Children Born to Mothers with Intrahepatic Cholestasis During Pregnancy (ICP) More Likely to Have Developmental Delays Than Those Born to Mothers Without ICP

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Key Findings:

- Children born to mothers diagnosed with intrahepatic cholestasis of pregnancy (ICP) were 31% more likely to have a motor delay diagnosed by age 5 compared to those born to mothers without a diagnosis of ICP.
- ICP diagnosed in the mother was associated with a 28% higher likelihood of pervasive developmental disorder and a 19% higher likelihood of a speech or language delay diagnosis in the child by age five.

Intrahepatic cholestasis of pregnancy (ICP) is a liver condition during pregnancy that presents as itchy skin and elevated bile acid levels. Bile acids can cross the placenta, which has been linked to adverse fetal and perinatal outcomes.[1] The longer-term neurodevelopmental implications for offspring are less well characterized.

We studied 42,144 children born between January 1, 2010, and December 31, 2020, with follow-up through at least their fifth birthday. Children were included if they had a documented gestational age, a link to their mother's chart, at least one outpatient face-to-face encounter at least every 18 months from birth through age 4.5, and at least one visit after age 5. We excluded children with neonatal abstinence syndrome or genetic abnormalities. We matched each child born to a mother with ICP to four children who were not exposed based on race, ethnicity, infant sex, delivery method, and whether they were diagnosed as small for their gestational age. We additionally accounted for prematurity, maternal age, multiple gestation, maternal comorbidities, social vulnerability, birth weight, and APGAR scores.

Motor delays and pervasive developmental delays were diagnosed in fewer than 4% of all children in the study. Speech and language delays were more common, with nearly 20% of all children studied having a speech or language delay diagnosis.

Compared with children who were not born to mothers diagnosed with ICP, those born to mothers diagnosed with ICP were 31% more likely to have a motor delay, 28% more likely to have a pervasive developmental disorder, and 19% more likely to have a speech or language delay by age 5.

Likelihood of Developmental Delays by Maternal ICP Diagnosis

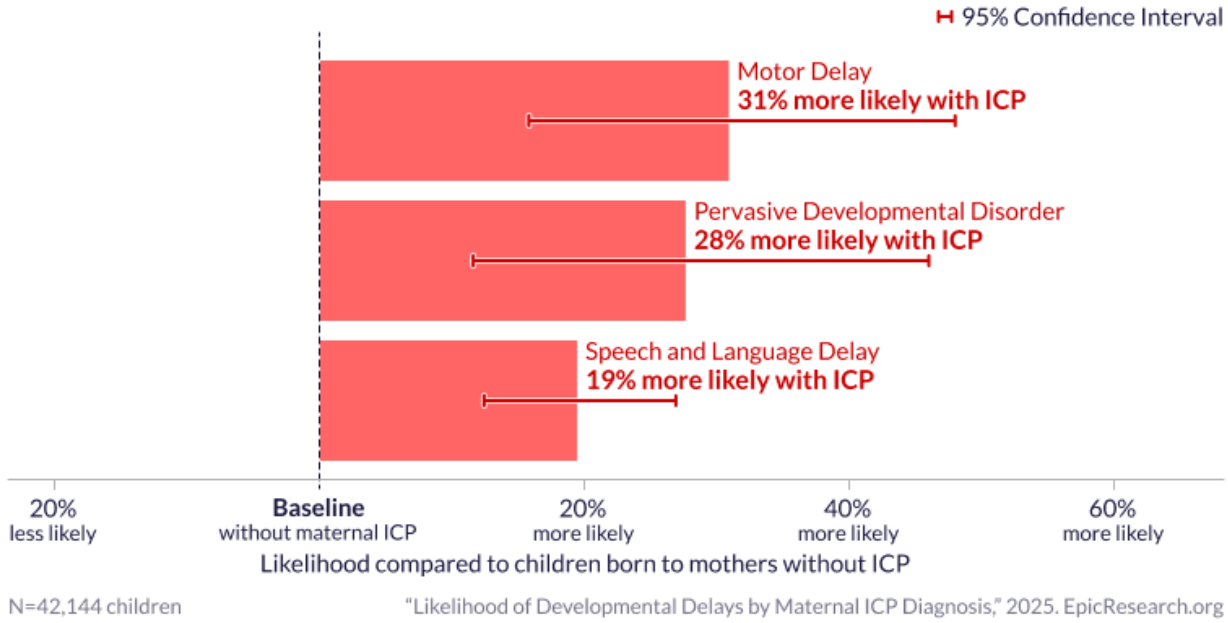

Figure 1. The likelihood of early childhood developmental delays by age 5 among children born to a mother diagnosed with ICP compared to those born to mothers not diagnosed with ICP.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 41,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Lindor KD, Lee RH. Intrahepatic cholestasis of pregnancy. UpToDate. September 17, 2025. Accessed October 10, 2025. https://www.uptodate.com/contents/intrahepatic-cholestasis-of-pregnancy

