BRIEF REPORT

Beyond "Asian": Specific East and Southeast Asian Races or Ethnicities Associated With Jaundice Readmission

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ABSTRACT

OBJECTIVES: Clinical practice guidelines have recognized "Asian" and "East Asian" as risk factors for newborn jaundice and readmission. We sought to identify more detailed and specific, parent-identified races or ethnicities associated with jaundice readmission.

METHODS: We conducted a case control study of 653 newborn infants born (2014–2016) at a West-Coast, urban hospital to examine specific parent-described races or ethnicities that are associated with newborn hospital readmissions for hyperbilirubinemia. Parent-reported race or ethnicity was abstracted from the California Newborn Screening Test.

RESULTS: Our sample included 105 infants readmitted for jaundice (cases) and 548 infants as controls. In the full cohort, 66 infants (10.1%) were Coombs positive, 39 infants (6.0%) were born before 37 weeks' gestational age, and 405 infants (62.0%) were born to first-time mothers. The parents described the 653 infants using 45 unique races and ethnicities. In a multivariable model that controlled for Coombs positivity, gestational age <37 weeks, and primiparity, infants described as "Far East Asian" (odds ratio [OR] = 3.17; 95% confidence interval [CI] = 1.94–5.18) or "Southeast Asian" (OR = 3.17; 95% CI = 1.66–6.08) had increased risk for jaundice readmission. Infants described as Southeast Asian (eg, Laotian, Cambodian, Indonesian, Vietnamese, and Filipino) and Far East Asian (eg, Chinese, Korean, Taiwanese, Japanese, and Mongolian) had an increased risk of readmission. Finally, we did not find an association between South Asian (OR = 0.79; 95% CI = 0.33–1.92) race or ethnicity and risk of jaundice readmission.

CONCLUSIONS: In this study, we help clarify and move beyond the term "Asian" as a risk factor for readmission due to hyperbilirubinemia.

www.hospitalpediatrics.org
DOI:https://doi.org/10.1542/hpeds.2017-0234

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HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Mr Bentz designed the study, collected and analyzed the data, and drafted the initial manuscript; Ms Carmona, Ms Bhagwat, Ms Thimmig, Dr Saleh, Dr Eke, Ms Kokroko, Dr Dadasovich, and Ms Rice developed the data collection instruments, collected the data, and analyzed the data; Dr Cabana conceptualized the study and analyzed the data; and all authors approved the final manuscript as submitted.

Hyperbilirubinemia requiring phototherapy is a common cause of newborn hospital readmissions. Understanding and identifying risk factors for readmissions is important to clinicians evaluating newborns in the nursery to ensure that readmissions can be minimized.

In previous studies, terms such as "Asiatic race,"[1] "Oriental,"[2,3] "East Asian,"[4] and "mixed Asian/white"[4] have been used as risk factors for jaundice. More recently, the American Academy of Pediatrics clinical practice guideline for the management of newborn hyperbilirubinemia states that East Asian race is a risk factor for the development of hyperbilirubinemia.[5] However, for practicing clinicians, there is little guidance provided for what constitutes Asian or East Asian.

As a result, in our study, we sought to investigate specific parent-described races or ethnicities that are associated with newborn hospital readmissions for hyperbilirubinemia, while controlling for known risk factors.

METHODS

We performed a case-control study with 653 infants who were born into the XXX Children's Hospital well-baby nursery during from 2014 to 2016. The case patients were 105 infants who were born into the well-baby nursery and later readmitted for hyperbilirubinemia within 30 days of discharge. To be considered a case patient, it was required that an infant had a primary diagnosis of hyperbilirubinemia and received phototherapy on readmission. Infants readmitted for direct hyperbilirubinemia were not included in the analysis. Each case patient was matched with 5 control patients born during the same week as a case patient infant. Because there were more than 5 potential control patients for each case, the control patients were first selected on the basis of a random number generator. The control patients were 548 infants who were admitted to the well-baby nursery and not readmitted for hyperbilirubinemia within 30 days of discharge. For 4 instances, case patients were made control patients when during data abstraction, it was determined that the patient did not have a primary diagnosis of hyperbilirubinemia and did not receive phototherapy on readmission.

