Neonatal Jaundice in Asian, White, and Mixed-Race Infants

Sabeena Setia, MPH; Andrés Villaveces, MD, PhD; Preet Dhillon, MPH; Beth A. Mueller, DrPH

Background: East Asians have inherently higher bilirubin levels at birth than whites. The potential for unnecessary treatment makes jaundice a problem of public health and clinical significance.

Objectives: To report the occurrence of jaundice diagnoses in East Asian and mixed East Asian/white infants in Washington State in recent years, and to compare the risk of diagnosis with neonatal jaundice among these infants, relative to white infants.

Design: Population-based cohort study in Washington state. Participants were infants of full East Asian parentage (n=3000), maternal Asian parentage (n=2997), paternal Asian parentage (n=2048), and white parentage (n=3000). Diagnoses of jaundice and “severe jaundice” were identified using International Classification of Diseases, Ninth Revision (ICD-9) diagnosis and procedure codes from hospital discharge records.

Results: Infants of full East Asian parentage were more likely to be diagnosed with jaundice than were white infants (relative risk [RR], 1.37; 95% confidence interval [CI], 1.16-1.62). For infants with Asian mothers and white fathers, the RR was 1.09 (95% CI, 0.91-1.30). Infants with Asian fathers and white mothers had an RR of 1.26 (95% CI, 1.05-1.52). The risk of severe jaundice requiring phototherapy, blood transfusion, or rehospitalization, however, was significantly elevated only for infants of full East Asian parentage (RR, 1.7; 95% CI, 1.12-2.58).

Conclusions: Diagnoses of neonatal jaundice occurred more often among East Asian and mixed Asian/white infants than among white infants. However, the risk of jaundice requiring extended hospital stay, rehospitalization, phototherapy, or blood transfusion was elevated only for infants of full East Asian parentage.

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PARTICIPANTS AND METHODS

SUBJECT IDENTIFICATION

We conducted a population-based cohort study of infants born in Washington state from 1987-1993. Data were obtained from the Washington State Birth Events Records Database. This database, created by the Washington State Department of Health Office of Hospital and Patient Data, links birth certificates to hospital discharge information for the birth hospitalizations of mother and child. Four cohorts of infants defined by parental race/ethnicity as indicated on the birth certificate (based on prenatal record or self-reported) were identified: those born to 2 white parents, those born to 2 East Asian (hereafter called “Asian”) parents, those born to an Asian mother and white father, and those born to a white mother and Asian father. Asian infants included those of Chinese, Japanese, or Filipino descent. We selected these infants because much of the existing literature on jaundice focuses on these ethnicities and because they were the largest Asian cohorts. We excluded other ethnicities such as Korean and Vietnamese to create more homogeneity and to increase our power to examine associations within groups. We also excluded groups such as “Samoan” and “Pacific Islander” because of their small numbers and the “other Asian” category because it was not well defined. Infants with parents identified as Native American or other nonwhite classifications were not included.

A random sample of 3000 infants born from 1987-1995 to white parents was the reference group. The 3 comparison groups included a random sample of 3000 infants born to 2 Asian parents, a random sample of 3000 infants born to an Asian mother and white father, and all 2048 infants born to a white mother and Asian father.

OUTCOME MEASUREMENTS

Infants with neonatal jaundice were identified by screening all available International Classification of Diseases, Ninth Revision (ICD-9) diagnosis fields in the child’s hospital discharge record for codes indicating jaundice (774.1, 774.2, 774.39, 774.4, and 774.6). Information concerning rehospitalization 28 or fewer days after birth was obtained by linking subjects’ records with Comprehensive Hospital Abstract Reporting System (CHARS) records for 1987-1996. Created by the Washington State Department of Health, CHARS contains discharge data for all hospitalizations in nonmilitary hospitals.

