Annals of Internal Medicine | Review

Reducing Risk for Mother-to-Infant Transmission of Hepatitis C Virus: A Systematic Review for the U.S. Preventive Services Task Force

Erika Barth Cottrell, PhD, MPP; Roger Chou, MD; Ngoc Wasson, MPH; Basmah Rahman, MPH; and Jeanne-Marie Guise, MD, MPH

Background: Mother-to-infant transmission is the leading cause of childhood hepatitis C virus (HCV) infection, with up to 4000 new cases each year in the United States.

Purpose: To evaluate effects of mode of delivery, labor management strategies, and breastfeeding practices on risk for mother-to-infant transmission of HCV.

Data Sources: MEDLINE (1947 to May 2012), the Cochrane Library Database, clinical trial registries, and reference lists.

Study Selection: Randomized trials and observational studies on mode of delivery, labor management strategies, and breastfeeding practices and risk for mother-to-infant transmission of HCV.

Data Extraction: Investigators abstracted and reviewed study details and quality using predefined criteria.

Data Synthesis: Eighteen observational studies evaluated the association between mode of delivery, labor management strategies, or breastfeeding practices and risk for mother-to-infant HCV transmission. Fourteen studies (2 good-quality, 4 fair-quality, and 8 poor-quality studies) found no clear association between mode of delivery (vaginal versus cesarean delivery) and risk for transmission. Two studies (1 good-quality and 1 poor-quality study) reported an association between prolonged duration of ruptured membranes and increased risk for transmission. Fourteen studies (2 good-quality, 2 fair-quality, and 10 poor-quality studies) found no association between breastfeeding and risk for transmission.

Limitations: Only English-language articles were included. Studies were observational, and most had important methodological shortcomings, including failure to adjust for potential confounders and small sample sizes.

Conclusion: No intervention has been clearly demonstrated to reduce the risk for mother-to-infant HCV transmission. Avoidance of breastfeeding does not seem to be indicated for reducing transmission risk.

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For author affiliations, see end of text.

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An estimated 40 000 children are born to hepatitis C virus (HCV)–positive women each year (1). Mother-to-infant (vertical) transmission is the main route of childhood HCV infection (2). Estimates for the rate of vertical transmission range from 3% to 10% (2–5). Risk for transmission is highest among women with a high viral load at delivery (2–6) and those co-infected with HIV (5, 7). Although antiviral therapies are contraindicated in pregnancy because of teratogenic risks, prenatal HCV screening to identify HCV-infected women unaware of their status might lead to other interventions during labor and delivery or in the perinatal period that reduce risk for mother-to-infant transmission (8).

The purpose of this review was to synthesize the evidence on the effects of mode of delivery, labor management strategies, and breastfeeding practices on risk for mother-to-infant transmission. This review was performed as part of a larger report on HCV screening (9) and will be used by the U.S. Preventive Services Task Force (USPSTF) to inform its prenatal HCV screening recommendations.

Methods

Scope

We developed a review protocol by using a standardized process with input from experts and the public to address the following key question: "What is the effect of mode of delivery, labor management strategy, or breastfeeding on risk for mother-to-infant transmission of HCV?" Detailed methods and data for the review, including the full USPSTF analytic framework on screening, search strategies, detailed abstraction tables, and quality ratings of individual studies, are available in the full report (9).

Data Sources and Searches

A research librarian searched Ovid MEDLINE (1947 to May 2012), EMBASE, the Cochrane Library Database, Scopus, PsycINFO, clinical trial registries (including clinicaltrials.gov), and grants databases. We supplemented electronic searches by reviewing reference lists of retrieved articles. Searches were peer reviewed by a second librarian.

Study Selection

At least 2 reviewers independently evaluated each study to determine inclusion eligibility. We selected for full-review randomized trials, cohort studies, and case–control studies that evaluated the association between mode of delivery (cesarean versus vaginal delivery), labor management strategies (use of internal fetal monitoring or management of premature rupture of membranes), or breastfeeding on risk for mother-to-infant transmission. We restricted inclusion to English-language articles and

See also:

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Related articles 101, 114

excluded studies published only as abstracts. Women co-infected with HIV are advised to avoid breastfeeding and deliver by elective cesarean if they are viremic in order to reduce risk for HIV transmission (10). Therefore, we excluded studies of HIV co-infected women, unless results for women not co-infected with HIV were reported separately or co-infected women made up less than 10% of the study sample.

