

Is Pacific Race a Retinopathy of Prematurity Risk Factor?

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Background: Black race affords some protection from retinopathy of prematurity (ROP), but more ROP was previously found in another darkly pigmented race, the Alaskan natives.

Design: From fall 1989 through summer 2003, all Alaskan infants with a birth weight of 1500 g or less were examined, documenting mother's stated race, prenatal care, and neonatal intensive care unit course.

Results: Retinopathy of prematurity was classified as to predefined threshold for peripheral ablative treatment (region of avascular retina and fibrovascular ridge and vessel tortuosity) in 873 infants. Threshold ROP was more prevalent in Alaskan natives (24.9%) and Asians (15.9%) (10% overall), with no significant difference between Alaskan natives and Asians ($P = .24$). Alaskan native males had

more threshold ROP (69%) compared with non-Alaskan native males (51%). Compared with threshold nonnatives, Alaskan native threshold infants had greater birth weights (829 ± 222 vs 704 ± 186 g), required less time on ventilation (46 ± 22 vs 70 ± 75 days), and progressed to treatment at a younger age (35.5 ± 2.2 vs 36.2 ± 2.6 weeks' gestational age) (data are given as mean \pm SD).

Conclusions: In this limited study, we find increased risk of threshold ROP in 2 northern Pacific races. Threshold Alaskan natives had similar or better prenatal and neonatal intensive care unit variables than did threshold nonnatives; however, Alaskan native males were still at a greater risk.

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RETINOPATHY OF PREMATURITY (ROP), despite improvements in neonatal intensive care unit (NICU) care and survival, remains a major cause of childhood blindness. Race is a risk factor for threshold ROP. The Multicenter Trial of Cryotherapy for Retinopathy of Prematurity found a threshold rate of 7.5% for white and 3.2% for black persons.¹ Latin American persons may have more ROP than white persons.² Although black race affords some protection from threshold ROP,³⁻⁶ a higher preponderance of ROP in another darkly pigmented race, the Alaskan natives, was previously noted.⁷ We sought to determine if this trend persisted and was predictive of ROP severity in Alaska.

METHODS

From September 1989 through July 2003, all infants with birth weights of less than 1500 g, receiving care at Alaska's levels 3 and 2 NICUs in Anchorage, underwent serial ophthalmic and retinal examinations to diagnose and/or treat

ROP by one of us (R.W.A.). This observational study received approval from the Institutional Review Board of Providence Hospital, Anchorage. We prospectively recorded birth date, mother's stated race,⁸ birth weight, gestational age, severity of intraventricular hemorrhage, date of extubation, prenatal care, birth location, maternal substance use, and details related to either cryotherapy or diode laser therapy. The threshold for ROP treatment was defined by the Multicenter Trial of Cryotherapy for Retinopathy of Prematurity¹; the region of immature avascular retina (zone), the degree of fibrovascular ridge (stage), and the level of retinal vascular tortuosity from abnormal arteriovenous shunting (Plus disease) were carefully documented. These observations preceded recent 2003 NICU adaptation of decreased early oxygen saturation⁹ and the adoption of modified ROP threshold criteria.¹⁰

The variables were compared using statistical software (JMP 5.01a; SAS Institute Inc, Cary, NC) using the χ^2 test, an unpaired t test, and an analysis of variance.

RESULTS

Retinopathy of prematurity was classified as to the presence or absence of thresh-

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Table 1. Distribution of Alaskan Infants With Threshold ROP Divided by Race*

Race	Do Not Have Threshold ROP	Have Threshold ROP	Total
Black	103	5	108
White	401	27	428
Latin American	31	2	33
Alaskan native	148	49	197
Asian	37	7	44
Other†	63	0	63
Total	783	90	873

Abbreviation: ROP, retinopathy of prematurity.

*Data are given as number of infants in each group.

†Infants for whom race was not easily discerned because of mixed parents and lack of both parents available for reporting.

old in 873 infants (**Table 1**). Threshold ROP was more common in the Alaskan native and the Asian Pacific races ($\chi^2_{810,4}=48, P<.001$). There was no significant difference in threshold ROP rate between Alaskan natives and Asians ($P=.24$). The sex of the infant was not predictive of progression to threshold for any race, except that Alaskan native males were more likely to progress to threshold ROP ($\chi^2_{197,1}=7.8, P=.005$). Comorbid prenatal and NICU variables were collated by race (**Table 2**). Compared with nonnatives who progressed to threshold ROP (41 of 676), Alaskan native threshold infants had greater birth weights ($t=2.9, P=.005$), required less time on ventilation ($F_{81,4}=4.2, P=.004$), and were younger at age of treatment ($F_{89,4}=3.7, P=.008$). For the infants requiring peripheral ablative therapy for threshold ROP, 3 of 41 nonnatives and 7 of 49 Alaskan natives had adverse retinal outcomes (ie, progression to stage 4-5 ROP).

