Current management of retinopathy of prematurity in sub-Saharan Africa

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PURPOSE To survey current oxygen management, screening criteria, and methods for treating retinopathy of prematurity (ROP) in sub-Saharan Africa.

METHODS An online survey was sent to ophthalmologists and neonatologists practicing in sub-Saharan Africa.

RESULTS Ophthalmologists and neonatologists from 15 of 49 countries (31%) in sub-Saharan Africa responded. Neonatologists reported treating a median of 15 infants with supplemental oxygen per week but only had a median of 3.5 oxygen-measuring devices and a median of zero oxygen blenders in their units. Ophthalmologists reported screening a median of 5 infants per week for ROP and treating 2 infants each month for ROP. Most ophthalmologists (24/27 [89%]) had access to anti-vascular endothelial growth factor drugs to treat ROP, but only 13 of 27 (48%) had access to a laser.

CONCLUSIONS Survey results reveal an urgent need for additional oxygen- management equipment in hospitals in sub-Saharan Africa. (J AAPOS 2020;24:151.e1-6)

Recent advances in neonatal intensive care and treatments for retinopathy of prematurity (ROP) have dramatically reduced the incidence of blindness from ROP in high-income countries.[1] These advancements include regulation of oxygen levels, fluorescein angiography, laser photocoagulation, intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF), and telemedicine.[2-4] In low- and middle-income countries, however, the trend is toward a rising incidence of treatment-requiring ROP,[1] as the survival rate for premature infants improves. Many of these countries lack the infrastructure and equipment necessary to properly screen for and effectively treat ROP.[5] This is particularly a problem in sub-Saharan Africa, where it has been estimated there are 31 million births annually, of which 4 million are preterm.[6] The purpose of the current study was to report the results of a survey of neonatologists and ophthalmologists in sub-Saharan Africa to better understand the magnitude of this problem.

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Subjects and Methods

The Stanford University Institutional Review Board exempted this study from approval. On September 3-4, 2018, the International Pediatric Ophthalmology and Strabismus Council (IPOSC) held a symposium in Cape Town, South Africa, to develop strategies and models to enhance research, education, and clinical care for ROP in sub-Saharan Africa. After the symposium, an online survey was developed by a task force consisting of interested members of the IPOSC (Africa ROP Task Force) for neonatologists/pediatricians and ophthalmologists practicing in sub-Saharan Africa to gather information about the prevalence and current management of ROP. Unique surveys were developed for neonatologists (19 questions) and ophthalmologists (15 questions). See eSupplements 1 and 2, available at jaapos.org. The questions were not field tested. The surveys were initially sent to the neonatologists and ophthalmologists who attended the 2018 symposium and practice in sub-Saharan Africa. They were then sent to personal contacts of the authors that practice ophthalmology or neonatology in sub-Saharan Africa, secondary referrals from these contacts, and to medical school deans in sub-Saharan Africa that had publicly accessible websites. There was no preference for any region and no differentiation by type of center. An email directory was created for these contacts. A total of 173 doctors were sent surveys. If no response was received, the survey was resent.

Each contact received an email from the IPOSC with an introduction describing our overall goals and an invitation to complete the online survey. The surveys were created using the website SurveyGizmo and were accessible through a hyperlink. They were only available in English. Reminder emails (median, 3; range, 1-6) were sent to all contacts between May 9, 2019, and August 5, 2019, or until they had completed the survey.

If a respondent did not answer a question in the survey, it was listed as unstated. If a specific response was an outlier presumably due to a data entry error, attempts were made to contact the respondent to verify the response. If no confirmation was received, these responses were not included in the analyses.

Results

Neonatologists/Pediatricians

The survey was completed by 28 of 97 (29%) neonatologists from 8 of 49 (16%) countries in sub-Saharan Africa (Figure 1). The location of all sites (either a neonatologist or ophthalmologist) responding to our survey are shown in Figure 2. We received only 1 of 21 responses (5%) from neonatologists practicing in French-speaking countries in sub-Saharan Africa. One-half of the responses (14/28) were from neonatologists/pediatricians practicing in Nigeria.

The median number of beds or incubators in each unit was 32, with a median of 30 patients treated each week (Table 1). A median of 15 infants were on supplemental oxygen each week, with a median of zero oxygen blenders and a median of 3.5 oxygen measurement instruments (eg, pulse oximetry, blood gas determination, or transcutaneous measurements). Twenty-two neonatal units with ≤2 oxygen blenders were subsequently queried about in-wall air and oxygen lines. Thirteen of the 16 respondents (81%) indicated that they did not have in-wall air and oxygen lines, precluding the use of oxygen blenders. The median number of infants requiring ROP treatment each month was one.

