

Supplementary Table 1 Patient characteristics of all patients and trimesters

Parameters	Normal range ¹	ICP	Control
		N = 117	N = 488
Age (years)		30.6 ± 4.2 ^c	32.2 ± 4.9
Number per trimester			
1		0	60
2		2	162
3		98	228
postpartal		17	38
Bile acids (μmol/L)	2 - 5	37.8 ± 28.7 ^d	5.9 ± 6.1
AST (U/L)	<35	112 ± 103 ^d	25 ± 23
ALT (U/L)	<35	199 ± 193 ^d	18 ± 23
GGT (U/L)	<40	27 ± 27	25 ± 46
AP (U/L)	35 - 105	179 ± 69	135 ± 122
Bilirubin total (mg/dL)	<1.3	0.63 ± 0.33 ^d	0.51 ± 0.28
M30 (U/L)	<200	519.8 ± 309.7 ^a	277.7 ± 171.6
M65 (U/L)	<400	1045.7 ± 544.1 ^d	385.9 ± 192.2
Creatinine (mg/dL)	<1.3	0.75 ± 0.39 ^d	0.56 ± 0.11
Urea (mg/dL)	< 50	21.8 ± 7.1 ^d	17.5 ± 4.6
Uric acid (mg/dL)	3.5-7.2	5.84 ± 2.53 ^d	3.74 ± 1.11
Total protein (g/L)	6.6-8.3	66.9 ± 5.2	66.4 ± 5.7
Albumin (g/L)	3.8-5.9	35.6 ± 3.6	36.5 ± 2.7
Leukocytes (1/nL)	3.7 - 10.0	9.3 ± 2.8 d	11.8 ± 4.1
Erythrocytes (1/pL)	4.1-5.1	3.88 ± 0.41	3.91 ± 0.44
Hemoglobin (g/dL)	12-16	11.27 ± 1.26	11.63 ± 1.35
Hematocrit (%)	36-43	33 ± 3	
MCV (fL)	80-96	86.1 ± 4.3	
Platelets (1/nL)	150-360	229 ± 71	236 ± 65
Haptoglobin (g/L)	0.3-2.0	0.82 ± 0.40	1.60 ± 1.20 ²
Quick (%)	70 - 120	122.8 ± 9.1	122.4 ± 10.2
INR	< 1.1	0.91 ± 0.04	0.91 ± 0.03

Grade of steatosis in US (0-3)	0	0.35 ± 0.49^a	0.16 ± 0.41
Spleen size (cm)	<11	11.4 ± 1.8	10.9 ± 1.4
Liver stiffness (kPa)	< 6	7.0 ± 2.9^d	5.3 ± 2.0
CAP (dB/m)	< 290 (S3)	207 ± 48^d	226 ± 43

¹Normal range for women.

²Values from reference cohort.

^a $P < 0.05$, ^b $P < 0.01$, ^c $P < 0.001$, ^d $P < 0.0001$ *vs* controls.

ICP: Intrahepatic cholestasis of pregnancy; CAP: Controlled attenuation parameter; M65: Soluble cytokeratin 18; M30: Caspase-cleaved cytokeratin 18 fragment.

Supplementary Table 2 Spearman Rho correlation with bile acids for women with ICP, controls and all

Parameter	Spearman Rho correlation with bile acids		
	ICP	Control	All
	N = 100	N = 450	N = 550
	r	r	r
M30 (U/L)	0.810 ^a	0.088	0.185
Pruritus (1 or 0)	0.539 ^b	-0.172	0.578 ^d
Gestational diabetes (1 or 0)	0.434 ^a	0.053	0.124
Haptoglobin (g/L)	-0.412 ^c		
Leukocytes (1/nL)	-0.370 ^c	0.135	-0.393 ^d
LS (kPa)	0.368 ^c	0.085	0.438 ^d
ALT (U/L)	0.324 ^b	0.471 ^b	0.688 ^d
AST (U/L)	0.279 ^b	0.255	0.643 ^d
Bilirubin total (mg/dL)	0.244 ^a	0.365 ^a	0.264 ^b
Quick (%)	-0.169	0.006	-0.157
CAP (dB/m)	-0.140	-0.095	-0.283 ^c
AP (U/L)	0.281	0.194	0.432 ^c
Spleen size (cm)	0.263	0.032	0.189
RR systolic (mmHg)	0.363	-0.102	-0.230
Albumin (g/L)	-0.110	-0.258	-0.202
M65 (U/L)	0.286	0.076	0.291 ^a
Uric acid (mg/dL)	0.150	0.027	0.398 ^c
Age (years)	-0.059	0.131	-0.177 ^a
Erythrocytes (1/pL)	0.058	0.003	-0.126
GGT (U/L)	-0.025	0.416 ^b	0.178 ^a

^a $P < 0.05$, ^b $P < 0.01$, ^c $P < 0.001$, ^d $P < 0.0001$.

Note that parameters are sorted first by levels of significance in the ICP group (p) and then the absolute correlation coefficient in descending order. Most relevant parameters are on top. ICP: Intrahepatic cholestasis of pregnancy; LS: Liver stiffness; CAP: Controlled attenuation parameter; M65: Soluble cytokeratin 18; M30: Caspase-cleaved cytokeratin 18 fragment.

Supplementary Table 3 Uni- and multivariate Logistic regression (N = 550) with elevated levels of bile acids (> 20 µM). Note that liver stiffness remains sole independent variable associated with elevated bile acids

Parameter	Univariate Odds ratio	Multivariate Odds ratio
ALT (U/L)	1.00 (1.00 - 1.01) ^b	1.01 (0.99-1.02)
Urea (mg/dL)	1.18 (1.04 - 1.33) ^b	1.12 (0.95-1.32)
AP (U/L)	1.01 (1.00 - 1.02) ^a	
AST (U/L)	1.00 (1.00 - 1.01) ^a	1.00 (0.97 - 1.03)
CAP (dB/m)	0.99 (0.99 - 1.00)	
Liver stiffness (kPa)	1.10 (0.96 - 1.26)	1.74 (1.09 - 2.76) ^a
GGT (U/L)	1.01 (0.99 - 1.02)	1.01 (1.00 - 1.02)
Bilirubin total (mg/dL)	1.62 (0.39 - 6.69)	
Creatinine (mg/dL)	1.36 (0.16 - 11.66)	
Platelets (1/nL)	1.00 (0.99 - 1.00)	
Erythrocytes (1/pL)	1.01 (0.35 - 2.91)	

^aP < 0.05, ^bP < 0.01. CAP: Controlled attenuation parameter