Evaluation of Children Exposed to Perinatal Hepatitis C in the US : A Literature Review

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Background

- Incidence of Hepatitis C virus (HCV) infection is rising in the US, largely due to the ongoing opioid epidemic.
- In children, perinatal transmission is the most common route of HCV infection with estimated MTCT rate of 5-15%.
- HCV infection in infants is almost always asymptomatic. Therefore, diagnosis is confirmed by HCV antibody testing by ≥18 months due to persistence of maternal antibodies.
- Identification of HCV-infected infants is critical as up to 50%-75% of perinatally infected infants go on to develop chronic HCV infection with significant morbidity and mortality.

Objective

- In this review, we examine the US studies evaluating rates of HCV testing amongst infants at risk of perinatal HCV transmission.

Methods

- PubMed and Embase were searched (through April 2022) for studies evaluating optimal testing of children exposed to perinatal HCV in the US.
- We included full text, English language, human studies, age birth-18 years, US location. We excluded conference proceedings.
- 1,093 and 2564 articles from PubMed and Embase were screened, respectively. 13 articles were selected for final analysis.

Results

Table 1. Summary of the US Studies Evaluating Appropriate Hepatitis C Testing in Perinatally Exposed Children

Author/ Publication Date	Location	Study Duration	Design	Database/Registry	Intervention	Infants Born to HCV + Mothers	Infants Completed Diagnostic Work up		HCV MTCT Rate
							Number	%	
Delgado-Borrego 2012	Miami FL	2000-2009	Retrospective	State and county database	--	12311	1444	12%	--
Kuncio 2016	Philadelphia PA	2011-2013	Retrospective	State Hepatitis Registry, Laboratory database, Immunization Registry	--	537	38	7%	10.5%
Watts 2017	Wisconsin	2011-2015	Retrospective	State Medicaid database	--	92	31	34%	4%
Chappell 2018	Pittsburgh PA	2006-2014	Retrospective	Institutional database/EMR	--	1025	95	9%	8.4%
Epstein 2018	Boston MA	2006-2016	Retrospective	Registry database for women with drug use	--	404	180	45%	2.8%
Bell 2019	Portland MA	2013-2018	Retrospective	Institutional EMR State Laboratory database	--	177	94	53%	7.4%
Protopapas 2019	Cincinnati OH	2014-2016	Retrospective	Institutional EMR	--	702	259	37%	3.6 - 5.2%
Gowda 2020	Columbus OH	2008-2018	Retrospective	Institutional EMR	--	770	253	33%	3.5%
Lopata 2020	Tennessee	2005-2014	Retrospective	Birth Certificate records/ EMR	--	4072	733	18%	--
Bhardwaj 2021	Cleveland OH	1993-2016	Retrospective	Institutional EMR	--	407	108	27%	11%
Towers 2019	Knoxville TN	2015-2016	Prospective	Database for HCV+ pregnant women	Follow up provided at discharge	127	55	43%	--
Abughali 2014	Cleveland OH	1993-2005 2006-2011	Pre- and post-intervention	Institutional EMR	Consultation + follow up, HCV Education, Perinatal HCV exposure documentation, Annual HCV testing review, PCP notification for HCV testing	121 (Pre) 72 (Post)	10 (Pre) 36 (Post)	8%(Pre) 50 % (Post)	--
Hojat 2020	Cleveland OH	2011-2015 2015-2018	Pre- and post-intervention	Institutional EMR	EMR-based reminder to test HCV Ab at 18 months	79 (Pre) 140 (Post)	11 (Pre) 86 (Post)	14% (Pre) 61% (Post)	--

Table 2. Maternal/Infant Risk Factors Associated with Perinatal Hepatitis C Testing in US Studies

	Adequate HCV testing	Inadequate HCV testing	No association found
Maternal Characteristics	White Race [1] Hispanic Ethnicity [2] Residence rurality [1] Opioid use [3] Methadone therapy during pregnancy [2,4] HCV medical care [2] HIV coinfection [4] Tobacco use [1], [4] $ HCV viremia $ [4]	Intravenous drug use [2]	Age [1,2,3] Gravidity [2] Parity [1,2] HBV coinfection [1,2] Psychiatric diagnosis [4] Healthcare use- Prenatal visits [1,5] ICU admission [1] Clinic distance (≥ 8 miles or < 8miles) [4] Insurance [3] Education [1,3]
Infant Characteristics	Birth weight [1] Small for Gestation [1] NICU admission [1] † [5] Healthcare use- Well-child visit [1,5] Female sex [4] $	None reported	Gestational age [1,2,4] Mode of delivery [2] Feeding practices [2] Congenital or Neonatal disorder [1] Foster care placement [4] [5] †

References (Author/Year): 1. Lopata (2020), 2. Bhardwaj (2021), 3. Chappell (2018), 4. Epstein (2018), 5. Protopapas (2019)
$ Higher odds for adequate HCV testing but no significance reached
† Associated with adequate testing in univariate analysis but no significance after adjusted analysis

- Most studies were retrospective, except for one prospective and two before-and-after intervention [Table1].
- **Appropriate HCV testing:** defined by all studies as HCV Ab testing at ≥ 18 month of age. Nine studies additionally included RNA testing at ≥ 2 months, and one study included negative HCV Ab between 12-18 months of age.
- **Rates of optimal testing widely varied** with vast regional differences, with rates as low as 7%. Only 3 studies reported ≥ 50% appropriate testing, with the highest rate (61%) reported by a study that adopted EMR-reminders for testing.
- 2 interventional studies showed > 40% increase of adequate testing. Interventions included early engagement of caregivers at time of birth (consultation, education, and close follow-up), and EMR leverage to document HCV-exposure and send reminders for final testing at 18 months of age.
- 8 studies estimated the rate of mother-to-child transmission (ranged from 2.6% to 11%).
- 5 studies retrospectively evaluated maternal and infant risk factors associated with complete perinatal HCV testing [Table2].

Discussion/Conclusions

- Overall, rates of perinatal HCV appropriate testing were suboptimal and varied widely.
- Prospective and EMR-based interventional studies showed higher rates of testing. Innovative testing schemes, public health and social support programs, similar to perinatal HIV model, are strongly needed to substantially improve perinatal HCV management.
- Further prospective and interventional studies are needed to formulate effective guidelines for perinatal HCV evaluation, and to identify and address barriers and enablers to optimal perinatal HCV care.