Of the 28 respondents, 27 (96%) reported they had at least 1 oxygen measurement device in their unit. Only 1 (4%) had enough oxygen measurement devices for all beds in their unit; 22 (75%) reported that they had oxygen measurement devices for <25% of the beds in their unit. Eighteen (64%) reported zero oxygen blenders in their unit.

One neonatologist did not state whether ROP screening criteria were being used. Of the 27 neonatologists who reported information on screening criteria, 4 (15%) did not have clearly established criteria or have not started to screen for ROP. Two (7%) reported that they recommended screening any infant receiving supplemental oxygen. Two (7%) stated that they recommended screening all premature infants. Nineteen (70%) reported that they relied on gestational age and birth weight to determine which infants to screen. These ages ranged from <32 to <37 weeks (median, <32 weeks), and birthweight ranged from <1000 g to <2000 g (median, <1500 g). See Table 2.

Ophthalmologists

We received responses from 34 of 76 (45%) ophthalmologists. The ophthalmologists practiced in 14 of 49 (29%) countries (Figure 1). Ophthalmologists from 4 of 21 (19%) French-speaking countries in sub-Saharan Africa responded to the survey. A large proportion (15/34) of the

FIG 1. Map of sub-Saharan Africa showing the countries that had at least one neonatologist or ophthalmologist complete our survey.

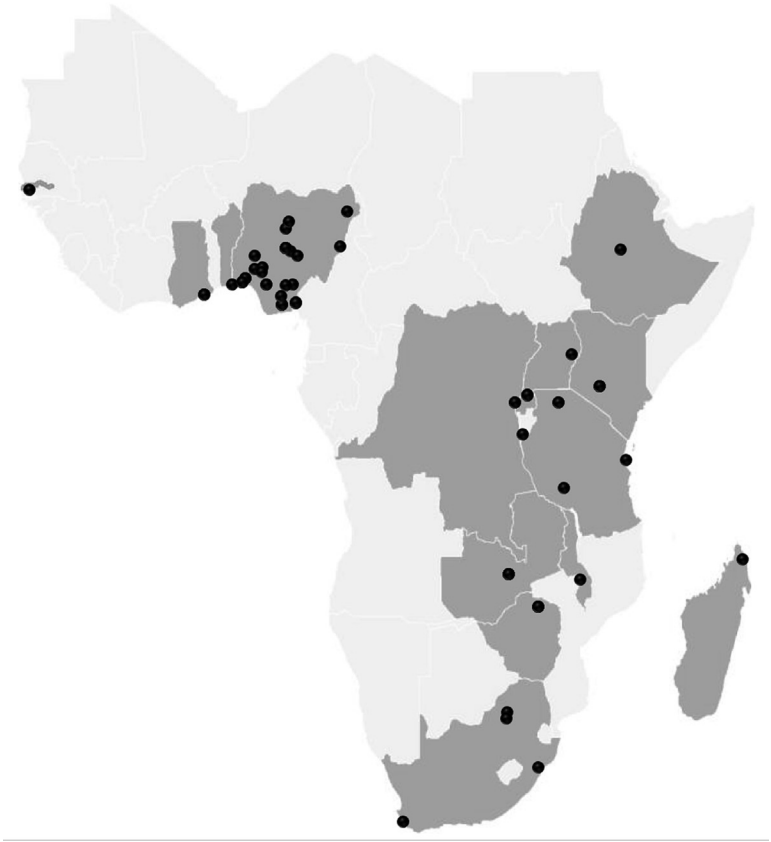

FIG 2. Map of sub-Saharan Africa showing the location of the clinical sites (circle) that responded to our survey. The countries in which the clinical sites are located that responded to our survey are also shaded.

total responses were from ophthalmologists practicing in Nigeria. Ophthalmologists reported screening a median of 4.5 infants once per week, and a median of 2 infants required treatment each month (Table 3).

Information on ROP screening criteria was provided by 30 of 34 ophthalmologists (88%). Of the 30, 27 (90%) screened for ROP. Nine (30%) had regional or national guidelines. Nearly all ophthalmologists that screened for ROP reported screening based on gestational age and birth weight (26/27 [96%]). The gestational ages meeting the criterion for screening ranged from <32 to <37 weeks (median, <34 weeks), and birthweights ranged from <1500 g to <2500 g (median, <2000 g). See Table 2. One ophthalmologist reported screening every premature infant receiving supplemental oxygen regardless of gestational age or birthweight. Three ophthalmologists (10%) reported that their hospital either did not participate in ROP screening or did not have screening criteria. Of the 34, 7 (21%) did not specify the treatment criteria used for ROP. For the ophthalmologists who reported treatment criteria, 19 of 27 (70%) based their treatment on whether or not the infant had type 1 ROP.