STATISTICAL ANALYSES

Stratified analyses were conducted to calculate Mantel-Haenszel relative risk estimates and to evaluate the presence of confounding and/or effect modification. Variables considered for their potential effects included maternal age (<20, 20-24, 25-29, 30-34, or ≥35 years), sex, gravidity, parity (0, 1, 2, or ≥3 prior births), duration of gestation (20-36, 37-42, or >42 weeks), maternal established or gestational diabetes, prenatal smoking or alcohol use (yes/no), birth weight (<2500, 2500-4500, or >4500 g), and preeclampsia (ICD-9 code 642.4 or 642.5). Factors that altered risk estimates more than 10% were considered confounders. Other factors possibly related to jaundice, such as maternal hepatitis (ICD-9 code 070), congenital anemia (ICD-9 code 776.5), and newborn sepsis (per the birth certificate), were also considered.

Initially, we evaluated jaundice from any cause as a single outcome. However, we were concerned that infants with jaundice might differ across cohorts with respect to short gestational duration (20-36 weeks), preterm delivery, hepatitis, hemolysis/bruising, maternal hepatitis, or congenital anemia. To isolate relationships of interest, we excluded infants with these potential causes to identify infants with presumed physiologic jaundice.

Infants with hospital stays of more than 5 days, procedure codes indicating phototherapy or blood transfusion during birth hospitalization, or rehospitalization for jaundice 28 or fewer days after birth were classified as having “severe” jaundice.

Adjustment for maternal age, infant sex, parity, duration of gestation, diabetes, smoking and alcohol consumption during pregnancy, birth weight, and preeclampsia did not appreciably change the estimates, nor were suppression during pregnancy, birth weight, and preeclampsia considered for their potential effects included maternal age (<20, 20-24, 25-29, 30-34, or ≥35 years), sex, gravidity, parity (0, 1, 2, or ≥3 prior births), duration of gestation (20-36, 37-42, or >42 weeks), maternal established or gestational diabetes, prenatal smoking or alcohol use (yes/no), birth weight (<2500, 2500-4500, or >4500 g), and preeclampsia (ICD-9 code 642.4 or 642.5). Factors that altered risk estimates more than 10% were considered confounders. Other factors possibly related to jaundice, such as maternal hepatitis (ICD-9 code 070), congenital anemia (ICD-9 code 776.5), and newborn sepsis (per the birth certificate), were also considered.

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Infants with hospital stays of more than 5 days, procedure codes indicating phototherapy or blood transfusion during birth hospitalization, or rehospitalization for jaundice 28 or fewer days after birth were classified as having “severe” jaundice.

Infants with 2 Asian parents were more likely to be diagnosed with jaundice regardless of their parents’ country of ethnic origin. Relative to white infants, the RR of diagnosis with neonatal jaundice for infants identified as being born to Chinese parents was 1.25 (95% CI, 1.00-1.57). For infants of Japanese parents, the RR was 1.85 (95% CI, 1.34-2.55), and for infants of Filipino parents, the RR was 1.34 (95% CI, 1.10-1.63). The RR among infants of mixed-heritage Asian parents was 1.26 (95% CI, 0.81-1.97). When infants with other known causes of jaundice were excluded, the risks of diagnosis with physiologic jaundice increased even more for infants in all Asian subgroups, except those born to Filipino parents.

The risk of severe jaundice significantly increased among infants with 2 Asian parents (RR, 1.70; 95% CI, 1.12-2.58) (Table 3). Infants with Asian mothers/white fathers and white mothers/Asian fathers had RRs of 1.36 (95% CI, 0.87-2.11) and 1.15 (95% CI, 0.69-1.91), respectively. Among specific Asian groups, significantly increased risk of severe jaundice was observed for Japanese (RR, 2.64; 95% CI, 1.27-5.51) and Filipino (RR, 1.68; 95% CI, 1.02-2.76) infants.

