Characteristics of Infants With Severe Retinopathy of Prematurity in Countries With Low, Moderate, and High Levels of Development: Implications for Screening Programs

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ABSTRACT. *Objective.* **Retinopathy of prematurity (ROP) is a potentially avoidable cause of blindness in children. The proportion of blindness as a result of ROP varies greatly among countries depending on their level of development, being influenced by the availability of neonatal care, neonatal outcomes, and whether effective screening and treatment programs are in place. The objective of this study was to compare characteristics of premature infants who developed severe ROP between 1996 and 2002 in highly developed countries with less developed countries.**

Methods. **This was an observational study. A questionnaire was completed by ophthalmologists in countries with low, moderate, and high development rankings (3 highly developed countries and from 10 less well-developed countries) who screen for ROP in which they supplied birth weights and gestational ages (GAs) of infants who were treated for threshold ROP or identified with more advanced stages of the disease. Birth weights and GAs of infants with severe ROP were measured.**

Results. **The mean birth weights of infants from highly developed countries ranged from 737 to 763 g compared with values ranging from 903 to 1527 g in less developed countries. Mean GAs of infants from highly developed countries ranged from 25.3 to 25.6 weeks compared with 26.3 to 33.5 weeks in less developed countries. A total of 13.0% of 1091 infants from poorly developed countries exceeded United Kingdom screening criteria; 3.6% exceeded a criteria of <34 weeks' GA and/or <1750 g birth weight.**

Conclusions. **These findings suggest that larger, more mature infants are developing severe ROP in countries with low/moderate levels of development compared with highly developed countries. ROP screening programs need to use criteria that are appropriate for their local population.** *Pediatrics* **2005;115:e518–e525. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-1180;** ***retinopathy of prematurity, screening, development index.***

ABBREVIATIONS. ROP, retinopathy of prematurity; UNDP, United Nations Development Programme; HDI, Human Development Index; GA, gestational age.

Retinopathy of prematurity (ROP) is a potentially avoidable cause of blindness in children. The proportion of blindness as a result of ROP varies greatly among countries (Table 1),[1,2] being influenced both by levels of neonatal care (in terms of availability, access, and neonatal outcomes) and by the availability of effective screening and treatment programs. This raises important questions concerning strategies to reduce the incidence of blindness as a result of ROP, which should include ensuring that all infants who are at risk are examined in screening programs.

In highly developed, industrialized countries (ie, those ranked highly by the United Nations Development Programme [UNDP] on the basis of their Human Development Index [HDI]), the population of premature infants who are currently at risk for the advanced stages of ROP that requires treatment is extremely premature, with birth weights almost always <1000 g.[3,4] However, this has not always been the case: during the first epidemic of ROP, in the 1940s and 1950s, larger, more mature infants became blind from retrolental fibroplasia (the term used earlier to describe the condition). At that time, the mean birth weight of affected infants in the United Kingdom was 1370 g (range: 936–1843 g) and in the United States was 1354 g (range: 770–3421 g).[5] More premature infants generally did not survive. The population of infants who are at risk for blinding ROP, therefore, has changed over time in highly developed countries. These changes can be attributed to a better understanding of the risk factors and pathogenesis of ROP, leading to improvements in neonatal care. More conservative use of supplemental oxygen, meticulous monitoring of blood oxygen levels, and aggressive management of instability of the infant are probably the most important factors that are responsible for the lower risk in more mature infants. In many countries of Latin America and the Former Socialist Economies of Eastern Europe (ie,

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TABLE 1. Proportion of Childhood Blindness as a Result of ROP in Countries Ranked by Their UNDP HDI