We abstracted the following variables from the electronic health record of each infant: history of readmission for

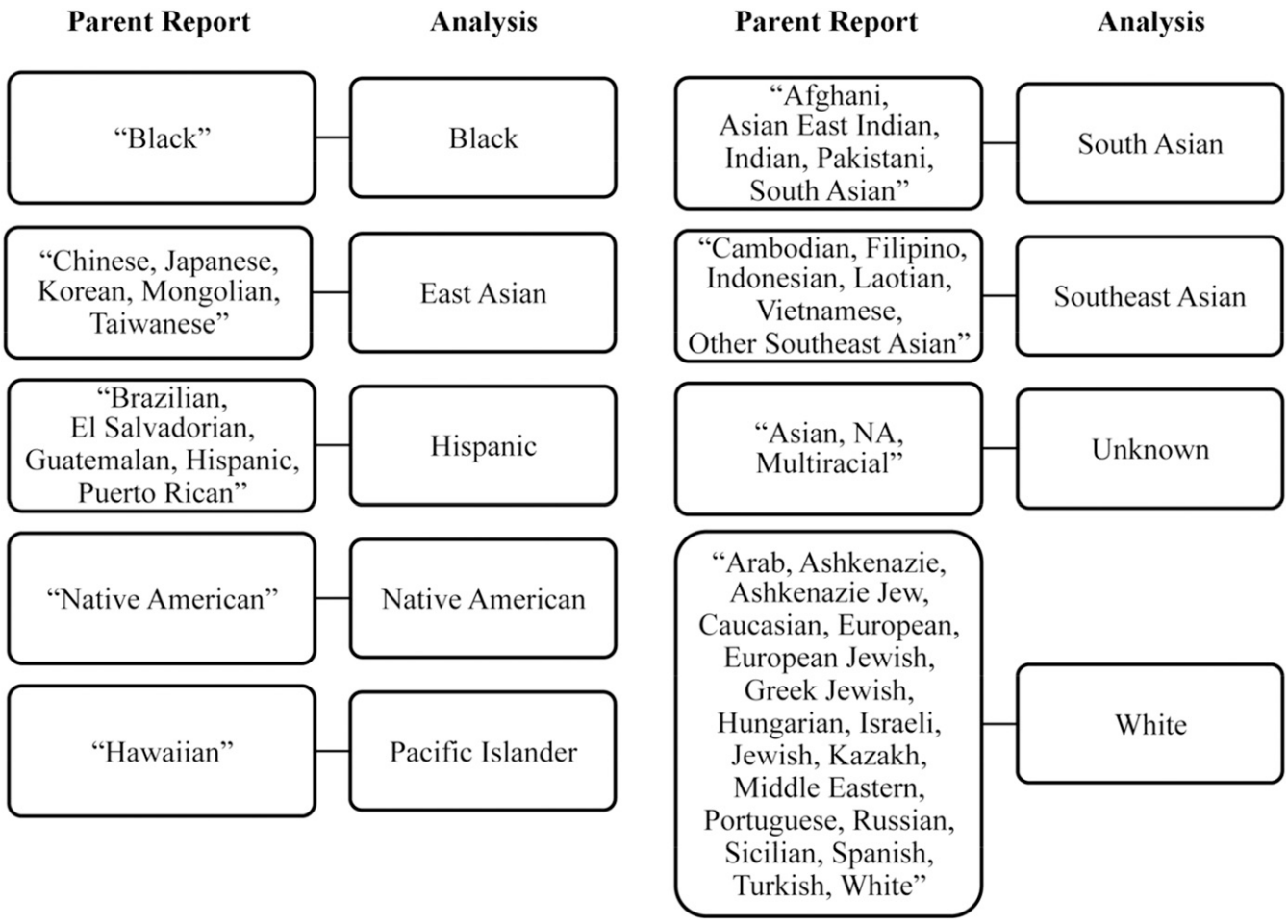

FIGURE 1 Consolidation of parent-reported races and ethnicities. NA, Not applicable

hyperbilirubinemia, Coombs positivity, gestational age, sex, maternal parity, feeding method, and race or ethnicity. Variables were abstracted twice, by separate, independent abstractors to confirm the data. Discrepancies were checked by a third party and resolved by consensus and re-abstracting the necessary data.

Readmission for indirect hyperbilirubinemia was the dependent variable. Coombs positivity, gestational age, sex, maternal parity, feeding method, and race or ethnicity were the independent variables. Coombs status was routinely determined during the initial admission for infants that had an O blood type or were Rh negative. Gestational age, sex, maternal parity, and feeding method were determined on the basis of documentation during the initial admission note.

Parent-reported race or ethnicity was abstracted from electronic medical records of the California Newborn Screening Test, which is performed by state law for each infant born in California at least 24 hours after birth. The screening test form has a semistructured question for the parent(s) to describe the races and/or ethnicities of their infant.[6] The form states, "Race/Ethnicity: Fill all that apply." The responses are "White," "Hispanic," "Black," "Chinese," "Japanese," "Korean," "Vietnamese," "Filipino," "Cambodian," "Laotian (Laos)," "Other S.E. Asian," "Middle Eastern," "Hawaiian," "Samoan," "Asian-East Indian," "Guamanian," "Native American," and "Other (Specify)." If the parent(s) select Other (Specify), then there is an open-ended space that includes up to 11 characters to describe the race or ethnicity.