COMMENTS

Infants of East Asian parentage were more likely to be diagnosed with jaundice than white infants. This is consistent with the results of other studies.10,13 In our study, it is possible that clinicians had a lower threshold for testing for, and thus diagnosing, jaundice in Asian infants because of awareness of higher jaundice rates in Asians, or possibly because of skin coloration. To the extent that a diagnosis of jaundice in our data accurately indicates jaundice, we found that, among infants with 2 Asian parents, Japanese infants had the greatest risk, whereas risks for Filipino and Chinese infants were elevated to a lesser
Ho\(^5\) found that not all Asian groups had similar risks of jaundice, and recent investigations provide evidence of elevated mutation levels in the bilirubin uridine diphosphate–glucuronosyltransferase gene associated with jaundice in Japanese infants.\(^{15,16}\)

The rate of jaundice diagnosis among infants with Asian mothers and white fathers was not substantially different from that of white infants. However, infants with Asian fathers and white mothers had a 32% greater risk relative to white infants, suggesting a stronger paternal influence in determining an infant’s risk of jaundice. At this time, a possible genetic basis for paternal influence is unknown.

Asian infants were more likely to have severe jaundice requiring phototherapy and/or blood transfusion, rehospitalization for jaundice, or birth hospitalization greater than 5 days. The subgroup analysis by Asian ancestry suggests that infants of full Filipino and Japanese ancestry may be contributing to this increased risk.

The rate of jaundice diagnosis among infants with Asian mothers and white fathers was not substantially different from that of white infants. However, infants with Asian fathers and white mothers had a 32% greater risk relative to white infants, suggesting a stronger paternal influence in determining an infant’s risk of jaundice. At this time, a possible genetic basis for paternal influence is unknown.

**Table 1. Maternal, Infant, and Pregnancy Characteristics of East Asian, Mixed Asian/White, and White Study Cohorts**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>White Mother/White Father (n = 3000)</th>
<th>Asian Mother/Asian Father (n = 3000)</th>
<th>Asian Mother/White Father (n = 2997)</th>
<th>White Mother/Asian Father (n = 2048)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>185 (6.2)</td>
<td>65 (2.2)</td>
<td>94 (3.1)</td>
<td>172 (8.4)</td>
</tr>
<tr>
<td>20-24</td>
<td>745 (24.8)</td>
<td>353 (11.8)</td>
<td>476 (15.9)</td>
<td>436 (21.3)</td>
</tr>
<tr>
<td>25-29</td>
<td>1029 (34.3)</td>
<td>895 (29.8)</td>
<td>943 (31.5)</td>
<td>660 (32.2)</td>
</tr>
<tr>
<td>30-34</td>
<td>703 (23.4)</td>
<td>1046 (34.9)</td>
<td>926 (30.9)</td>
<td>510 (24.9)</td>
</tr>
<tr>
<td>≥35</td>
<td>336 (11.2)</td>
<td>641 (21.4)</td>
<td>556 (18.6)</td>
<td>270 (13.2)</td>
</tr>
<tr>
<td>Male infant</td>
<td>1515 (50.5)</td>
<td>1577 (52.6)</td>
<td>1505 (50.2)</td>
<td>1029 (50.2)</td>
</tr>
<tr>
<td>No. of prior births</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1209 (40.8)</td>
<td>1363 (46.6)</td>
<td>1364 (46.1)</td>
<td>888 (44.0)</td>
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<tr>
<td>1</td>
<td>1037 (35.0)</td>
<td>1039 (35.5)</td>
<td>1020 (34.5)</td>
<td>668 (33.1)</td>
</tr>
<tr>
<td>2</td>
<td>464 (15.7)</td>
<td>362 (12.4)</td>
<td>386 (13.1)</td>
<td>305 (15.1)</td>
</tr>
<tr>
<td>≥3</td>
<td>250 (8.5)</td>
<td>161 (5.5)</td>
<td>188 (6.4)</td>
<td>156 (7.7)</td>
</tr>
<tr>
<td>Gestational length, wk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-36</td>
<td>188 (7.0)</td>
<td>209 (8.4)</td>
<td>232 (8.6)</td>
<td>133 (7.4)</td>
</tr>
<tr>
<td>37-42</td>
<td>2258 (84.4)</td>
<td>2141 (86.0)</td>
<td>2306 (85.3)</td>
<td>1519 (84.0)</td>
</tr>
<tr>
<td>≥42</td>
<td>229 (8.6)</td>
<td>139 (5.6)</td>
<td>156 (6.1)</td>
<td>156 (6.6)</td>
</tr>
<tr>
<td>Maternal diabetes</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Established</td>
<td>4 (0.1)</td>
<td>9 (0.3)</td>
<td>11 (0.4)</td>
<td>9 (0.5)</td>
</tr>
<tr>
<td>Gestational</td>
<td>49 (1.6)</td>
<td>138 (4.9)</td>
<td>112 (3.9)</td>
<td>56 (2.9)</td>
</tr>
<tr>
<td>Maternal prenatal smoking</td>
<td>556 (19.5)</td>
<td>68 (2.4)</td>
<td>207 (7.2)</td>
<td>315 (16.1)</td>
</tr>
<tr>
<td>Maternal prenatal alcohol</td>
<td>77 (3.7)</td>
<td>0 (0.0)</td>
<td>16 (0.6)</td>
<td>36 (2.7)</td>
</tr>
<tr>
<td>consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried parents</td>
<td>356 (11.9)</td>
<td>176 (5.9)</td>
<td>195 (6.6)</td>
<td>329 (16.1)</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>105 (3.5)</td>
<td>150 (5.0)</td>
<td>112 (3.7)</td>
<td>82 (4.0)</td>
</tr>
<tr>
<td>2500-4500</td>
<td>2804 (93.5)</td>
<td>2826 (94.2)</td>
<td>2825 (94.3)</td>
<td>1930 (94.2)</td>
</tr>
<tr>
<td>&gt;4500</td>
<td>91 (3.0)</td>
<td>24 (0.8)</td>
<td>60 (2.0)</td>
<td>36 (1.8)</td>
</tr>
</tbody>
</table>