Country	UNDP Rank Based on HDI in 2002	Source of Data	*N*	% ROP
Highly developed: HDI ranking 1–30[2]				
Sweden[20]	2	Register	2048	4
United States[21]	8	Blind school study; national	2553	13
Eire[22]	10	Multiple sources; national	172	11
Nordic countries[23]	1, 7, 13, 17	Register; national	2527	10
United Kingdom[24]	12	Surveillance; national	439*	3
Moderately developed: HDI ranking 31–100[2]				
Czech Republic[25]	32	Blind school study; national	229	41.9
Argentina[26]	34	Blind school study; 1 province	177	60.0
Hungary[27]	38	Blind school study; national	491	11
Chile[28]	43	Blind school study; national	267	17.6
Cuba[1]	52	Blind school study; 2 provinces	70	38.6
Bulgaria[1]	56	Blind school study; national	135	22.9
Malaysia[29]	59	Blind school study; national	332	6.0
Albania[1]	65	Blind school study; national	37	0.0
Romania[1]	69	Blind school study; national	103	2.0
Brazil[UPD]	72	Blind school study; 1 region	148	14.2
Colombia[UPD]	73	Blind school study; 2 regions	226	23.9
Thailand[1]	76	Blind school study; 2 regions	65	16.9
Kazakhstan[UPD]	78	Blind school study; national	45	4.4
Philippines[1]	83	Blind school study; 2 regions	179	8.4
Peru[UPD]	85	Blind school study; 4 cities	217	16
Paraguay[1]	89	Blind school study; national	36	33.3
China[30]	94	Blind school study; sample of schools	1131	1.9
Sri Lanka[31]	96	Blind school study; national	226	0.0
Ecuador[UPD]	100	Blind school study; national	142	14.1
Poorly developed: HDI ranking 101 and above[2]				
Uzbekistan[32]	107	Blind school study; national Blind school study; 19 regions	506	0.0
Mongolia[33]	117	Blind school study; national Blind school study; 19 regions	24	0.0
Guatemala[UPD]	121	Blind school study; national	73	4.1
India[34–36]	127	Blind school study; 10 states, Delhi	2360	0.2
Cambodia[UPD]	130	Blind school study; 1 city	24	0.0
South Africa[10]	119	Blind school study; national	564	10.6†
Ghana/Togo/Benin[1]	131	Blind school study; national	284	0.0
Pakistan[UPD]	142	Blind school study; national	760	0.0
Uganda[UPD]	146	Blind school study; sample of schools	30	0.0
Kenya[UPD]	148	Blind school study; sample of schools	77	0.0
Nigeria[1]	151	Blind school study; 1 state	210	0.5
Eritrea[1]	156	Blind school study; national	61	0.0
Malawi[1]	165	Blind school study; national	137	0.0
Ethiopia[37]	170	Blind school study; sample of schools	295	0.0

UPD indicates unpublished data held in a database at the London School of Hygiene and Tropical Medicine.
* Incident cases of blindness.
† Blindness from ROP was found only in Asian and white children and not in African children.

those that are moderately developed, with HDI rankings in the range 31–100), ROP is emerging as a major cause of blindness (Table 1). This has been referred to as the "third epidemic."[1] Indeed, it is thought that two thirds of the 50 000 children who are blind from ROP worldwide live in Latin America.[6,7] There are several possible reasons for this third epidemic: first, birth rates and rates of premature birth are higher[8,9]; second, neonatal care may be compromised as a result of lack of resources, leading to higher rates of severe ROP not only in extremely premature infants but also in larger, more mature infants; and third, because of lack of awareness, skilled personnel, and because of financial constraints, screening and treatment programs are not in place in all neonatal units in many cities. Indeed, in Lima, Peru, a city with 8 million residents, 1 of the authors (L.G.) single-handedly provides the ROP service for the whole city, and in Rio de Janeiro, Brazil, another author (A.Z.) examines infants in 7 of the largest units in the city that cater to two thirds of all premature births. In poorly developed countries (ie, those with UNDP rankings <100, which includes most of sub-Saharan Africa and much of Asia), blindness from ROP is virtually unknown. South Africa is the exception, where ROP accounts for 11% of blindness in children.[10] In the majority of other sub-Saharan African countries, services for the care of premature infants are not well developed, and preterm infants do not survive long enough to develop severe ROP.[11] Accurate delineation of the population of infants who are at risk for potentially blinding ROP is essential, providing the evidence on which to base guidelines regarding which infants need to be examined. The United Kingdom, the United States, and Canada,[4,12–16] along with several other countries, have developed evidence-based screening criteria, which continue to be reviewed as the population of infants who are at risk changes over time. Information on the population of infants who develop treatable ROP is required from less developed countries, to develop screening programs that include all premature infants who are at