Data Extraction and Quality Rating

One investigator abstracted details about the study design, patient population, setting, interventions, analysis, follow-up, and results. A second investigator reviewed data for accuracy. Two investigators independently applied predefined criteria to assess the quality of each study as good, fair, or poor (11–13). Discrepancies were resolved through a consensus process.

Data Synthesis

We assessed the overall strength of each body of evidence as "high," "moderate," "low," or "insufficient" in accordance with the AHRQ "Methods Guide for Comparative Effectiveness Reviews" (14), based on the quality of studies, consistency between studies, precision of estimates, and directness of evidence.

Role of the Funding Source

This research was funded by AHRQ's Effective Health Care Program. Investigators worked with AHRQ staff to develop and refine the scope, analytic framework, and key questions. AHRQ staff had no role in study selection, quality assessment, synthesis, or development of conclusions. AHRQ staff provided project oversight, distributed the draft report for peer review, and reviewed the draft report and manuscript. The investigators are solely responsible for the content of the manuscript and the decision to submit for publication.

Results

The search and selection of articles are summarized in the study flow diagram (**Appendix Figure**, available at www.annals.org). Of 2580 potentially relevant citations, 444 articles were selected for full-text review and 18 met inclusion criteria.

Mode of Delivery

Fourteen observational studies reported in 16 publications (sample sizes of 56 to 1034 mother–infant pairs) evaluated the association between mode of delivery and vertical transmission of HCV (**Appendix Table**, available at www.annals.org) (4, 5, 15–28). Nine studies were conducted in Europe (4, 15–17, 19–21, 23, 25, 27, 28), 2 in Australia (18, 24), 2 in Japan (22, 26), and 1 in the United States (5). Two studies were rated as good quality (5, 15, 16), 4 fair quality (4, 19, 21, 23), and the remainder poor quality. Two reports from the European Pediatric Hepatitis C Network evaluated overlapping populations (15, 16), and 2 studies evaluated nonoverlapping (different periods of enrollment) populations in Dublin, Ireland (19, 21). Only 4 studies adjusted for potential confounders in analyses (4, 5, 15, 16, 19); no study reported baseline characteristics according to mode of delivery or matched women on key potential confounders.

Four studies (5, 15, 19, 21) totaling 2080 mother–infant pairs (2 good-quality [5, 15] and 2 fair-quality [19, 21] studies) compared risk for transmission after elective cesarean delivery before the onset of labor versus vaginal or emergency (after onset of labor) cesarean delivery (**Appendix Figure**, available at www.annals.org). Three of these studies (5, 19, 21) reported higher transmission risk after vaginal or emergent cesarean delivery, but the difference was statistically significant in only 1 fair-quality study (19). That study ($n = 424$) reported no cases of transmission after elective cesarean delivery, compared with 7.4% after vaginal or emergency cesarean delivery (adjusted odds ratio, 0.0 [95% CI, 0.0 to 0.87]) (19). The 2 good-quality studies reported conflicting results. One ($n = 181$) reported a direction of effect that was not statistically significant but was similar to that of the fair-quality study, with a vertical transmission rate of 4.1% (7 of 169) after vaginal or emergent cesarean delivery compared with no cases after 12 elective cesarean births (relative risk, 1.1 [CI, 0.07 to 19]) (5). The other, larger ($n = 1034$) good-quality study found elective cesarean to be associated with increased risk for vertical transmission compared with vaginal or emergency cesarean delivery (adjusted odds ratio, 1.6 [CI, 0.88 to 2.9]) (15).