*Data given as number (percentage) of subjects. Numbers may not add to totals because of missing data.

**Table 2. Incidence of Neonatal Jaundice in East Asian and Asian/White Infants Relative to White Infants**

<table>
<thead>
<tr>
<th>Parentage</th>
<th>No. of Infants</th>
<th>No. (%) With Jaundice</th>
<th>RR‡ (95% CI)</th>
<th>No. of Infants</th>
<th>No. (%) With Jaundice</th>
<th>RR‡ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White mother/white father</td>
<td>3000</td>
<td>221 (7.4)</td>
<td>1.00</td>
<td>2784</td>
<td>169 (6.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Asian mother/white father</td>
<td>2997</td>
<td>240 (8.0)</td>
<td>1.09 (0.91-1.30)</td>
<td>2724</td>
<td>182 (6.7)</td>
<td>1.10 (0.90-1.35)</td>
</tr>
<tr>
<td>White mother/Asian father</td>
<td>2048</td>
<td>190 (9.3)</td>
<td>1.26 (1.05-1.52)</td>
<td>1868</td>
<td>151 (8.0)</td>
<td>1.32 (1.07-1.63)</td>
</tr>
<tr>
<td>Asian mother/Asian father</td>
<td>3000</td>
<td>303 (10.1)</td>
<td>1.37 (1.16-1.62)</td>
<td>2748</td>
<td>235 (8.6)</td>
<td>1.41 (1.17-1.70)</td>
</tr>
<tr>
<td>Both Chinese</td>
<td>1095</td>
<td>101 (9.2)</td>
<td>1.25 (1.00-1.57)</td>
<td>1029</td>
<td>84 (8.2)</td>
<td>1.35 (1.05-1.73)</td>
</tr>
<tr>
<td>Both Japanese</td>
<td>279</td>
<td>38 (13.7)</td>
<td>1.85 (1.34-2.55)</td>
<td>259</td>
<td>31 (12.0)</td>
<td>1.97 (1.37-2.84)</td>
</tr>
<tr>
<td>Both Filipino</td>
<td>1483</td>
<td>146 (9.8)</td>
<td>1.34 (1.10-1.63)</td>
<td>1332</td>
<td>106 (8.0)</td>
<td>1.31 (1.04-1.66)</td>
</tr>
<tr>
<td>Mixed Asian</td>
<td>143</td>
<td>18 (12.6)</td>
<td>1.26 (0.81-1.97)</td>
<td>128</td>
<td>14 (10.9)</td>
<td>1.80 (1.07-3.03)</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; CI, confidence interval.
†Excludes infants with jaundice because of anemia/isoimmunization, hepatitis, preterm delivery at less than 37 weeks’ gestation, hemolysis/bruising, or congenital anemia.
‡Risk relative to infants of white mother/white father.
Ethnic variation in the rates of neonatal jaundice has been recognized, and gene mutations associated with hyper-
bilirubinemia among some Asian groups have been identified. Greater knowledge of characteristics, including race/ethnicity, that may be associated with an increased risk of jaundice may be helpful, particularly as earlier hospital discharge after birth limits opportunity for cli-
nicians to detect progression to more serious disease.

