission serum bilirubin $+ 50.0 \times$ admission INR	

				respectively 153, 297, 173, and 212 as originally reported.
Devarbhavi model	WDALF	Encephalopathy, serum bilirubin (mg/dL)	2.87 × encephalopathy + 1.07 × serum bilirubin	Cutoff value of 10.4 for predicting mortality. Higher score signals higher risk of death.
PALF-Ds	PALF	Peak serum bilirubin (mg/dL), daily INR, peak ammonia (µmol/L),	(0.232 × peak serum bilirubin) + (2.263 × daily INR) + (0.013 × peak ammonia) - 4.498	Cutoff value of 0.02 for predicting mortality. Higher score signals higher risk of death.

KCHC: King's College Hospital Criteria; MELD: Model for End-stage Liver Disease; PELD: Pediatric End-stage Liver Disease;

LIU: Liver Injury Unit; aLIU: admission LIU; LIU-PT: LIU score using PT; LIU-INR: LIU score using INR; PALF-Ds: Pediatric

Acute Liver Failure-Delta score; WD: Wilson disease; PALF: pediatric acute liver failure; WDALF: WD with acute liver failure. AST: aspartate aminotransferase, INR: international normalized ratio; PT: prothrombin time; Na: serum natrium = serum sodium; LT: liver transplant;*Growth failure as based on gender, height, and weight.

For PALF-Ds, serum bilirubin, INR, and ammonia values are determined for up to 7 days after diagnosis of PALF, and $\triangle$peak serum bilirubin = the difference between the peak serum bilirubin and serum bilirubin at enrollment, with $\triangle$daily INR = the maximum change between serial INR levels.

Supplementary Table 3 *ATP7B* variants by patient, with predicted ATP7B effects

Patient No.	*ATP7B* / ATP7B variants	RS	*ATP7B* / ATP7B variants	RS
1	c.314C>A, p.Ser105X	rs753236073	c.3700delG, p.Val1234Leufs*96	rs193922108
2	c.2333G>T, p.Arg778Leu/c.2310C>G, p.Leu770Leu	rs28942074, rs398123136	c.3517G>A, p.Glu1173Lys	rs756029120
3	c.2333G>T, p.Arg778Leu/c.2310C>G, p.Leu770Leu	rs28942074, rs398123136	c.3089Gly>A, p.Gly1030Asp	Novel
4	c.2975C>T, p.Pro992Leu	rs201038679	c.2975C>T, p.Pro992Leu	rs201038679
5	c.994G>T, p.Glu332X	rs761084829	c.1529T>C, p.Leu510Pro	Novel
6	c.2455C>T, p.Gln819X	novel	c.1842_1845delins23	Novel
7	c.2975C>T, p.Pro992Leu	rs201038679	c.2975C>T, p.Pro992Leu	rs201038679
8	c.994G>T, p.Glu332X	rs761084829	c.994G>T, p.Glu332X	rs761084829
9	c.2621C>T, p.Ala874Val/c.4072delG, p.Ala1358Profs*35	rs121907994, HGDM, CM980195	c.2975C>T, p.Pro992Leu	rs201038679

11	c.2333G>T, p.Arg778Leu	rs28942074	c.3182G>A, p.Gly1061Glu	rs764131178
12	c.2333G>T, p.Arg778Leu	rs28942074	c.2621C>T, p.Ala874Val	rs121907994
13	c.2975C>T, p.Por992Leu	rs201038679	c.3443T>C, p.Ile1148Thr	rs60431989
14	c.2333G>T, p.Arg778Leu/c.2310C>G, p.Leu770Leu	rs28942074, rs398123136	c.1708-5T>G	rs770829226
15	c.3517G>A, p.Glu1173Lys	rs756029120	c.3884C>T, p.Ala1295Val	rs1340942427
16	c.2356-2A>G	HGDM, HS050008	c.2333G>T, p.Arg778Leu/c.2310C>G, p.Leu770Leu	rs28942074, rs398123136
17	c.2333G>T, p.Arg778Leu/c.2310C>G, p.Leu770Leu	rs28942074, rs398123136	c.2975C>T, p.Pro992Leu	rs201038679
18	c.2333G>T, p.Arg778Leu/c.2310C>G, p.Leu770Leu	rs28942074, rs398123136	c.3809A>G, p.Asn1207Ser	rs121907990
20	c.3646G>A, p.Val1216Met	rs77680797	c.3809A>G, p.Asn1207Ser	rs121907990
21	c.2932_2933insG, pVal978Glyfs*50	Novel	c.2333G>T, p.Arg778Leu	rs28942074

22	c.1708-1G>C	rs137853280	c.2333G>T,p.Arg778Leu	rs28942074
23	c.1708-1G>C	rs137853280	c.2333G>T,p.Arg778Leu	rs28942074
24	c.2528G>A, p.Gly843Glu§	Novel	c.2975C>T,p.Pro992Leu	rs201038679
25	c.2975C>T, p.Pro992Leu	rs201038679	c.2975C>T, p.Pro992Leu	rs201038679
26	c.2543dupG, p.Asn849Glnfs*5	Novel	c.2924C>A, p.Ser975Tyr	rs778163447
27	c.2333G>T, p.Arg778Leu	rs28942074	c.2975C>T, p.Pro992Leu	rs201038679
28	c.2975C>T, p.Pro992Leu	rs201038679	c.2668G>A, p.Val890Met	rs786204718
29	c.2924C>A, p.Ser975Tyr	rs778163447	c.2128G>A, p.Gly710Ser	rs137853285
30	c.2620G>C, p.Ala847Pro	rs376355660	c.2621C>T, p.Ala874Val	rs121907994
31	c.2939G>A, p.Cys980Tyr	rs1038582488	c.2333G>T, p.Arg778Leu	rs28942074
32	c.2719C>T, p.Gln907X	rs757595812	c.2924C>A, p.Ser957Tyr	rs778163447
34	c.1168A>G, p.Ile390Val	rs770903362	c.2975C>T, p.Pro992Leu, c.1708-1G>C	rs201038679 rs137853280
35	c.2157>A, p.Tyr719X	rs1057516380	c.3452G>A, p.Arg1151His	rs377297166
38	c.2333G>T, p.Arg778Leu	rs28942074	c.2333G>T, p.Arg778Leu	rs28942074
39	c.314C>A, p.Ser105X	rs753236073	c.2620G>C,p.Asn874Pro	rs376355660
40	c.2333G>T, Arg778Leu/c.2310C>G,	rs28942074 rs398123136	c.3809A>G,p.Asn1270Ser	rs121907990