TABLE 2. Sources of Information and Screening Criteria

Country	Source	Provider(s) of Neonatal Care	Year	Screening Criteria		
				Birth Weight, g	GA, wk	Other
Highly developed countries: UNDP HDI 1–30[2]						
Canada	14 units	Government	1996 and 1997	<1500	<30	Yes[22]
United States	3 units in 1 city	Government, PP	1998–2001	<1500	<32	Yes
United Kingdom	Through national surveillance	Government	12.97–03.99	<1500	<32	No
Moderately developed countries: UNDP HHDI ranking 31–100[2]						
Argentina (C)	1 unit in provincial state capital	Government	2000 and 2001	<1500	<32	Yes*
Argentina (M)	1 unit in provincial state capital	Government	2000 and 2001	<1500	<32	Yes*
Argentina (P)	1 unit in provincial state capital	Government	1999–2002	<1500	<32	Yes*
Argentina (T)	1 unit in provincial state capital	Government	2000 and 2001	<1500	<32	Yes*
Lithuania (V)	1 unit in provincial state capital	University	2000–2002	2500	35	No
Lithuania (K)	1 unit in provincial state capital	University	2001 and 2002	NA	36	Yes
Cuba	4 units in Havana	Government	1998–2001	<1700	<32	Yes
Brazil	1 unit in Rio de Janeiro	Government	2000 and 2002	<1500	<33	No†
Colombia	7 units in Bucaramanga	Mixture	1997–2001	<1500	<31	Yes‡
Peru	2 units in Lima	Government, SS	2000–2002	2000	34	Yes*
Ecuador	1 unit in Guayaquil	Charitable	1999–2002	1900	36	No
National treatment referral center						
Argentina (G)	Infants throughout the country	Mixture	1999–2002	NA	NA	NA
From national program						
Chile	27 units throughout country	Mixture	1996–1999	<1750§	<32‖	No
From low vision clinic						
Argentina (L)	1 clinic in Buenos Aires	Mixture	Born 1992–1996	NA	NA	NA
Poorly developed countries: UNDP HDI >100[2]						
Vietnam	3 units: Hanoi, Ho Chi Minh	Government	2001–2003	<1601	NA	No
India (D)	1 unit in Delhi	Government	2000	<1500	<32	Yes
India (H)	8 units	Government, PP	1999–2002	<2000	<35	
India (M)	1 neonatal unit; 1 surgical unit	Charitable	1999–2002	<2000	NA	

SS indicates Social Security; NA, not applicable; PP, private.
* Criteria: >72 hours in oxygen, prolonged ventilation, blood transfusion, hyperoxia, hypoxia, apnea, resuscitation, acidosis, and sepsis.
† Criteria changed in 2001 to 1750 g, and all who had 30 days in oxygen regardless of birth weight or GA.
‡ Criteria for infants 1500 to 1700 g: >30 days in oxygen.
§ In government sector.
‖ In private sector.
¶ Any with a stormy neonatal course and whose GA is unknown irrespective of birth weight.

risk. The purpose of this study was to describe and compare the birth weight and gestational age (GA) of infants who develop severe ROP in countries with a range of development indices to determine whether screening criteria used in highly developed countries would be applicable worldwide. We did not attempt to describe rates of severe ROP or to explore other risk factors for ROP, particularly those in relation to neonatal care. In this study, we use the term "severe ROP" to encompass infants who are treated for threshold stage 3 disease as well as those with stages 4 and 5 ROP, or cicatricial disease.

METHODS

For the purposes of this study, countries were grouped into 3 categories according to their rank for the year 2002, based on their UNDP HDI.[2] "Highly developed" countries are those ranked among the top 30 most developed countries in the world, where ROP accounts for 3% to 11% of blindness in children; countries that are ranked 31 to 100 are termed "moderately developed," and in these countries, ROP accounts for up to 60% of blindness; "poorly developed countries" are those that are ranked <100 and where blindness in children as a result of ROP is not currently a major problem.

Information on the population of infants with severe ROP was obtained via several different approaches. The following individuals were contacted: ophthalmologists who screen for ROP in Latin America and who had presented their data at workshops held annually in the region since 1997 (from Argentina, Brazil, Colombia, Ecuador, Mexico, and Peru); authors of papers describing large case series of infants who were screened for ROP in Canada[14] or large series of infants with stage 5 disease (from India[17]); individuals who have undertaken research on ROP in the United Kingdom and the United States; an ophthalmologist who runs a low vision clinic for children in Argentina; other ophthalmologists who are known to the authors and screen for ROP (in Lithuania, Vietnam, and India); the ophthalmologist responsible for the national ROP screening program in Chile; and neonatologists who manage infants who are referred to a national ROP treatment center in Argentina. All were sent a questionnaire, in which they were asked to indicate the following: (1) the city, (2) the level of neonatal care provided, (3) the health sector providing the service (eg, government, private, social security), (4) and the screening criteria used (if relevant). They were also sent a spreadsheet in which they were asked to supply the birth weight and GA of individual infants who were treated for threshold ROP, who had presented too late for treatment, who had been treated for stage 5 ROP, or who were being treated in the low vision clinic. They were asked to supply data for infants who were seen during the preceding 1 to 2 years or, in the case of published series, for the years relevant to those series. Infants who were referred to the unit just for treatment were excluded, apart from the unit in Argentina, which is the national referral unit for treatment ("Argentina G"). Information on the number of infants who were examined during the relevant time period was not requested as we were not intending to report rates of ROP, which would be difficult to interpret in light of variation in case mix, level of care, and screening criteria. Ethical approval for release of these routinely collected data was obtained, when necessary.