Eleven studies (total of 2308 mother–infant pairs) compared the risk for vertical transmission after vaginal versus cesarean delivery, without specifying whether the cesarean delivery was elective or emergent (**Appendix Figure**) (4, 16–18, 20, 22–28). Ten of the 11 studies (1 good-quality [16], 2 fair-quality [4, 23], and 8 poor-quality [17, 18, 20, 22, 24–28] studies) found no association between mode of delivery and risk for HCV transmission (4, 16–18, 20, 23–28). The exception was 1 small ($n = 59$), poor-quality Japanese prospective cohort study that reported a statistically significant increase in risk with vaginal delivery in a subgroup of women with high viral load ($\geq 2.5 \times 10^6$ RNA copies/mL) (22).

Labor Management

Internal Fetal Monitoring

Three studies (2 good-quality [5, 16] studies and 1 fair-quality [21] study) reported conflicting findings on the relationship between use of internal fetal monitoring and risk for vertical transmission (**Appendix Figure**). One good-quality study ($n = 181$) (5) found internal fetal monitoring versus no monitoring was associated with increased risk (adjusted odds ratio, 6.7 [CI, 1.1 to 36]), but another, larger good-quality study ($n = 724$) found no association (relative risk, 1.2 [CI, 0.70 to 2.2]) (16).

Table. **Summary of Evidence: Effect of Mode of Delivery, Labor Management Strategies, or Breastfeeding Practices on Risk for Mother-to-Child Transmission of HCV***

Variable	Overall Strength of Evidence	Studies Identified, *n* Participants, *n*	Overall Quality	Consistency (High, Moderate, Low)	Directness (Direct or Indirect)	Precision (High, Moderate, Low)	Summary of Findings
Mode of delivery							
Elective cesarean versus vaginal delivery	Low	4 cohort studies 2080	Fair	Moderate	Direct	Low	The 2 good-quality studies found no statistically significant difference in risk for transmission with elective cesarean versus vaginal delivery, with trends in opposite directions
Any cesarean versus vaginal delivery	Moderate	11 cohort studies 2308	Fair	High	Direct	Low	Ten of 11 studies (1 good-quality) found no statistically significant difference in risk for transmission with cesarean (not specified whether elective or emergent) versus vaginal delivery
Labor management							
Internal fetal monitoring versus no internal fetal monitoring	Insufficient	3 cohort studies 928	Fair	Moderate	Direct	Low	Three studies (2 good-quality) found inconsistent evidence on the risk for transmission with fetal monitoring, with no association in 2 studies and increased risk for transmission in 1 of the good-quality studies (adjusted OR, 6.7 [95% CI, 1.1–36])
Prolonged rupture of membranes versus less prolonged rupture of membranes	Low	2 cohort studies 245	Fair	High	Direct	Low	Two studies (1 good-quality, 1 poor-quality) found an association between longer duration of rupture of membranes and risk for transmission, with the good-quality study reporting higher risk for transmission with membrane rupture >6 hours (adjusted OR, 9.3 [CI, 1.5–180])
Breastfeeding							
Breastfeeding versus no breastfeeding	Moderate	14 cohort studies 2971	Fair	High	Direct	High	Fourteen studies found no significant association between breastfeeding and risk for transmission

HCV = hepatitis C virus; OR = odds ratio.
* The full report is available on the Agency for Healthcare Research and Quality Web site at www.effectivehealthcare.ahrq.gov (9).

Duration of Rupture of Membranes

One good-quality study (5) and 1 poor-quality study (24) (total of 245 mother–infant pairs) found an association between longer duration of rupture of membranes and increased risk for transmission (**Appendix Figure**). The good-quality study reported greater risk for vertical transmission in women with membrane rupture longer than 6 hours (odds ratio, 9.3 [CI, 1.5 to 180]) (5). The poor-quality study reported longer average duration of membrane rupture in women who transmitted virus to their infant than in those who did not transmit virus (28 versus 16 hours; $P = 0.03$) (24).

