

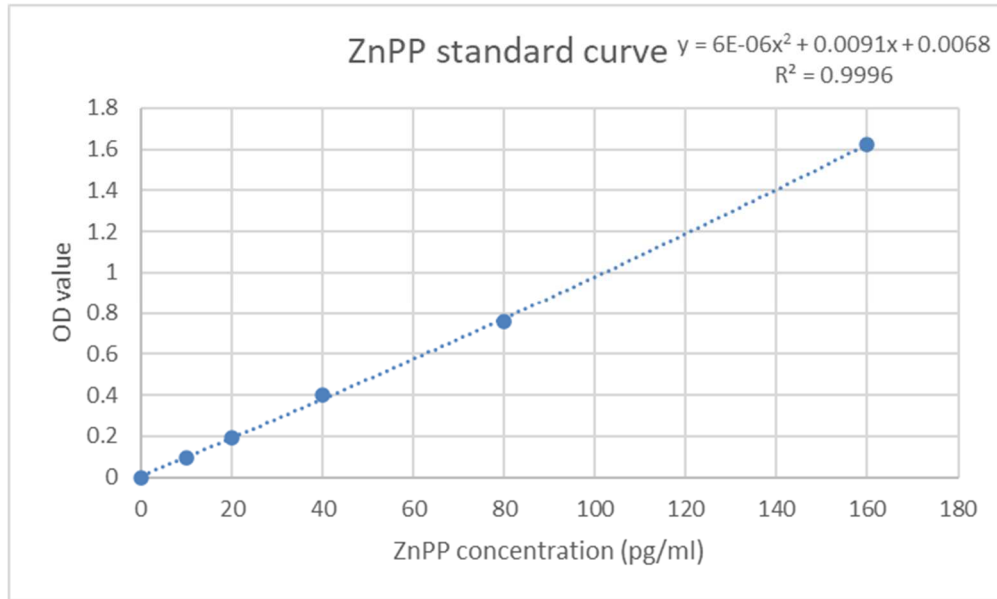


Fig. S1: The standard curve of the double antibody sandwich ELISA for ZnPP.
(OD, optical density; ZnPP, zinc protoporphyrin; ELISA, enzyme-linked immunosorbent assay).

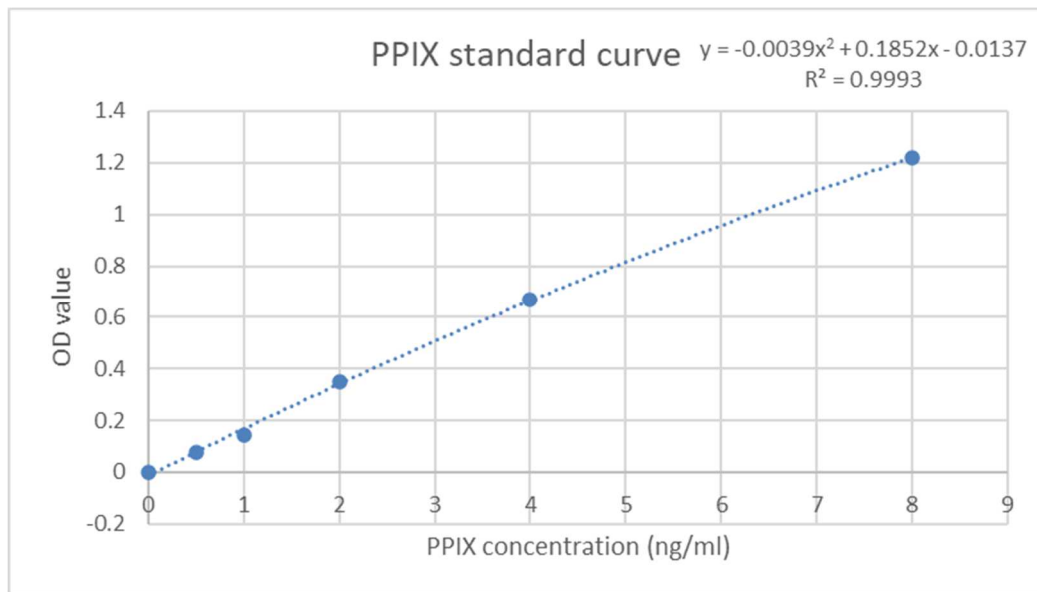


Fig. S2: The standard curve of the double antibody sandwich ELISA for PPIX.
(OD, optical density; PPIX, protoporphyrin IX; ELISA, enzyme-linked immunosorbent assay).

Table S1: ROC curve of traditional biomarkers for discrimination of ATDH.