Because there were 45 unique combinations of parent responses to this question, for our analyses, we consolidated the specific races and ethnicities into the following groups, as determined by the National Institutes of Health definitions of racial and ethnic categories[7]: Black, Far East Asian, Hispanic, Native American, Pacific Islander, Southeast Asian, South Asian, White, and Unknown. In Fig 1, we outline the consolidation process and the grouping of each of the 45 individual categories. The following self-reported races or ethnicities were placed into the Unknown group: Asian, "Multiracial," and those responses that were left unanswered by the parent(s). We included Asian in this group because this parent description is ambiguous and spans multiple categories such as Far East Asian, South Asian, and Southeast Asian. Infants identified as multiple races or ethnicities (up to 2) were included in both categories.

We performed bivariate analyses (logistic regression) to establish which variables are associated with newborn hospital readmissions for hyperbilirubinemia. We then performed multivariable logistic regression with all variables that were significant in the bivariate analyses to determine factors associated with newborn hospital readmissions for hyperbilirubinemia.

With a total of over 100 readmission cases, we had sufficient power to analyze ~5 to 10 independent variables for our final multivariable logistic regression.[8] We used Stata (Version 14.0; Stata Corp, College Station, TX) to perform all analyses. The study was approved by the XXX Committee on Human Research (Institutional Review Board).

RESULTS

Our sample included 653 infants, of which 105 infants were from the group of case patients who were readmitted for hyperbilirubinemia within 30 days of discharge. There were 3 records with missing data, and these infants were excluded from analysis. In terms of risk factors for jaundice readmission, 66 infants (10.1%) were Coombs positive, 39 infants (6.0%) were born before 37 weeks' gestational age, 327 infants were boys (50.1%), 525 infants (80.4%) were exclusively breastfed, and 405 infants (62.0%) were born to first-time mothers.

On the basis of data from the California Newborn Screening Test, the parents described the 653 infants using 45 unique races and ethnicities. In Fig 2, we describe the distribution of the raw number of infants in each race or ethnicity category. The majority (65.4%) were white. The sample's racial or ethnic breakdown equals more than 653 infants (100%) because parents were able to self-report more than 1 race or ethnicity.

In Table 1, we list the unadjusted and adjusted odds ratios (ORs) for each of the variables associated with newborn readmissions for hyperbilirubinemia. Of the race and ethnicity variables, only Far East Asian (OR = 3.05; 95% confidence interval [CI] = 1.92–4.83) and Southeast Asian (OR = 2.88; 95% CI = 1.59–5.22) were associated with an increased likelihood for

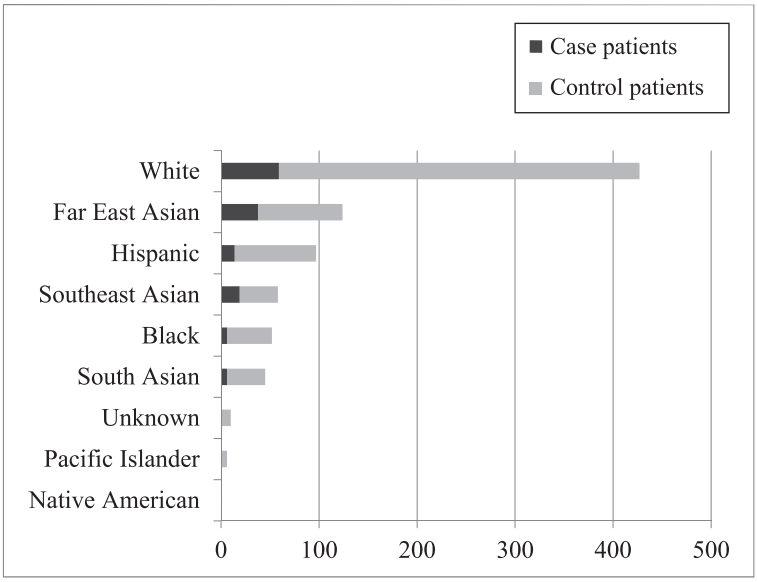

FIGURE 2 Number of newborns in each race and ethnicity subgroup.