	Leu770Leu		
41	c.3836A>G, p.Asp1279Gly	rs778914828	c.2333G>T, p.Arg778Leu	rs28942074

RS: Rs number, standing for reference SNP cluster ID; Novel: Not identified as previously reported. HGDM: Human Gene Mutation Database.

Supplementary Table 4 Clinical features, 41 Wilson disease with acute liver failure children at admission

Gastrointestinal		Neurologic		Other	
Jaundice	32	Fatigue or lethargy	9	Fever	9
Hepatomegaly	11	Encephalopathy	7	Petechiae or ecchymosis	8
Splenomegaly	15	Anorexia	6	Epistaxis	4
Ascites	16	Headaches	2	Rash	2
Abdominal distension	12	Numbness over limbs	2	Dark urine	2
Vomiting	10	Tremors	1	Joint pain	3
Melena or hematemesis	3				

Supplementary Table 5 Scores assigned Wilson disease with acute liver failure patients in different systems

Patient No.	KCHC	KCHC (max)	MELD/PELD score	MELD/PELD score (max)	LIU-PT	LIU-INR	aLIU-PT	aLIU-INR	Devarbhavi model	Devarbhavi model (max)	Outcome	Interval to death or liver transplant[1]
1	14	15	33	33	298	412	470	572	55.6	59.1	Liver transplant	10 d
2	10	10	16	25	125	284	130	152	2.8	3.6	Liver transplant	29 d
3	3	3	15	15	57	113	94	102	1.8	1.8	Survival	
4	9	10	35	35	180	378	249	347	10.0	11.7	Survival	
5	15	15	29	32	276	374	463	561	60.4	60.4	Survival	
6	7	7	14	15	99	196	125	152	1.2	2.6	Survival	
7	6	6	8	11	83	155	103	116	1.4	3.9	Survival	
8	5	5	13	13	69	140	123	140	4.3	6.0	Survival	
9	12	14	33	33	269	402	385	478	42.0	45.3	Death	6 d
10	5	7	8	15	80	168	104	114	3.3	4.6	Survival	
11	13	15	23	33	240	361	265	307	25.2	38.7	Survival	

12	11	12	46	46	217	544	359	522	24.3	27.0	Death	3 d
13	7	7	14	16	101	197	124	145	4.1	7.6	Survival	
14	13	13	24	27	141	283	206	250	13.1	14.5	Survival	
15	14	14	27	30	252	375	372	444	43.0	43.0	Liver transplant	24 d
16	5	5	16	16	52	97	100	113	1.9	1.9	Survival	
17	12	12	18	18	128	186	193	221	17.4	17.4	Survival	
18	10	12	19	30	171	276	153	177	6.9	24.4	Survival	
19	7	7	17	17	87	203	148	180	1.8	2.5	Survival	
20	7	7	18	21	81	149	107	120	8.3	10.7	Survival	
21	4	4	21	21	64	122	119	133	5.5	5.5	Survival	
22	10	10	20	20	96	159	129	145	6.3	6.3	Survival	
23	7	8	22	23	129	256	174	216	4.0	7.1	Survival	
24	5	5	16	16	79	140	94	114	2.1	2.1	Survival	
25	10	10	26	31	136	349	192	255	1.5	3.8	Survival	
26	6	6	17	17	73	148	92	103	1.8	1.8	Survival	
27	5	10	22	22	106	167	162	184	11.8	11.8	Survival	
28	5	6	19	19	66	130	105	116	2.0	2.2	Survival	

29	12	12	30	30	143	275	187	228	7.3	13.1	Survival	
30	4	4	3	3	79	132	84	93	1.1	1.4	Survival	
31	8	8	24	24	75	138	170	194	12.1	2.9	Survival	
32	11	11	15	15	115	192	134	151	5.7	5.7	Survival	
33	14	14	27	27	126	230	174	207	6.5	10.5	Survival	
34	14	14	33	34	204	369	360	443	33.1	33.1	Survival	
35	10	10	11	34	197	404	115	124	8.0	14.2	Survival	
36	8	8	9	9	71	136	110	121	2.8	2.8	Survival	
37	11	11	35	35	179	327	315	401	25.1	25.1	Death	15 d
38	13	13	25	26	159	286	254	305	21.0	21.0	Survival	
39	12	12	30	33	147	408	166	206	3.3	4.3	Survival	
40	5	5	7	7	67	128	100	106	1.7	1.7	Survival	
41	8	8	17	17	75	167	133	152	1.9	1.9	Survival	

[1]Interval from admission of Wilson disease with acute liver failure to death or liver transplant. Scores were calculated using data for the first day of admission. Max: maximum score during hospital. KCHC: King's College Hospital criteria; PELD/MELD: Pediatric end-stage liver disease/model for end-stage liver disease; PT: Prothrombin time; INR: International normalized ratio; LIU: Liver Injury Unit; aLIU: Admission to Liver Injury Unit.