Breastfeeding

Fourteen cohort studies (total of 2971 mother–infant pairs) found no association between breastfeeding by women infected with HCV and risk for transmission to infants (**Appendix Figure**) (5, 15, 17, 19, 20, 23–32). Most studies prospectively followed infants for at least 1 year. Sample sizes ranged from fewer than 50 (29, 31, 32) to more than 1000 (15). Two studies were rated good quality (5, 15), 2 fair quality (19, 23), and 10 poor quality (17, 20, 24–32). Methodologic shortcomings in the poor-quality studies included failure to perform statistical adjustment on potential confounders and insufficient information to determine comparability of groups at baseline stratified by breastfeeding status.

Discussion

Vertical transmission is the leading cause of childhood HCV infection, and identification of effective management strategies to reduce risk for transmission is an important clinical and public health concern. However, the primary finding of this review as summarized in the **Table** is that no perinatal management strategy has clearly been shown to reduce risk for HCV transmission. Observational studies consistently found no evidence of an association between breastfeeding and risk for vertical transmission, consistent

with data suggesting that transmission typically occurs in utero (23, 33). Evidence on the effects of labor management strategies and mode of delivery on risk for transmission was somewhat conflicting. Two studies (5, 24) reported increased risk for HCV transmission with more prolonged duration of ruptured membranes, similar to findings for other infectious agents transmitted vertically (such as group B streptococcus and HIV). However, other studies did not find vaginal delivery associated with increased risk for vertical transmission versus cesarean delivery, and the largest single study (15) reported a non–statistically significant trend toward decreased risk, even though vaginal delivery is associated with longer duration of ruptured membranes. Possible explanations for the failure to find an association between vaginal delivery and increased risk for transmission could include threshold or modifying effects related to the duration of rupture, viral load, or other factors. Cohort studies that focus on women with longer rupture of membranes or high viral load and perform statistical adjustment on other potential confounding factors could help clarify the effects of mode of delivery on transmission risk. Randomized trials are less susceptible to confounding but would involve potential challenges related to the acceptability of randomly assigning HCV-infected women to elective cesarean delivery versus planned vaginal birth.

Other reviews and reports were consistent with our findings. A review of cesarean delivery versus vaginal delivery for preventing mother-to-infant HCV transmission found no randomized trials and concluded that a systematic review of observational studies is needed (34). A 2007 American College of Obstetricians and Gynecologists report identified a possible association between prolonged rupture of membranes after labor and increased risk for vertical transmission but concluded that no preventive measures have been proven effective for reducing the risk for mother-to-infant transmission (35).

Our review has limitations. Evidence on the effects of interventions to prevent mother-to-infant transmission was restricted to observational studies, most with methodological shortcomings (including failure to adjust for confounders) and small sample sizes. If practices that are more effective at reducing transmission are preferentially used in women at higher risk, this could have biased results toward null findings. We excluded non–English-language articles, which could result in language bias. We were also unable to formally assess publication bias due to small numbers of studies and methodological shortcomings in the studies.

This review was conducted as part of a larger review on HCV screening (9). For prenatal screening to be effective, there must be an effective intervention. Our findings indicate that avoidance of breastfeeding is not warranted to reduce risk for vertical transmission. Given limited evidence of an association between prolonged rupture of membranes and increased transmission risk, clinicians may consider avoiding prolonged rupture of membranes in HCV-infected women until more definitive data are available.

From Oregon Health & Science University, Portland, Oregon.

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Requests for Single Reprints: Roger Chou, MD, 3181 SW Sam Jackson Park Road, Mail Code BICC, Portland, OR 97239; e-mail, chour@ohsu.edu.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Drs. Cottrell, Chou, Wasson, Rahman, and Guise: 3181 SW Sam Jackson Park Road, Mail Code BICC, Portland, OR 97239.

