Maternal liver-related symptoms during pregnancy in primary sclerosing cholangitis

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Fig. S1. Study design and subject disposition.

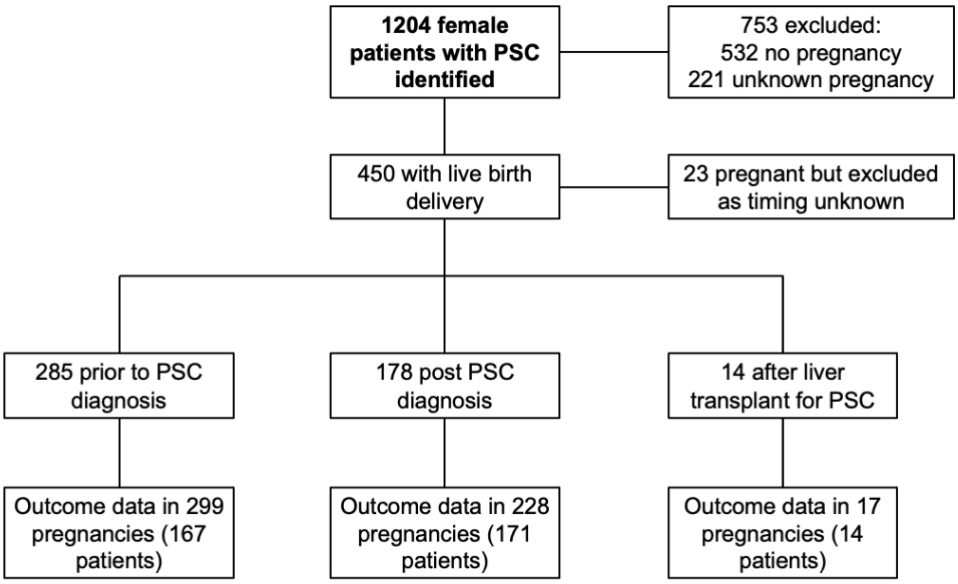
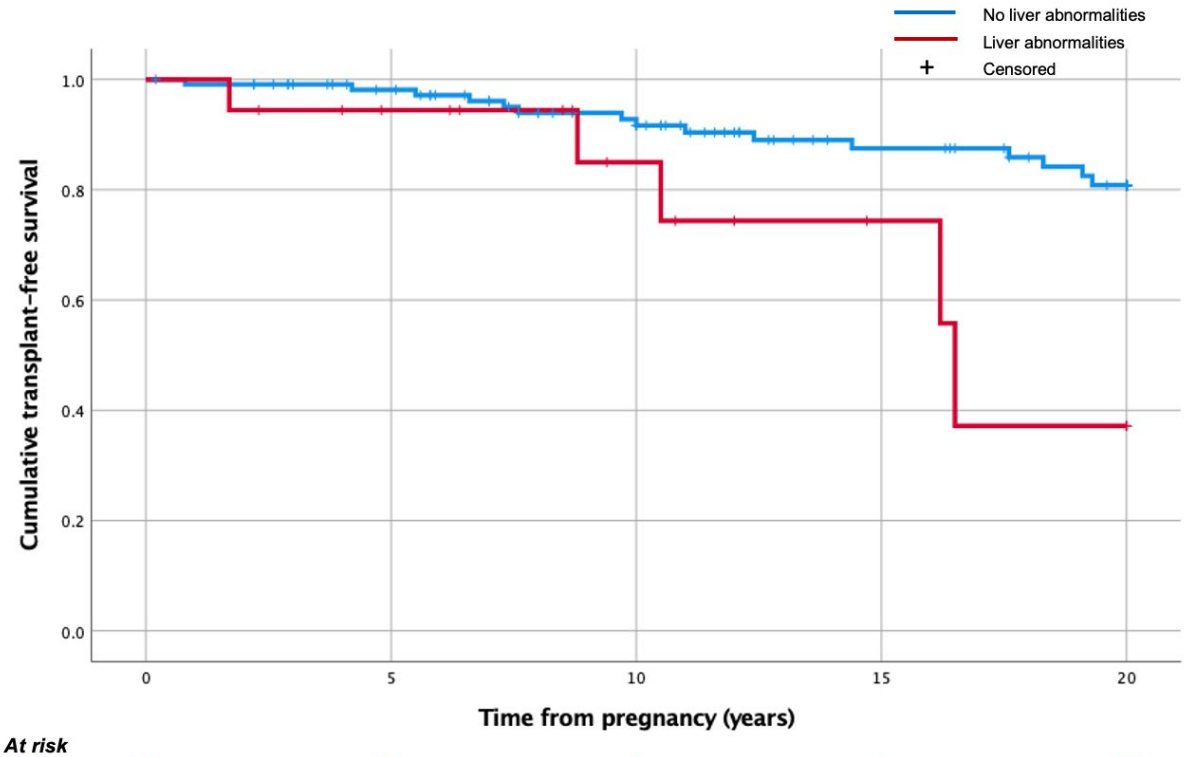
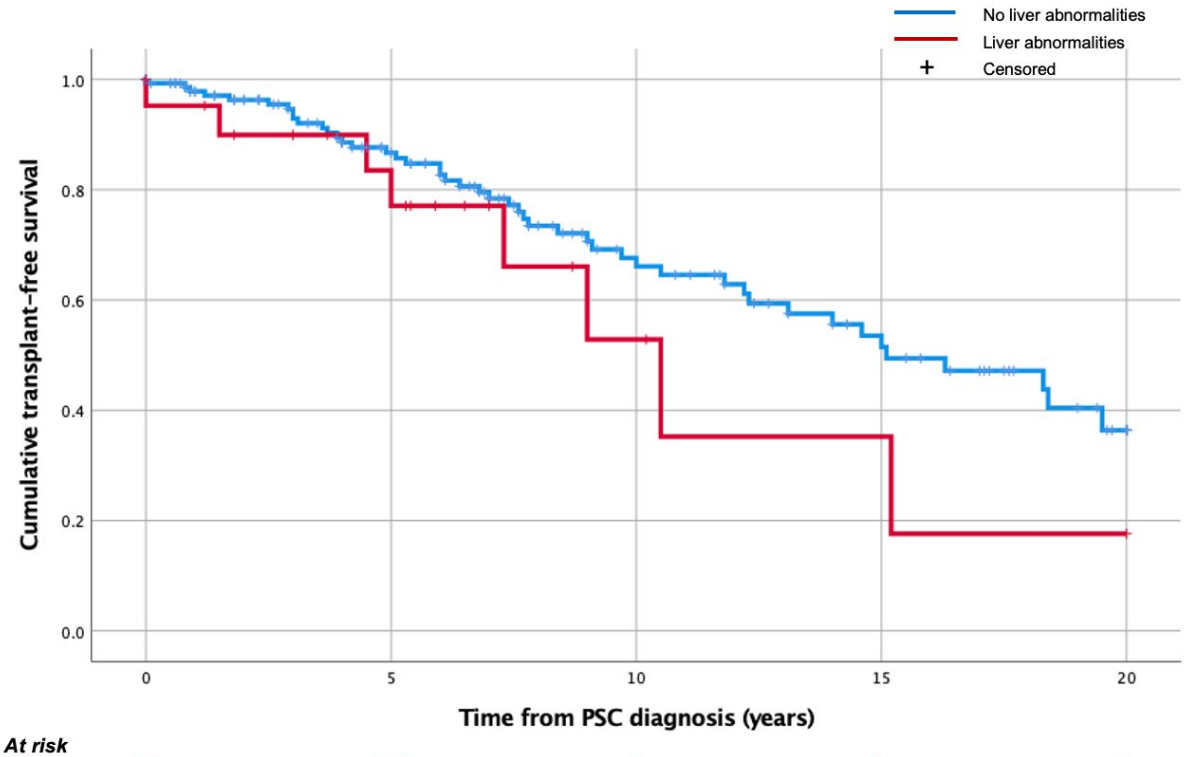


