

Evaluating intrahepatic cholestasis of pregnancy in twin pregnancies – a systematic review and meta-analysis

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Introduction

- Intrahepatic cholestasis of pregnancy (ICP) increases the risk of adverse perinatal outcomes in singleton pregnancy¹
- Adverse outcomes (e.g., stillbirth, preterm birth) increase with higher peak bile acid concentrations
- Spontaneous preterm birth is reduced in singleton pregnancy by treatment with ursodeoxycholic acid (UDCA)²
- Multifetal pregnancy is a risk factor for developing ICP, likely due to elevated reproductive hormone metabolites and assisted conception³
- However, the association of disease severity and perinatal outcome, and benefit of UDCA are not clear for twin pregnancies

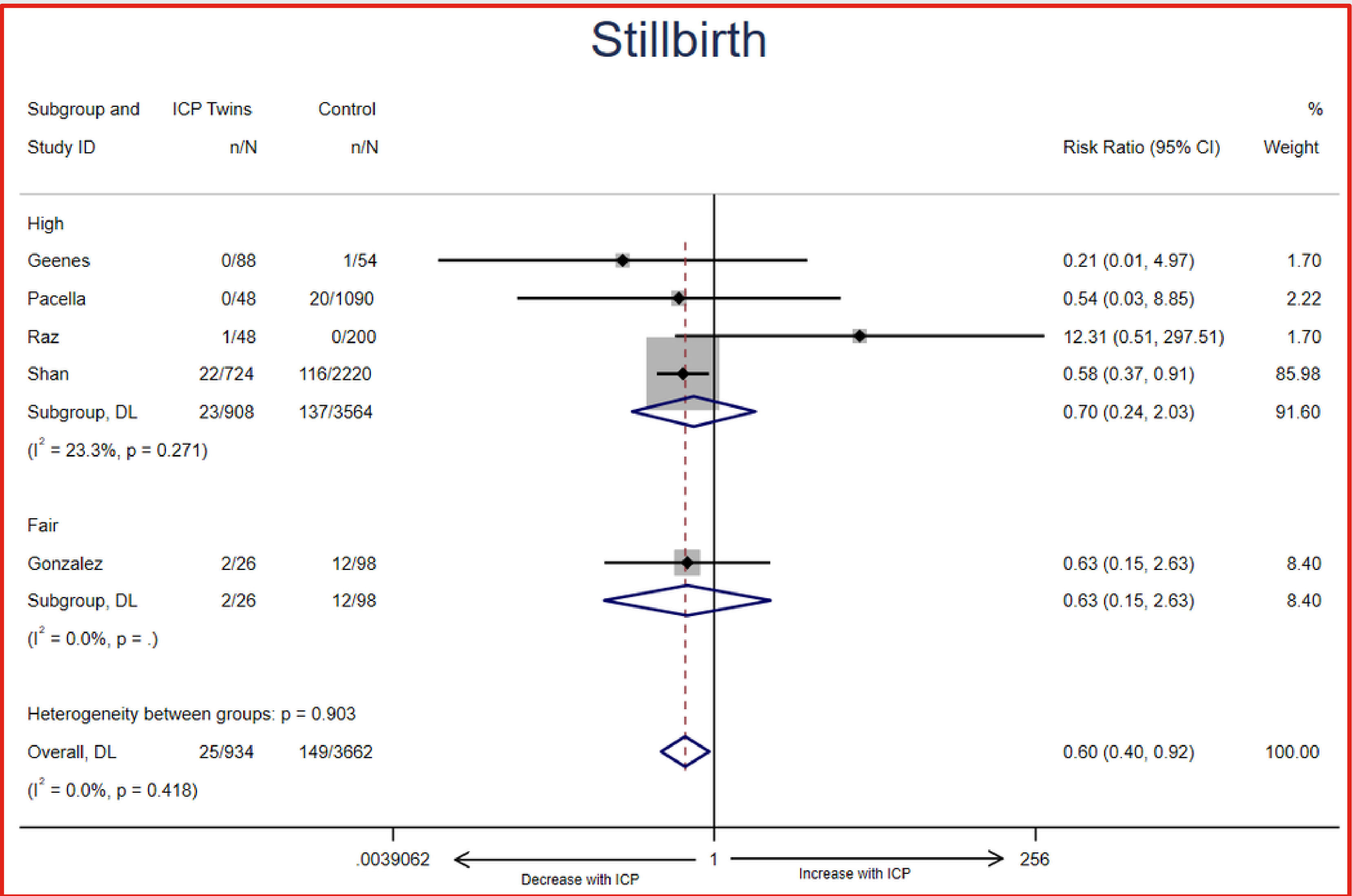
Methods

- Systematic review and aggregate data meta-analysis
- PubMed, Embase, Web of Science, Cochrane Library and Clinicaltrial.gov databases searched
- Study quality determined using a modified NHLBI scoring system
- Random effects meta-analysis using the DerSimonian and Laird model (Stata 16.0)
- Adverse perinatal outcomes were compared between twin ICP and uncomplicated pregnancies, and twin versus singleton ICP pregnancies

Results

- Outcomes reported for 815 women with ICP and twin pregnancies, 5310 women with uncomplicated twin pregnancies, and 3607 women with singleton ICP pregnancies
- Insufficient data to determine the impact of treatment with ursodeoxycholic acid

Perinatal Outcome	Number of cases	Number of controls	Risk Ratio / SMD	L 95% CI	U 95% CI	P
ICP Twin vs Control						
Stillbirth	25/934	149/3662	0.60	0.40	0.92	0.018
Preterm Birth	970/1214	4286/7240	1.33	1.23	1.44	0.004
MSAF	133/930	232/3356	2.49	2.02	3.08	<0.001
Apgar < 7 at 5 Mins	35/1219	297/7278	1.04	0.75	1.45	0.820
Neonatal Unit Admission	300/844	831/2479	1.02	0.91	1.13	0.049
Gestational age at birth (wks)	35.9	35.6	-2.06	-0.42	0.01	0.061
Mean birthweight (grams)	2262.5	2423.1	-0.30	-0.42	-0.17	0.743
ICP Twin vs Singleton						
Stillbirth	7/383	29/1931	1.05	0.18	6.04	0.080
MSAF	53/346	346/1842	0.74	0.41	1.34	0.113
Apgar < 7	1/126	19/825	0.60	0.11	3.24	0.480
Neonatal Unit Admission	40/130	95/889	3.11	2.28	4.25	0.939



Conclusions

- There was a decrease in the relative risk of stillbirth in ICP twins compared with uncomplicated twin pregnancies
- This was likely related to the increased rates of preterm birth, and did not account for the resultant neonatal morbidity or mortality
- Aggregate data meta-analyses are limited by the restricted fields reported in individual studies; we plan to address this in an individual participant data meta-analysis

References

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3. Gonzalez MC, Reyes H, Arrese M *et al.* Intrahepatic cholestasis of pregnancy in twin pregnancies. *J Hepatol* 1989; 9: 84-90