Variables	AUC (95% CI)	P value
ALT (U/L)	0.575 (0.490~0.660)	0.083
AST (U/L)	0.621 (0.536~0.706)	0.005
TBil (μmol/L)	0.574 (0.495~0.652)	0.099
DBil (μmol/L)	0.549 (0.467~0.631)	0.259
ALP (U/L)	0.538 (0.455~0.622)	0.376

ATDH, anti-tuberculosis drug-induced hepatotoxicity; ALT, alanine transaminase; AST, aspartate transaminase; TBil, total bilirubin; DBil, direct bilirubin; ALP, alkaline phosphatase; ROC, receiver operating characteristic curve; AUC, area under curve; 95%CI, 95% confidence interval.

Table S2: Characteristics of moderate-severe and mild ATDH.

Variables	Moderate-severe (n=29)	Mild (n=29)	P value
Age (years) ^a	47.4±17.0	45.9±17.2	0.736 ^c
Sex (male/female)	18/11	22/7	0.259 ^d
Hepatoprotectant (use/not use)	12/17	10/19	0.589 ^d
Liver disease history (yes/no)	9/20	5/24	0.225 ^d
Smoke history (yes/no)	4/25	1/28	0.193 ^d
Drink history (yes/no)	1/28	1/28	1.000 ^d
Baseline value			
ALT (U/L) ^b	16.0 (9.8-20.4)	16.0 (9.0-16.4)	0.644 ^e
AST (U/L) ^b	22.0 (17.9-24.1)	22.0 (19.5-25.5)	0.361 ^e
TBil (μmol/L) ^b	10.5 (7.4-13.9)	10.5 (9.4-11.1)	0.737 ^e
DBil (μmol/L) ^b	3.3 (2.1-3.8)	3.5 (2.0-4.2)	0.657 ^e
ALP (U/L) ^b	83.0 (67.6-84.4)	83.0 (71.5-94.9)	0.295 ^e
During treatment (peak value)			
ALT (U/L) ^b	316.0 (236.0-475.5)	150.0 (120.5-163.0)	<0.001 ^e
AST (U/L) ^b	255.0 (120.3-499.5)	98.7 (50.5-145.5)	<0.001 ^e
TBil (μmol/L) ^b	25.0 (17.9-34.3)	17.0 (14.9-22.0)	0.007 ^e
DBil (μmol/L) ^b	10.4 (6.0 -16.9)	6.8 (5.7-9.7)	0.072 ^e
ALP (U/L) ^b	123.0 (107.5-178.0)	128.0 (85.1-168.0)	0.680 ^e

ATDH, anti-tuberculosis drug-induced hepatotoxicity; ALT, alanine transaminase; AST, aspartate transaminase; TBil, total bilirubin; DBil, direct bilirubin; ALP, alkaline phosphatase.

Normal range: ALT < 40U/L; AST < 40U/L; TBil < 21μmol/L; DBil < 6.9μmol/L; ALP < 130U/L.

^a Values are presented the mean ± standard deviation (range).

^b Values are presented as median (interquartile range).

^c Independent-samples t-test.

^d Unconditional logistic regression.

^e Wilcoxon rank-sum test.

Table S3: Comparison of serum indexes between moderate-severe and mild ATDH.

Variables	Time points	Moderate-severe (n=29)	Mild (n=29)	P value*
ZnPP (pg/ml) ^a	Baseline	109.4 (69.3-159.3)	116.8 (75.6-211.0)	0.414
	Time 2 ^b	146.7 (84.2-197.4)	124.7 (78.8-220.8)	0.635
	Time 3 ^c	125.1 (74.2-172.3)	113.8 (83.3-234.3)	0.658
	ΔT1 ^d	18.1 (-15.1-53.4)	3.2 (-11.7-25.2)	0.519
	ΔT2 ^e	-2.3 (-21.0-21.1)	-10.2 (-28.9-31.6)	0.669
PPIX (ng/ml) ^a	Baseline	8.6 (5.2-19.1)	8.1 (5.7-14.9)	0.907
	Time 2 ^b	9.8 (5.8-28.2)	8.9 (5.8-22.8)	0.858
	Time 3 ^c	9.1 (5.6-36.7)	8.8 (6.5-41.4)	0.846
	ΔT1 ^d	2.2 (0.42-13.6)	0.97 (-0.86-9.1)	0.432
	ΔT2 ^e	1.3 (-0.82-11.8)	1.3 (-0.53-1.3)	0.570

ATDH, anti-tuberculosis drug-induced hepatotoxicity; ZnPP, zinc protoporphyrin; PPIX, protoporphyrin IX.

^a Values are presented as median (interquartile range).^b The time 2 in the case group refer to the first abnormal liver function detection time point.^c The time 3 in the case group refer to the peak liver function detection time point.^d The change at time 2 relative to the baseline.^e The change at time 3 relative to the baseline.

* Wilcoxon rank-sum test.