Fig. S2A. Cumulative incidence of clinical events with Kaplan-Meier estimates for time to liver transplantation or death (transplant-free survival) from time of pregnancy prior to PSC diagnosis. 20 year transplant-free survival in those with liver abnormalities in pregnancy (log-rank, P=0.01).



At risk					
Liver abnormalities	18	14	8	4	2
No liver abnormalities	113	100	81	58	47

Fig. S2B. Cumulative incidence of clinical events with Kaplan-Meier estimates for time to liver transplantation or death (transplant-free survival) from time of PSC diagnosis in those with pregnancy prior to diagnosis. 20 year transplant-free survival in those with liver abnormalities in pregnancy (log-rank, P=0.21).



At risk					
Liver abnormalities	21	13	4	2	1
No liver abnormalities	146	90	44	26	7

Table S1. Clinical characteristics of subgroup of patients who were pregnant prior to their diagnosis of PSC (n=167).

	N=167
Age at delivery, median (IQR), years	28.7 (25.2-31.8),
Age at PSC diagnosis, median (IQR), years	38.8 (32.4-48.1)
Interval between delivery and PSC diagnosis, median (IQR), years	5.8 (1.7-17.1)
Large duct	132 (79.0%)
Small duct	14 (8.4%)
PSC/AIH overlap	19 (11.4%)
IgG4-SC	2 (1.2%)
IBD	85 (50.9%)

Abbreviations: PSC, primary sclerosing cholangitis; AIH, autoimmune hepatitis; IgG4-SC, immunoglobulin G4 sclerosing cholangitis; IBD, inflammatory bowel disease.

Continuous variables are expressed as median (IQR), categorical variables are represented as number (%).

Table S2. Clinical characteristics of subgroup of patients who were pregnant after their diagnosis of PSC (n=178).

	N=178
Age at PSC diagnosis, median (IQR), years	26.8 (21.5-30.7)
Age at delivery, median (IQR), years	32.3 (28.7-35.7)
PSC duration at time of delivery, median (IQR), years	4.4 (2.2-8.9)
Large duct	146 (82.0%)
Small duct	8 (4.5%)
PSC/AIH overlap	24 (13.5%)
IBD	122 (66.5%)

Abbreviations: PSC, primary sclerosing cholangitis; AIH, autoimmune hepatitis; IBD, inflammatory bowel disease.

Continuous variables are expressed as median (IQR), categorical variables are represented as number (%).

Table S3. Univariate analysis of continued UDCA use during pregnancy and change in liver blood tests from baseline values.

	UDCA not used previously or stopped	UDCA continued	P
Bilirubin			
Normal prior to conception	33/38 (86.8%)	53/65 (81.5%)	0.48
>25% rise from baseline during pregnancy	4/34 (11.8%)	10/51 (19.6%)	0.34
>25% rise post from baseline after delivery	8/32 (25.0%)	17/53 (32.1%)	0.49
ALP			
Normal prior to conception	19/42 (45.2%)	33/68 (48.5%)	0.74
>25% rise from baseline during pregnancy	7/36 (19.4%)	16/55 (29.1%)	0.30
>25% rise post from baseline after delivery	17/36 (47.2%)	27/58 (46.6%)	0.95
ALT			
Normal prior to conception	9/22 (40.9%)	24/46 (52.2%)	0.39
>25% rise from baseline during pregnancy	2/20 (10.0%)	7/41 (17.1%)	0.70
>25% rise post from baseline after delivery	8/29 (27.6%)	12/34 (35.3%)	0.51
AST			
Normal prior to conception	14/32 (43.8%)	12/42 (28.6%)	0.18
>25% rise from baseline during pregnancy	5/30 (16.7%)	6/32 (18.8%)	0.83

>25% rise post from baseline after delivery	10/18 (55.6%)	16/39 (41.0%)	0.31
GGT			
Normal prior to conception	9/27 (33.3%)	16/51 (31.4%)	0.86
>25% rise from baseline during pregnancy	**7/23 (30.4%)**	**3/35 (8.6%)**	**0.04**
>25% rise post from baseline after delivery	9/24 (37.5%)	8/39 (20.5%)	0.14

Abbreviations; UDCA, ursodeoxycholic acid; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

Categorical variables are represented as number (%), or where data is missing number/number available (%). Subgroup differences were analysed by Chi-squared or Fisher's exact tests.

Table S4. Reported symptoms during pregnancy after PSC diagnosis (n=228).

	N=228
Clinical diagnosis of intrahepatic cholestasis of pregnancy	33 (14.5%)
Pruritus	
Stable or improved from baseline	33 (14.5%)
Worsened from baseline	23 (10.1%)
Newly developed	34 (14.9%)
Cholangitis	
Treated with antibiotics as outpatient	3 (1.3%)
Treated with antibiotics as inpatient	1 (0.4%)
Any worsening liver-related symptom during pregnancy	66 (28.9%)

Categorical variables are represented as number (%).

Table S5. Immunosuppression medications and combination regimens used during pregnancy in patients who had undergone liver transplantation for PSC.
Data was not available in 5 patients.

	N=12
Medications	
Corticosteroid	9 (75%)
Ciclosporin	2 (17%)
Tacrolimus	10 (83%)
Azathioprine	8 (67%)
Combination regimens	
Tacrolimus monotherapy	2 (17%)
Tacrolimus and corticosteroid	2 (17%)
Tacrolimus and azathioprine	1 (8%)
Tacrolimus, corticosteroid and azathioprine	5 (42%)
Ciclosporin, corticosteroid and azathioprine	2 (17%)

Categorical variables are represented as number (%).