To our knowledge, this is the first report of levels of jaundice diagnosis from population-based data in the
United States for infants of mixed Asian-white descent. These population-based findings of increased risks for
infants with Asian parents or one Asian parent and one white parent, may provide useful information to cli-
nicians and enhance our understanding of potential ge-
netic causes of jaundice.

Table 3. Risk of Severe Jaundice in East Asian
and Asian/White Infants, Relative to White Infants

<table>
<thead>
<tr>
<th>Parentage</th>
<th>No. of Infants</th>
<th>No. (%) With Severe Jaundice†</th>
<th>RR‡ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White mother/white father</td>
<td>2649</td>
<td>34 (1.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Asian mother/white father</td>
<td>2587</td>
<td>45 (1.7)</td>
<td>1.36 (0.87-2.11)</td>
</tr>
<tr>
<td>White mother/Asian father</td>
<td>1761</td>
<td>26 (1.5)</td>
<td>1.15 (0.69-1.91)</td>
</tr>
<tr>
<td>Asian mother/Asian father</td>
<td>2569</td>
<td>56 (2.2)</td>
<td>1.70 (1.12-2.58)</td>
</tr>
<tr>
<td>Both Chinese</td>
<td>962</td>
<td>17 (1.8)</td>
<td>1.38 (0.77-2.45)</td>
</tr>
<tr>
<td>Both Japanese</td>
<td>236</td>
<td>8 (3.4)</td>
<td>2.64 (1.27-5.51)</td>
</tr>
<tr>
<td>Both Filipino</td>
<td>1253</td>
<td>27 (2.2)</td>
<td>1.68 (1.02-2.76)</td>
</tr>
<tr>
<td>Mixed Asian</td>
<td>118</td>
<td>4 (3.4)</td>
<td>2.64 (0.98-7.11)</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; CI, confidence interval.
†Infants with severe jaundice included those with birth hospitalizations of more than 5 days, infants who underwent phototheraphy or blood transfusion
during birth hospitalizations, or infants rehospitalized for jaundice within 28
days of birth.
‡Risk relative to infants of white mother/white father.

Limitations of this study include reliance on birth
certificate and hospital discharge record coding of race/
ethnicity and jaundice, neither of which we could vali-
date. We also lacked data on other factors, such as fam-
ily history of neonatal jaundice, genetic traits that might
have varied by race, medicinal herbs in the diet, breast-
feeding, or the use of oxytocin to induce or augment
labor. Sepsis, preeclampsia, and preterm delivery are
also reportedly associated with jaundice. However, these
variables were not effect modifiers, nor did their
association have a significant effect on the risk of
severe jaundice.

Greater knowledge of characteristics associated with
risk of jaundice is helpful, particularly as earlier hospi-
 tal discharge after birth limits the opportunity for cli-
nicians to detect progression to more serious disease.
Racial differences have been observed in the time when peak serum bilirubin concentrations occur, with about 6%
of Asian infants diagnosed with jaundice more than 3 days
after birth, so early discharge may be of particular rel-

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This study was presented as a poster at the American
Public Health Association 127th Annual Meeting, Chi-
cago, Ill, November 7-11, 1999.

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