Author Contributions: Conception and design: R. Chou, J.M. Guise.
Analysis and interpretation of the data: E.B. Cottrell, R. Chou, N. Wasson, J.M. Guise.
Drafting of the article: E.B. Cottrell, R. Chou, B. Rahman, J.M. Guise.
Critical revision of the article for important intellectual content: E.B. Cottrell, R. Chou, N. Wasson, J.M. Guise.
Final approval of the article: E.B. Cottrell, R. Chou, N. Wasson, J.M. Guise.
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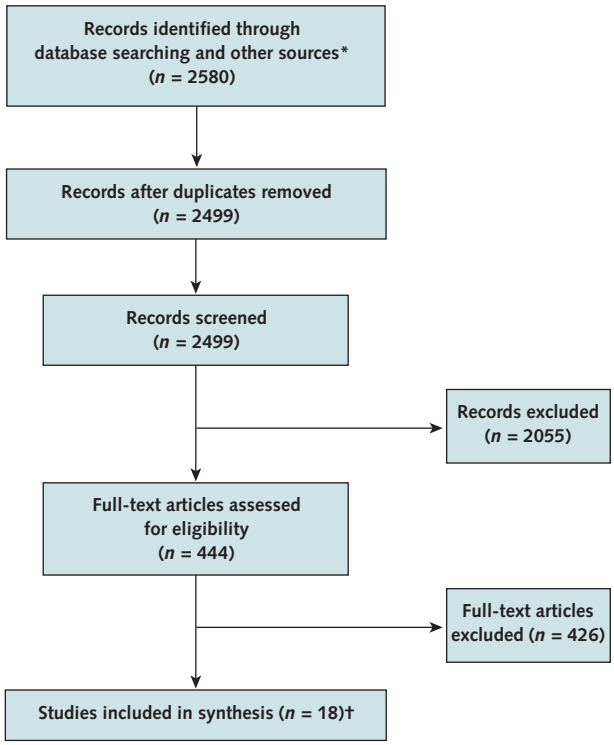
Appendix Figure. **Summary of evidence search and selection.**



The flow diagram summarizes the search and selection of articles addressing the effect of mode of delivery, labor management strategies, or breastfeeding practices on risk for mother-to-infant transmission of hepatitis C virus. Reproduced from reference 9.
* Includes hand searches and gray literature searches.
† One study resulted in 2 publications.

Appendix Table. **Studies on Mode of Delivery, Labor Management Strategies, and Breastfeeding Practices and Mother-to-Infant Transmission of HCV**