RESULTS

Data on the birth weight and GA of infants who were treated for threshold ROP were provided from 3 highly developed countries (262 infants) and from a range of sources in 8 moderately developed and 2 poorly developed countries (1091 infants; Table 2). All but 1 of the individuals contacted supplied the data requested. Because of the different sources, the data presented in Table 3 and in Figs 1 and 2 are for infants with threshold disease or more advanced stages. All have been included, as all infants with stage 4, 5, or cicatricial ROP would have passed through the threshold, treatable stage of disease. The data show that the mean birth weights of infants with severe ROP in highly developed countries are lower than in moderately and poorly developed countries. In the 3 highly developed countries, the mean birth weight values all were <800 g, whereas the mean values for the other countries all were >1000 g, apart from Chile and Brazil (903 and 952 g, respectively). The mean GA values of infants with severe ROP in highly developed countries all were <26 weeks, which was lower than the values for the other countries, which ranged from 26.3 weeks in Lithuania to 33.5 weeks in Ecuador. Overall, 142 (13%) of 1091 infants in this study with severe ROP from moderately and poorly developed countries had birth weights and GAs exceeding those recommended for screening by the Royal College of Ophthalmologists of the United Kingdom (ie, birth weight <1500 g and/or GA <32 weeks).[13] Only 5 (0.5%) infants had a GA of ≥37 weeks, whereas 39 (3.6%) exceeded a criterion of <34 weeks and/or <1750 g. Only 1 (0.4%) of the 262 infants who were treated for threshold disease in Canada, the United Kingdom, and the United States exceeded United Kingdom screening criteria.

DISCUSSION

This study suggests that the population of infants who develop severe ROP in highly developed countries differs from those who are affected in less well-developed countries. Given the complex interaction between case mix, neonatal care, and survival rates, as well as variation in screening practices and follow-up rates of discharged infants, this represents the best snapshot of the situation currently possible. Several limitations of this study need to be acknowledged. Different methods of assessing GA may have been used, the data come from a variety of sources (individual neonatal units, a treatment referral center; national data, a low vision clinic, and a national surgical referral center), and the data provided may not be representative of all units in the countries concerned. There are, therefore, potential sources of bias. For example, data from the treatment referral center in Argentina may have underascertained very low birth weight/GA infants who were too sick to be transferred to the regional center for treatment. Another potential source of bias relates to differences in the interpretation of the different signs of ROP by the screening ophthalmologists and inaccuracies in recording data. These limitations are almost inevitable in retrospective studies of this nature. Variation in

TABLE 3. Birth Weight and GA of Infants Reported With Severe ROP in Countries Ranked by Their HDI Between 1996 and 2002

Country and Level of Development	UNDP Rank	*N*	Birth Weight, g			GA, Wk		
			Mean	Range	SD	Mean	Range	SD
Highly developed countries with HDI ranking 1–30[2]								
Canada	4	117	759	440–1785	182	25.6	22–32	1.7
United States	8	36	763	415–1255	175	25.4	23–29	1.5
United Kingdom	12	109	737	450–1260	174	25.3	23–32	1.6
Moderately developed countries with HDI ranking 31–100[2]								
Argentina (C)	34	22	1150	620–1980	429	29.7	25–34	2.7
Argentina (G)	34	215	1199	550–2700	386	29.6	24–37	2.8
Argentina (L)*	34	12	1323	800–1940	417	29.4	26–35	2.7
Argentina (L)†	34	16	1231	820–2040	298	29.2	25–36	3.5
Argentina (M)	34	47	1051	550–1680	279	30.0	24–34	2.2
Argentina (P)	34	80	1357	650–2280	343	31.1	26–37	2.8
Argentina (T)	34	68	1527	410–3700	488	32.1	24–37	2.3
Lithuania (V)	41	67	1083	450–1920	315	28.0	24–33	2.2
Lithuania (K)	41	8	1021	732–1600	266	26.3	24–30	2.4
Chile	43	56	903	495–1550	248	26.8	24–35	2.1
Cuba	52	11	1285	990–2250	382	30.7	27–33	2.0
Brazil	72	12	952	640–1440	235	27.7	25–31	2.0
Colombia	73	59	1122	640–1900	262	29.2	25–35	2.3
Peru	85	82	1051	630–1710	241	29.1	25–34	2.2
Ecuador	100	62	1259	600–1900	309	33.5	30–36	1.6
Poorly developed countries with HDI ranking >100[2]								
Vietnam	112	26	1284	900–1600	202	29.9	27–34	1.8
India (D)	127	8	1307	767–1943	406	29.5	26–34	2.6
India (H)	127	115	1255	710–2000	280	29.6	26–36	2.1
India (M)‡	127	125	1167	600–2060	303	28.7	24–34	2.0

* Children who had low vision and had been treated as infants.
† Children who had low vision and had not been treated as infants.
‡ Includes infants who were screened locally and infants who were referred with stage 4 or 5 ROP from India and neighboring countries.