Data Definitions

Term	Definition
Study period	Births between 1/1/2010 and 8/31/2020
Study population: inclusion	Children with: • At least one **outpatient face-to-face** visit within each 18-month period after birth through age 4.5 and at least one visit after age 5 • A gestational age documented • A mother-baby link
Study population: exclusion	Children with: • Neonatal abstinence syndrome: A billing, encounter, or problem list diagnosis with ICD-10-CM code P96.1, P04.14, P04.16, P04.4, P04.40, P04.41, P04.42, or P04.49 • Genetic abnormalities: A billing, encounter, or problem list diagnosis with ICD-10-CM code Q*

Exposures	Mother diagnosed with intrahepatic cholestasis of pregnancy (ICP) during the pregnancy: A billing, encounter, or problem list diagnosis with ICD-10-CM O26.64* or K83.1*
Outcomes	Any developmental delay defined by one or more of the following recorded prior to fifth birthday: • Speech/language delay: A billing, encounter, or problem list diagnosis with ICD-10-CM code F80* • Motor delay: A billing, encounter, or problem list diagnosis with ICD-10-CM code F82* • Pervasive developmental disorders: A billing, encounter, or problem list diagnosis with ICD-10-CM code F84*
Matching	Matched 4:1 on: • Small for gestational age: A billing, encounter, or problem list diagnosis with ICD-10-CM code P05.1* • Race and ethnicity • Baby's sex • Delivery method
Confounders	Prematurity (<37 weeks' gestation) Maternal age at birth • 12-17 • 18-24 • 25-34 • 35+ Multiple gestation Maternal diagnoses • Maternal diabetes: A billing, encounter, or problem list diagnosis with ICD-10-CM code O24.1* or O24.4* • Maternal hypertension or pre-eclampsia: A billing, encounter, or problem list diagnosis with ICD-10-CM code O10*-O16* • Genetic abnormalities: A billing, encounter, or problem list diagnosis with O28.5*, O35.1* • Physical abnormalities: A billing, encounter, or problem list diagnosis with O28.3*, O35.0*, O35.8*, O35.A* • Alcohol/substance use affecting pregnancy: A billing, encounter, or problem list diagnosis with O35.4*, O35.5*, O99.31*, O99.32*, or O99.33* Maternal neuropsychiatric history: • Depression: A billing, encounter, or problem list diagnosis with ICD-10-CM code F32*, F33*, or F39* • Anxiety or OCD: A billing, encounter, or problem list diagnosis with ICD-10-CM code A billing, encounter, or problem list diagnosis with F40*, F41*, or F42* • Autism: A billing, encounter, or problem list diagnosis with ICD-10-CM code F84.0* or F84.5* • ADHD: A billing, encounter, or problem list diagnosis with ICD-10-CM code F90* Social Vulnerability Index quintile Birth weight APGAR: lowest result from 1, 5, and 10 minutes

Race and ethnicity	Patients were classified by self-reported race and ethnicity as Non-Hispanic Black (Black), Hispanic (any race), non-Hispanic White (White), non-Hispanic Asian (Asian), non-Hispanic Other (Other), non-Hispanic multiracial (Multiracial) and Unknown if no race/ethnicity information was present.
Model specifications	Matched exposure/control logistic regression, with an exposure of ICP during pregnancy and matching using the above criteria.
Limitations	Bile acid lab test results were not factored in due to inconsistent prevalence Paternal factors were not included as a factor

Table 1. Population Characteristics

Category	Subcategory	Had Any Developmental Delay < 5 yrs	Patients	% of Patients
Total	Total	No	33,947	77.5%
		Yes	9,848	22.5%
Sex	Female	No	18,780	42.9%
		Yes	3,815	8.7%
	Male	No	15,167	34.6%
		Yes	6,033	13.8%
Race/Ethnicity	Asian	No	883	2.0%
		Yes	247	0.6%
	Black	No	2,383	5.4%
		Yes	662	1.5%
	Hispanic	No	10,537	24.1%
		Yes	3,993	9.1%
	Other	No	3,663	8.4%
		Yes	1,047	2.4%
	Unknown	No	803	1.8%
		Yes	212	0.5%
	White	No	15,678	35.8%
		Yes	3,687	8.4%
Maternal Age	[12,17]	No	394	0.9%
		Yes	100	0.2%
	[18,24]	No	7,789	17.8%
		Yes	2,309	5.3%
	[25,34]	No	19,713	45.0%
		Yes	5,525	12.6%
	[35+]	No	6,051	13.8%
		Yes	1,914	4.4%
ICP During Pregnancy	No	No	27,523	62.8%
		Yes	7,513	17.2%

	Yes	No	6,424	14.7%
		Yes	2,335	5.3%

Table 2. Likelihood of Developmental Delays by Maternal ICP Diagnosis

Term	Odds Ratio	Lower CI	Upper CI
Motor Delay	1.31	1.16	1.48
Pervasive Developmental Disorder	1.28	1.12	1.46
Speech and Language Delay	1.19	1.12	1.27