COMMENT

Race continues to convey differential risk for progression to threshold ROP. We confirmed a protective effect for blacks and an exacerbating effect for Alaskan natives. Alaskan natives who progressed to threshold ROP had similar or better prenatal and NICU variables than their nonnative counterparts, but Alaskan native males fared worse. Because of a concerted maternal transport effort, most premature Alaskan natives are born adjacent to the level 3 NICU. Since the publication of a previous report,⁷ we also noted an increased risk for threshold ROP in Asian infants. We wonder if pooled data from US NICUs with more Asian infants would confirm these findings.

This study is limited by relatively few infants from a single center. Staging and treating ROP in Alaska's single level 3 NICU has primarily been done by only one clinician (R.W.A.). Our rate of progression to threshold ROP for nonnatives is similar to that from multicenter trials.^{10,11} This study also preceded NICU efforts to stringently avoid initial hyperoxia⁹ and adoption of revised threshold criteria.¹⁰

Why is race an important factor in ROP progression? The consistently increased risk of threshold ROP in Alaskan natives and this new observation of high ROP rates

Table 2. Prenatal and NICU Variables for Infants Who Progressed to Threshold ROP*

Comorbid Variable	Non-Alaskan Native	Alaskan Native
Birth weight, g	704 ± 186 (497-983)	829 ± 222 (591-1140)
Gestational age, wk	24.8 ± 1.6 (23-27)	25.2 ± 2.0 (23-28)
Male sex†	51.2	69.4
Age at treatment, wk	36.2 ± 2.6 (33.5-40.1)	35.5 ± 2.2 (32.7-38.7)
Interval to treatment, d	80 ± 8 (66-101)	72 ± 12 (54-91)
Time on ventilation, d	70 ± 75 (30-109)	46 ± 22 (16-78)
Intraventricular hemorrhage grade	1.0 ± 1.5	1.1 ± 1.4
Apgar score, min		
1	2.7 ± 1.7	3.5 ± 1.9
5	5.9 ± 1.4	6.3 ± 1.6
Outborn†	14.6	22.4
Lack prenatal care†	17.1	30.6

Abbreviations: NICU, neonatal intensive care unit; ROP, retinopathy of prematurity.

*Data are given as mean ± SD (10th-90th percentile) unless otherwise indicated. Outborn indicates born at another facility.

†Data are given as percentage of infants.

in our Asian infants may be related to ancestry across the Bering Land Bridge.¹² As a follow-up to an initial report,⁷ we were not able to ascribe a dietary influence related to ω-3 fatty acids and fish. In animal models of ROP, there is a differential propensity for ROP even in different strains and different retinal pigment levels of rats.^{13,14} We hope that a better understanding of risk factors and genetic markers might provide an answer that would be of benefit for infants at risk for ROP worldwide.¹⁵

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Correction

Errors in Tables. In the article “Associations of Body Mass Index and Perceived Weight With Suicide Ideation and Suicide Attempts Among US High School Students” by Eaton et al published in the June issue of the ARCHIVES (2005;159:513-519), 2 rows of data in the “Perceived Weight” section of Table 1 should have been deleted. The

corrected section of Table 1 is given in the tabulation below. Also, the subheadings for the “BMI Category” section in Tables 1, 2, 4, and 5 should have read as follows: Underweight, At Risk for Underweight, Normal Weight, At Risk for Overweight, and Overweight.

Table 1. Prevalence and Crude Odds Ratios (ORs) for Body Mass Index (BMI) Category, Perceived Weight, Suicide Ideation, and Suicide Attempt by Sex and Race/Ethnicity Among US High School Students—Youth Risk Behavior Survey, 2001¹⁷

Perceived Weight	Very Underweight		Slightly Underweight		About Right		Slightly Overweight		Very Overweight	
Sex										
Male	2.6	1.00 (Referent)	16.0	1.00 (Referent)	58.1	1.00 (Referent)	20.0	1.00 (Referent)	3.2	1.00 (Referent)
Female	1.7	0.66 (0.51-0.87)	10.7	0.63 (0.54-0.73)	52.6	0.80 (0.72-0.89)	30.1	1.72 (1.57-1.87)	4.8	1.53 (1.18-1.98)
Race/Ethnicity										
White	1.8	1.00 (Referent)	13.8	1.00 (Referent)	55.3	1.00 (Referent)	25.4	1.00 (Referent)	3.8	1.00 (Referent)
Black	3.2	1.88 (1.16-3.05)	11.1	0.78 (0.66-0.93)	60.0	1.21 (1.08-1.37)	21.6	0.81 (0.71-0.92)	4.1	1.10 (0.74-1.63)
Hispanic	2.4	1.40 (1.05-1.85)	11.3	0.80 (0.67-0.96)	51.4	0.86 (0.77-0.95)	29.1	1.20 (1.06-1.36)	5.7	1.55 (1.12-2.15)