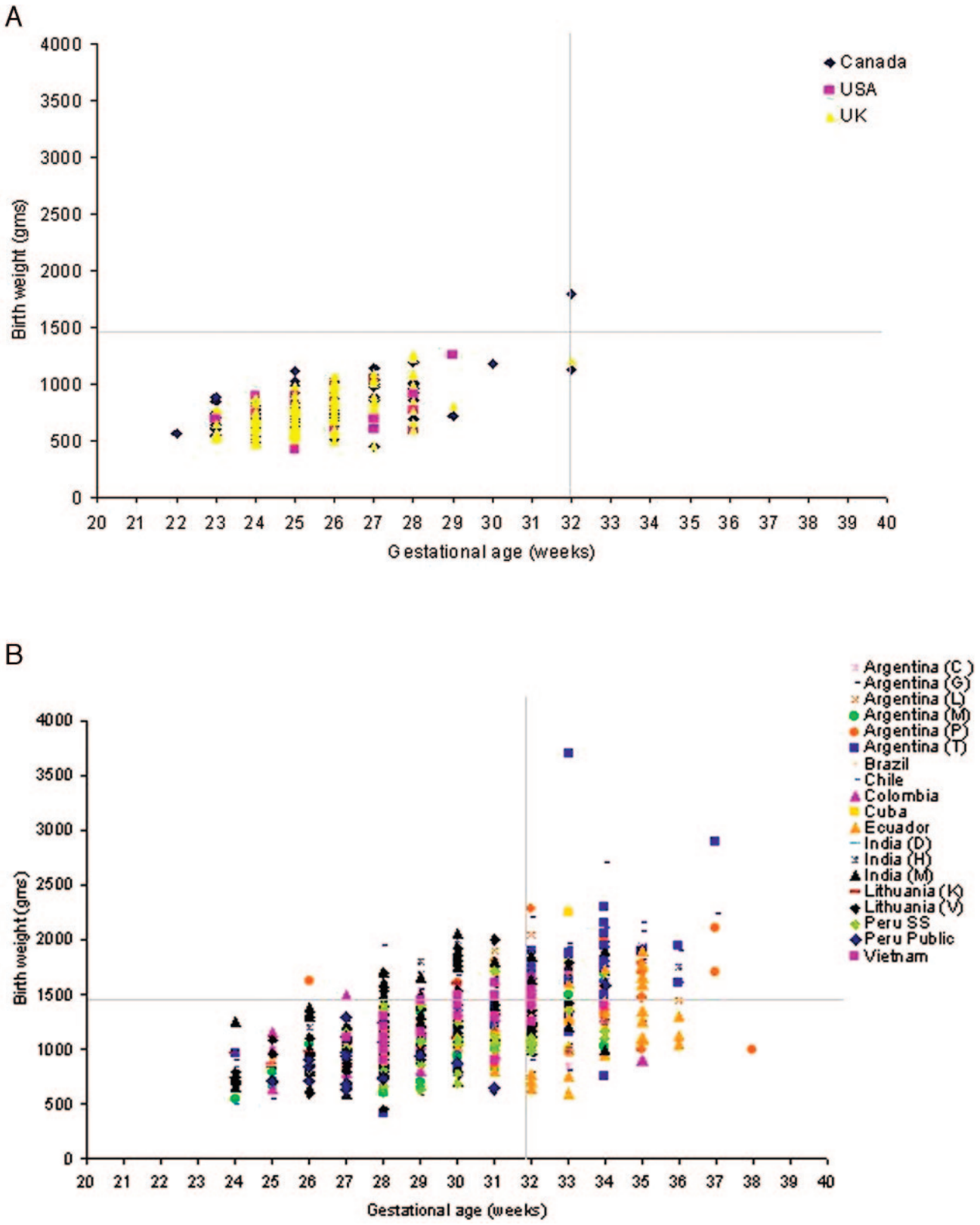

Fig 1. A, Birth weight and GA of infants reported with threshold disease from countries with high UNDP HDIs between 1996 and 2002. B, Birth weight and GA of infants reported with severe ROP from countries with low/middle HDIs between 1996 and 2002. The horizontal line indicates the boundaries of the United Kingdom screening data.

screening criteria may also explain the findings: some ophthalmologists in countries with moderate and poor levels of development follow the US guidelines, some follow the United Kingdom guidelines, and some have generated their own. One explanation for the "highly developed country" picture of some units in moderately developed countries (eg, Brazil) is that larger, more mature infants were not