TABLE 1 Factors Associated With Newborn Hospital Readmission for Hyperbilirubinemia ($N = 653$)

Risk Factor	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
EGA <37 wk	3.63 (1.83–7.18)	4.11 (1.96–8.60)
Far East Asian	3.05 (1.92–4.83)	3.17 (1.94–5.18)
Southeast Asian	2.88 (1.59–5.22)	3.17 (1.66–6.08)
Coombs positive	2.79 (1.58–4.92)	3.14 (1.69–5.83)
First-time mother	2.07 (1.29–3.33)	2.19 (1.31–3.65)
Male sex	1.22 (0.80–1.86)	—
Pacific Islander	1.04 (0.12–9.03)	—
Hispanic	0.86 (0.47–1.59)	—
South Asian	0.79 (0.33–1.92)	—
Black	0.66 (0.27–1.59)	—
White	0.63 (0.41–0.96)	—

The following variables included no readmitted infants and were unable to be analyzed in logistic regression: Native American race or ethnicity, Unknown race or ethnicity, and exclusive formula feeding. EGA, estimated gestational age; —, not applicable.

jaundice readmissions in the bivariate analysis.

In the multivariate analysis, by only using variables previously significant in bivariate analyses, Far East Asian (OR = 3.17; 95% CI = 1.94–5.18) and Southeast Asian (OR = 3.17; 95% CI = 1.66–6.08) both remained associated with an increased likelihood for jaundice readmission, even after controlling for Coombs positivity (OR = 3.14; 95% CI = 1.69–5.83), gestational age <37 weeks (OR = 4.11; 95% CI = 1.96–8.60), and primiparity (OR = 2.19; 95% CI = 1.31–3.65). Exclusive formula feeding perfectly predicted no readmission, and an OR could not be calculated in the bivariate analysis. As a result, infants that were exclusively formula fed ($n = 25$) were excluded from the multivariate analysis.

DISCUSSION

Asian race has long been identified as a risk factor for newborn hyperbilirubinemia. Our approach, based on parent-reported race or ethnicity of their newborn, allowed us to avoid potentially ambiguous terms and identify specific races and ethnicities associated with increased risk for jaundice. Overall, in this study, we help move beyond the term "Asian" as a risk factor for hyperbilirubinemia readmission. In our study, infants who were described as Southeast Asian (or Laotian, Cambodian, Indonesian, Vietnamese, and Filipino) or infants who were described as Far East Asian (or Chinese, Korean, Taiwanese, Japanese, and Mongolian) had an increased risk of readmission for hyperbilirubinemia, while controlling for Coombs positivity, gestational age <37 weeks, feeding method, and primiparity. Finally, in our analysis, we did not find an association between South Asian race or ethnicity and risk of readmission.

The ways in which Asian race has been defined in regards to jaundice have been varied and evolving. The 2004 American Academy of Pediatrics guidelines state that East Asian race is a risk factor for the development of hyperbilirubinemia but does not specify what this term includes or excludes.[5] Although authors of recent studies have taken more comprehensive approaches,[9–13] numerous studies still use "Asian" as a risk factor for the development of newborn hyperbilirubinemia.[14–21]

Differences in the risk of hyperbilirubinemia likely relate to the distribution of gene polymorphisms that are associated with hyperbilirubinemia. For example, mutations of the *UGT1A1* gene have been shown to be linked to an increased risk of neonatal hyperbilirubinemia in Asian populations, as compared with white populations.[22,23] In the absence of genetic testing, race or ethnicity is likely a rough approximation of the likelihood of these genetic variations related to hyperbilirubinemia.

The strength of our analysis is that we rely on parent report of their child's perceived ethnicity. However, there were some limitations. First, there were small sample sizes within race or ethnicity subgroups. As a result, we consolidated parent-reported race or ethnicity into larger groups. The small sample size for these less-frequently described ethnicities (eg, Samoan, Native American) led to low power, and we may have been unable to identify more specific groups at risk. Second, our study was limited to only 1 hospital, and the results may not be generalizable to other settings. Additionally, because data were abstracted from only 1 hospital system, it is possible that we were not able to identify some babies who were born at our institution but were readmitted into another hospital system.

Notwithstanding these limitations, there are some important clinical implications. We found that infants with specific Far East Asian or Southeast Asian races or ethnicities are at higher risk for readmission for jaundice. Furthermore, we also provided a list of specific races and ethnicities (Fig 1) associated with each of these categories. As a result, clinicians can use a more specific and patient-centric method for identifying those infants at risk for hyperbilirubinemia readmission. This approach is more specific and can help clinicians identify those infants who may benefit from close follow-up, nurse home visits, or increased lactation and feeding support to avoid jaundice readmission.

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Hospital Pediatrics 2018;8;269
DOI: 10.1542/hpeds.2017-0234 originally published online April 4, 2018;

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