Study, Year; Country (Reference)	Quality	Participants, *n*	Age, *y* Nonwhite Participants, % HIV-Positive Participants, % HCV Viral Load, *RNA copies* $\times 10^6$*/L*	Results* (95% CI)
Mode of delivery				
Elective cesarean versus vaginal delivery/emergent cesarean				
EPHN (Tovo), 2005; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (15)	Good	1034	Mean (SD), 31.7 (5.17) NR 0 NR	Rates NR OR, 1.57 (0.88–2.83); $P = 0.13$; unadjusted OR, 1.59 (0.88–2.86); $P = 0.13$; adjusted for sex, mode of delivery, prematurity, and breastfeeding
Gibb et al, 2000; Ireland, United Kingdom (19)	Fair	424	Mean (SD), 27 (6) 6 5 NR	0/31 (0%) versus 29/393 (7.4%) OR, 0 (0–0.87); $P = 0.04$; adjusted for HIV status and breastfeeding
Mast et al, 2005; United States (5)	Good	181	<20 y: 7 (2.9%) 20–29 y: 103 (42.9%) 30–39 y: 120 (49.6%) ≥40 y: 12 (4.9%) 67.4 0 Mean HCV RNA level at delivery: 2.38	0/12 (0%) versus 7/169 (4.1%) RR, 1.1 (0.07–19)
McMenamin et al, 2008; Ireland (21)	Fair	441	Median (range), 26 (16–44) NR 5.9 NR	1/33 (3%) versus 17/408 (4.2%) RR, 0.73 (0.09–5.30)
Total		2080		
Any cesarean (elective or emergent) versus vaginal delivery				
EPHN (Pembrey), 2001; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (16)	Good	884	<20 y: 219 (17%) 20–25 y: 563 (43%) 30–39 y: 495 (38%) ≥40 y: 34 (3%) NR 0 NR	15/218 (6.9%) versus 39/666 (5.9%) OR, 1.17 (0.59–2.31); adjusted for breastfeeding, maternal age at delivery, center category
Ceci et al, 2001; Italy (4)	Fair	78	Median (range), 30 (21–42) NR 0 <0.2: 9 (15%) >0.2: 51 (85%)	No association (data not reported)
Conte et al, 2000; Italy (17)	Poor	365	Mean (SD), 30.9 (5.2) NR 4% NR	1/106 (0.9%) versus 7/259 (2.7%) RR, 0.35 (0.04–2.80)
Garland et al, 1998; Australia (18)	Poor	83	NR NR 0 NR	0/22 (0%) versus 3/61 (4.9%) RR not calculated
La Torre et al, 1998; Italy (20)	Poor	80	NR NR 0 NR	1/14 (7.1%) versus 1/66 (1.5%) RR, 4.71 (0.31–70.94)
Okamoto et al, 1999; Japan (22)	Poor	59	NR NR 0 ≥2.5: 21 (25%)	0/18 (0%) versus 7/41 (14%) RR not calculated ($P = 0.045$) 0/10 (0%) versus 7/16 (44%) in women with high viral load ($P = 0.023$)
Resti et al, 1998; Italy (23)	Fair	275	NR NR 0 NR	4/62 (6.5%) versus 9/213 (4.2%) RR, 1.53 (0.48–4.79)
Spencer et al, 1997; Australia (24)	Poor	63	Mean: 30 NR 0 NR	1/7 (14%) versus 5/55 (9.1%) RR, 1.57 (0.21–11.6)
Syriopoulou et al, 2005; Greece (25)	Poor	56	Mean (SD), 29.6 (3) NR 2 NR	0/17 (0%) versus 2/39 (5.1%) RR not calculated ($P = 0.34$)
Tajiri et al, 2001; Japan (26)	Poor	114	NR NR 0 High: 46 (40%) Low: 27 (24%) NR: 41 (36%)	1/24 (4.2%) versus 8/90 (8.8%) RR, 0.46 (0.61–3.53)
Zanetti et al, 1998, (28) and 1999 (27); Italy	Poor	251	NR NR 0 NR	1/58 (1.7%) versus 7/193 (3.6%) RR, 0.48 (0.06–3.79)
Total		2308		
Labor management				
Internal fetal monitoring versus no internal fetal monitoring				
EPHN (Pembrey), 2001; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (16)	Good	724	<20 y: 219 (17%) 20–25 y: 563 (43%) 30–39 y: 495 (38%) ≥40 y : 34 (3%) NR 0 NR	11/93 (11.8%) versus 58/631 (9.2%) RR, 1.24 (0.70–2.2)

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Appendix Table—**Continued**