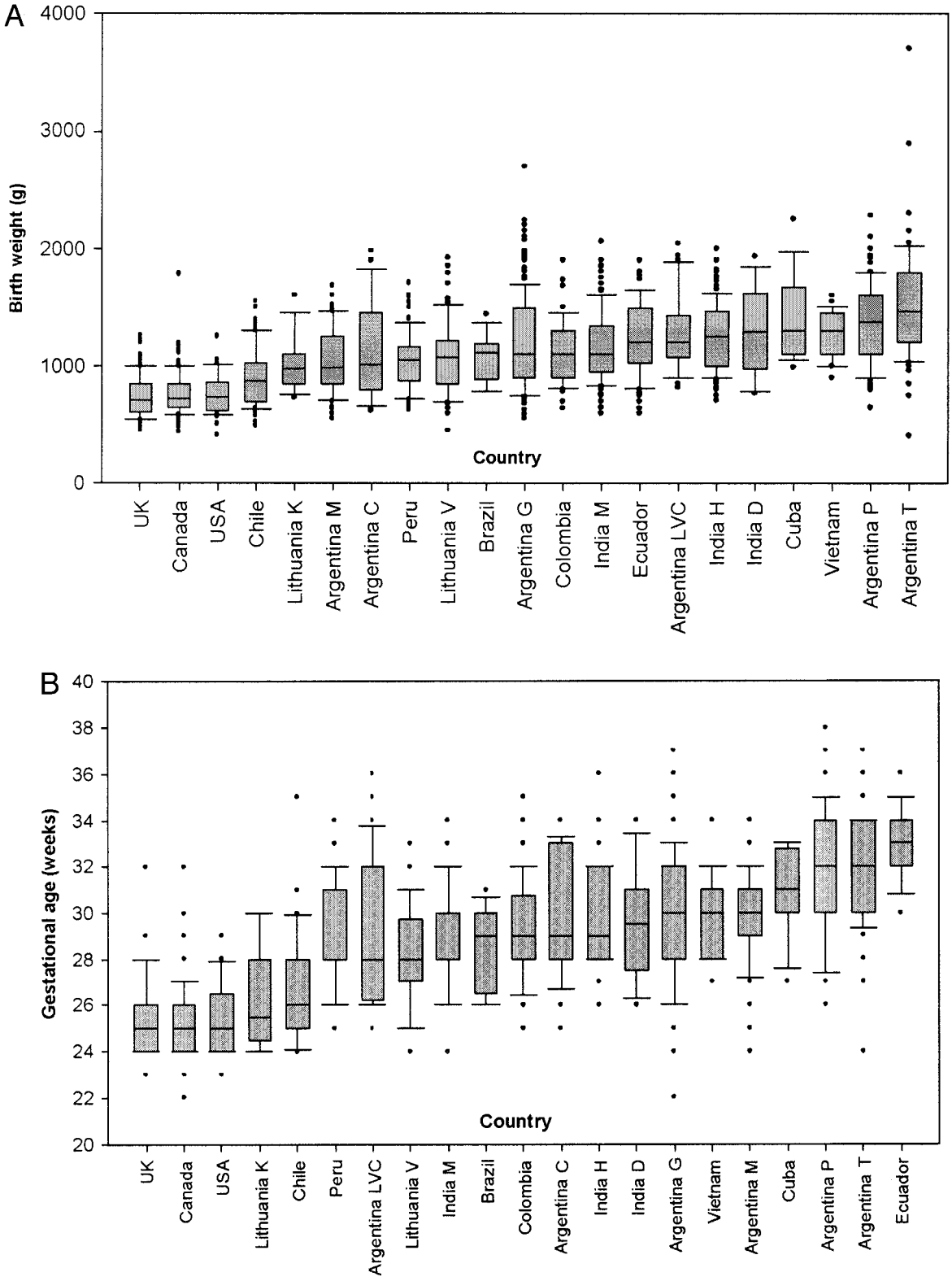

Fig 2. A, Box plots of birth weights of infants reported with severe ROP from 13 countries with varying levels of development. B, Box plots of GAs of infants reported with severe ROP from 13 countries with varying levels of development.

included in the screening program. However, it seems more likely that this reflects the excellent care that some infants are receiving. Variation in case mix may explain, in part, the findings but would not explain why larger, more mature infants are developing severe ROP. The implications of these findings are that screening guidelines developed in highly developed countries will not suit all situations. The finding that bigger, more mature infants are developing threshold ROP in less developed countries or present too late for treatment has led some ophthalmologists in Latin America to widen their inclusion

criteria for diagnostic screening. Some now examine infants with birth weights <2000 g and/or GA <37 weeks, and in Argentina, risk factor criteria have been expanded to include blood transfusion with adult blood, sepsis, or >36 hours in oxygen. In Ecuador, the ROP screening program started in 1994, and initially only infants with birth weights <1500 g were examined. The criteria were changed the following year to <1901 and/or <37 weeks because several unexamined infants with birth weights >1500 g presented with inoperable stage 5 ROP. Since adopting the wider criteria, no infant has become blind from ROP because of screening failure. A recent publication from Bangkok, Thailand, supports the findings of our study: the authors suggested region-specific criteria of <1500 g or <33 weeks' GA, emphasizing that these need to be evaluated and revised if necessary.[18]

The current picture of the infants who are affected by severe ROP in moderately and poorly developed countries seems to suggest a mixture of "first epidemic" risk factors (inadequately monitored oxygen) and the "second epidemic" risk factors (extreme prematurity), reflecting variation in levels of neonatal care. In this study, we did not attempt to address issues of variation in neonatal care in detail, but policies, practices, and levels of training and expertise do vary between countries and service providers. For example, in the unit in Brazil, all infants who receive oxygen are monitored, whereas in the unit in Peru, only ventilated infants who receive oxygen are being monitored. There is, therefore, an urgent need to monitor oxygen saturation levels in all infants who receive supplemental oxygen where this is currently not being done. Although this will not prevent all severe ROP, it will reduce its incidence, particularly in larger, more mature infants, as has happened in North America and Western Europe. From the ophthalmic perspective, there is a need to train and equip ophthalmologists to work with neonatologists and nurses so that comprehensive screening programs can be established in all units that admit high-risk infants, using local protocols developed from national guidelines. Establishing these services will not be straightforward, particularly in Latin America, where neonatal care is provided by a range of different service providers (government, private, charities, and through insurance schemes).

To provide the evidence on which to base decisions regarding appropriate screening criteria, standardize, prospective studies are needed to (1) identify the population of infants at risk and (2) determine whether the screening criteria need to vary according to case mix, levels of care, or neonatal outcomes. These issues are currently being explored in a prospective study in Rio de Janeiro, Brazil (principal investigators C.G. and A.Z.). If a single criterion of <37 weeks' GA were applied to the data presented in this article, then only a few infants with severe ROP would have been missed. However, increasing the GA criterion would significantly increase the number of infants who need examination, which may not be justifiable for the marginal gain. However, studies from the United Kingdom show that more mature infants need fewer examinations, and the majority of infants with GA >32 weeks are likely to need only 1 examination.[19] Broadening the criterion, therefore, may not increase the workload as much as might be anticipated. Another issue is that more mature infants are likely to be discharged before the first examination, making implementation of a screening program challenging. Ideally, decisions about appropriate screening criteria, as well as the timing of examinations, should be based on locally available data. Until those criteria are established, it is advisable for those who undertake screening to err on the side of caution and use wide screening criteria and not rely on published criteria from highly developed countries. The implications of this study are that communities with relatively sparse health resources have the greatest ROP screening workload. As this situation is likely to continue for the foreseeable future, innovative methods of screening, perhaps using nonmedical personnel, need to be explored.

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REFERENCES

1. Gilbert C, Rahi J, Eckstein M, O'Sullivan J, Foster A. Retinopathy of prematurity in middle-income countries. *Lancet*. 1997;350:12–14
2. United Nations Development Programme (UNDP). *Human Development Report, 2004*. Oxford, United Kingdom: Oxford University Press; 2004
3. Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol*. 2003;121:1684–1694
4. Reynolds JD, Dobson V, Quinn GE, et al, CRYO-ROP and LIGHT-ROP Cooperative Study Groups. Evidence-based screening criteria for retinopathy of prematurity: natural history data from the CRYO-ROP and LIGHT-ROP studies. *Arch Ophthalmol*. 2002;120:1470–1476
5. King M. Retrolental fibroplasia. *Arch Ophthalmol*. 1950;43:695–709
6. World Health Organization. *Preventing Blindness in Children: Report of WHO/IAPB Scientific Meeting (WHO/PBL/00.77)*. Geneva, Switzerland: World Health Organization; 2000
7. Gilbert CE, Foster A. Childhood blindness in the context of VISION 2020—the Right to Sight. *Bull WHO*. 2001;79:227–232
8. UNICEF. *State of the World's Children 2003*. New York, NY: UNICEF; 2003
9. World Health Organization. *Maternal Health and Safe Motherhood. Low Birth Weight: a Tabulation of Available Data. WHO/MCH/92.2*. Geneva, Switzerland: World Health Organization; 1992
10. O'Sullivan J, Gilbert C, Foster A. The causes of childhood blindness in South Africa. *S Afr Med J*. 1997;87:1691–1695
11. Baiyeroju-Agbeja AM, Omokhodion SI. Screening for retinopathy of prematurity in Idadan. *Nigerian J Ophthalmol*. 1998;6:23–25
12. American Academy of Pediatrics, American Association for Pediatric Ophthalmology and Strabismus, American Academy of Ophthalmology. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*. 2001;108:809–811
13. Report of a Joint Working Party of the Royal College of Ophthalmologists and British Association of Perinatal Medicine. Retinopathy of prematurity: guidelines for screening and treatment. *Early Hum Dev*. 1996;46:239–258