Study, Year; Country (Reference)	Quality	Participants, *n*	Age, *y* Nonwhite Participants, %	HIV-Positive Participants, % HCV Viral Load, *RNA copies* $\times 10^6$*/L*	Results* (95% CI)
Mast et al, 2005; United States (5)	Good	181	<20 y: 7 (2.9%) 20–29 y: 103 (42.9%) 30–39 y: 120 (49.6%) ≥40 y: 12 (4.9%) 67.4	0 Mean HCV RNA level at delivery: 2.38	3/16 (18.8%) versus 4/165 (2.4%) RR, 7.7 (1.9–31.6); $P = 0.02$; unadjusted OR, 6.7 (CI, 1.1–35.9); adjusted for maternal demographic characteristics, HCV RNA level, history of intravenous drug use, and cigarette smoking during pregnancy
McMenamin et al, 2008; Ireland (21)	Fair	23	Median (range), 26 (16–44) NR	5.9 NR	Infant HCV RNA–positive: 0/11 (0%) Infant not tested for HCV: 12 RR undefined
Total		928			
Prolonged rupture of membranes versus less prolonged rupture of membranes					
Mast et al, 2005; United States (5)	Good	182	<20 y: 7 (2.9%) 20–29 y: 103 (42.9%) 30–39 y: 120 (49.6%) ≥40 y: 12 (4.9%) 67.4	0 Mean HCV RNA level at delivery: 2.38	<1 versus 1–5 versus 6–12 versus ≥13 h: 0/53 versus 1/59 (1.7%) versus 4/40 (10%) versus 2/30 (6.7%); $P = 0.02$ Membrane rupture >6 h OR, 9.3 (1.5–179.7); adjusted for maternal demographic characteristics, HCV RNA level, fetal monitoring, history of intravenous drug use, and cigarette smoking during pregnancy
Spencer et al, 1997; Australia (24)	Poor	63	Mean: 30 NR	0 NR	Mean duration (SD), transmitted versus not transmitted: 28 (10) h versus 16 (4) h ($P = 0.03$)
Total		245			
Breastfeeding versus no breastfeeding					
Conte et al, 2000; Italy (17)	Poor	370	Mean (SD), 30.9 (5.2) NR	4 NR	2/90 (2.2%) versus 6/280 (2.1%) RR, 1.02 (0.30–3.45)
Gibb et al, 2000; Ireland, United Kingdom (19)	Fair	414	Mean (SD), 27 (6) 6	5 NR	7.7% versus 6.7% OR, 1.52 (0.35–5.12); adjusted for HIV status and mode of delivery
La Torre et al, 1998; Italy (20)	Poor	80	NR NR	0 NR	0/10 (0%) versus 2/46 (4.3%) RR not calculated
Lin et al, 1995; China (29)	Poor	15	NR NR	0 NR	0/11 (0%) versus 0/4 (0%) RR not calculated
Mast et al, 2005; United States (5)	Good	182	<20 y: 7 (2.9%) 20–29 y: 103 (42.9%) 30–39 y: 120 (49.6%) ≥40 y: 12 (4.9%) 67.4	0 Mean HCV RNA level at delivery: 2.38	2/62 (3.2%) versus 5/120 (4.2%) RR, 0.8 (0.2–3.9)
Moriya et al, 1995; Japan (30)	Poor	74	NR NR	0 NR	5/6 infected (83%) versus 54/68 uninfected (79%) were breastfed (case–control design) OR, 1.3 (0.14–12.0)
Pipan et al, 1996; Italy (31)	Poor	25	Mean (range), 26.4 (19–35) NR	0 NR	0/6 (0%) versus 0/19 (0%) RR not calculated
Resti et al, 1998; Italy (23)	Fair	275	NR NR	0 NR	6/87 (6.9%) versus 7/188 (3.7%) RR, 1.85 (0.64–5.35)
Spencer et al, 1997; Australia (24)	Poor	63	Mean: 30 NR	0 NR	2/33 (6.0%) versus 4/13 (13%) RR, 0.45 (0.09–2.31)
Syriopoulou et al, 2005; Greece (25)	Poor	56	Mean (SD), 29.6 (3) NR	2 NR	0/15 (0%) versus 2/41 (4.9%) RR not calculated ($P = 0.38$)
Tajiri et al, 2001; Japan (26)	Poor	114	NR NR	0 High: 46 (40%) Low: 27 (24%) NR: 41 (36%)	9/98 (9.2%) versus 0/16 (0%) RR not calculated ($P = 0.243$)
Tanzi et al, 1997; Italy (32)	Poor	18	NR NR	0.27% NR	0% (0/12) versus 0% (0/6) 12/18 HCV RNA–positive mothers breastfed, none infected at 3-mo follow-up
EPHN (Tovo), 2005; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (15)	Good	1034	Mean (SD), 31.7 (5.17) NR	0 NR	Rates NR OR, 0.88 (0.48–1.61); unadjusted OR, 0.92 (0.50–1.70); adjusted for sex, prematurity, and mode of delivery
Zanetti et al, 1998 (28) and 1999 (27); Italy	Poor	251	NR NR	0 NR	3/127 (2.4%) versus 5/124 (4.0%) RR, 0.59 (0.14–2.40)
Total		2971			

EPHN = European Paediatric Hepatitis C Virus Network; HCV = hepatitis C virus; NR = not reported; OR = odds ratio; RR = relative risk.
* Unadjusted unless otherwise indicated.