14. Lee SK, Normand C, McMillan D, et al. Evidence for changing guidelines for routine screening for retinopathy of prematurity. *Arch Pediatr Adolesc Med.* 2001;155:387–395
15. Wright K, Anderson ME, Walker E, et al. Should fewer premature infants be screened for retinopathy of prematurity in the managed care era? *Pediatrics.* 1998;102:31–34
16. Goble RR, Jones HS, Fielder AR. Are we screening too many babies for retinopathy of prematurity? *Eye.* 1997;11:509–514
17. Gopal L, Sharam T, Shanmugan MP, et al. Surgery for stage 5 retinopathy of prematurity: the learning curve and evolving technique. *Ind J Ophthalmol.* 2000;48:101–106
18. Trinavarat A, Atchaneeyasakul LO, Udompunturak S. Applicability of American and British criteria for screening of the retinopathy of prematurity in Thailand. *Jpn J Ophthalmol.* 2004;48:50–53
19. Brennan R, Gnanaraj L, Cottrell DG. Retinopathy of prematurity in practice. 1: screening for threshold disease. *Eye.* 2003;17:183–188
20. Blohme J, Bengtsson-Stigmar E, Tornqvist K. Visually impaired Swedish children. Longitudinal comparisons 1980–1999. *Acta Ophthalmol Scand.* 2000;78:416–420
21. Steinkuller PG, Du L, Gilbert C, Foster A, Collins ML, Coats D. Childhood blindness. *J AAPOS.* 1999;3:26–32
22. Goggin M, O'Keefe M. Childhood blindness in the Republic of Ireland: a national survey. *Br J Ophthalmol.* 1991;75:425–429
23. Rosenberg T, Flage T, Hansen E, Rudanko S-L, Viggosson G, Risse R. Visual impairment in Nordic children. II. *Aetiological factors. Acta Ophthalmol.* 1992;70:155–164
24. Rahi JS, Cable N; British Childhood Visual Impairment Study Group. Severe visual impairment and blindness in children in the UK. *Lancet.* 2003;362:359–365
25. Kocur I, Kuchynka P, Rodny S, Barakova D, Schwartz E. Causes of severe visual impairment and blindness in children attending schools for the visually handicapped in the Czech Republic Br. *J Ophthalmol.* 2001;85:1149–1152
26. Arrazola M. Retinopathy of Prematurity in Argentina. Master's Thesis. London, United Kingdom: International Centre for Eye Health, Institute of Ophthalmology; 1997
27. Czeizel A, Torzs E, Diaz LG, Kovacs J, Szabo G, Vitez M. An aetiological study on 6 to 14 years old children with severe visual handicap in Hungary. *Acta Pediatr Hung.* 1991;31:365–377
28. Gilbert CE, Canovas R, Kocksch R, Foster A. Causes of blindness and severe visual impairment in children in Chile. *Dev Med Child Neurol.* 1994;36:326–334
29. Reddy SC, Tan BC. Causes of childhood blindness in Malaysia: results from a national study of blind school students. *Int Ophthalmol.* 2001;24:53–59
30. Hornby SJ, Xiao Y, Gilbert CE, et al. The causes of childhood blindness in the People's Republic of China: results from 1131 blind school students in 18 Provinces. *Br J Ophthalmol.* 1999;83:929–932
31. Eckstein MB, Foster A, Gilbert C. Causes of childhood blindness in Sri Lanka. *Br J Ophthalmol.* 1995;79:633–636
32. Rogers NK, Gilbert CE, Zakhidov BO, McCollum CJ, Foster A. Childhood blindness in Uzbekistan. *Eye.* 1999;13:65–70
33. Bulgan T, Gilbert C. Prevalence and causes of severe visual impairment and blindness in children in Mongolia. *Ophthalmol Epidemiol.* 2002;9:271–281
34. Hornby SJ, Adolph S, Gothwal VK, Gilbert CE, Dandona L, Foster A. Evaluation of children in six schools for the blind in Andhra Pradesh. *Ind J Ophthalmol.* 2000;48:195–200
35. Rahi J, Sripathi S, Gilbert CE, Foster A. Childhood blindness in India: causes in 1,318 blind school students in 9 states. *Eye.* 1995;9:545–550
36. Jeewan ST, Pal N, Murthy GVS, et al. Causes and temporal trends of blindness and severe visual impairment in children in schools for the blind in North India. *Br J Ophthalmol.* 2003;87:941–945
37. Kello AB, Gilbert CE. Causes of severe visual impairment and blindness in children in schools for the blind in Ethiopia. *Br J Ophthalmol.* 2003;87:526–530

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