Seven ophthalmologists (21%) did not state which treatment method was used at their hospital. Of the 27 ophthalmologists who did report on treatment, 10 (37%) employed laser photocoagulation; 20 (74%), intravitreal anti-VEGF injections. Only 13 (48%) reported having access to a laser, whereas 24 (89%) reported access to anti-VEGF drugs. They reported that a median of 2 infants treated at their centers experienced severe vision loss due to ROP during the previous year.

Table 1. Reponses from neonatologists

Survey question	Median	Max	Min	IQR
No. incubators/beds in your unit	32	150	10	40
No. infants per incubator/bed	1	2	0	0
No. oxygen measurement instruments	3.5	70	0	7.75
No. oxygen blenders	0	50	0	2
No. patients per week	30	300	2	33
Infants on supplemental oxygen per week	15	100	4	28.25
Infants requiring ROP screening per week	7	25	0	8
Infants requiring ROP treatment per month	1	30	0	2
Estimated no. babies who had severe vision loss in last year	0	50	0	2

IQR, interquartile range.

Discussion

ROP screening criteria have been established in almost every unit that responded to our survey. Although some

Table 2. Sub-Saharan countries responding to survey

		ROP screening criteria				ROP treatment method				
Country	No. respondents	GA Median, weeks	Weight Median, g	Participates in telemedicine	ROP treatment criteria	Laser treatment only	Anti-VEGF treatment only	Both treatment methods	No treatment offered	Unstated
Benin	1	<37	Unstated	No	None	0	0	0	1/1	0
Democratic Republic of the Congo	2	<35	<2000	No	Zone 3 or 4	0	2/2	0	0	0
Ethiopia	1	<34	<2500	Yes	Type I	0	0	1/1	0	0
Gambia	1	Unstated	Unstated	No	Plus disease	0	1/1	0	0	0
Ghana	3	<34.5	<1600	No	Type I	1/3	0	2/3	0	0
Kenya	3	<32	<1500	No	Type I (2) Type I or APROP (1)	0	0	3/3	0	0
Madagascar	1	Unstated	Unstated	Yes	Unstated	0	0	0	0	1/1
Malawi	1	None	None	No	None	1/1	0	0	0	0
Nigeria	29	<34	<2000	No (22) Yes (7)	Type I (10) None (2) Stage 3 (1) Leukocoria (1) Plus disease (1) Retinal detachment (1) Type I, threshold, or APROP (1) Plus disease and stage 2-5 (1) Zone 1 or 2 with demarcation line or APROP (1) Unstated (10)	0	12/29	5/29	6/29	6/29
Rwanda	2	<33.5	<1500	No (1) Yes (1)	Type I (2)	0	0	1/2	1/2	0
South Africa	4	<32	<1500	No	Type I or APROP (1) Type I (1) Stage 3 (1) Unstated (1)	0	1/4	3/4	0	0
Tanzania	4	<36	<2000	No (3) Yes (1)	None (3) Type I (1)	0	1/4	1/4	2/4	0
Uganda	1	None	None	No	Unstated	0	0	0	0	1/1
Zambia	5	None	Low BW	No (2) Yes (1) Unstated (2)	Stage 3 (1) None (1) Unstated (3)	1/5	0	0	2/5	2/5
Zimbabwe	4	<32	<1500	No (2) Yes (1) Unstated (1)	Type I (1) Severe stage 2 (1) Unstated (2)	1/4	1/4	1/4	0	1/4

BW, birth weight; *GA*, gestational age.

Table 3. Responses from ophthalmologists

Survey question	Median	Max	Min	IQR
Screenings and/or treatments per week	1	3	0	0
Infants requiring ROP screening per week	4.5	20	1	1
Infants requiring ROP treatment per month	2	40	0	1.75
Estimated no. infants who had severe vision loss in last year	2	40	0	4

IQR, interquartile range.

units have oxygen blenders and oxygen-measuring devices, the equipment they have is insufficient for the need. We also found that most ophthalmologists use treatment guidelines for ROP, and there was greater availability of anti-VEGF drugs than lasers.

One of the most immediate concerns arising from our survey is that the median number of infants receiving supplemental oxygen per unit was 15, while the median number of oxygen blenders per unit was zero (Table 1). Most premature infants in sub-Saharan Africa placed on supplemental oxygen receive unregulated oxygenation. It has been shown that high levels of supplemental oxygen lead to higher rates of morbidity, including ROP, and the most important intervention to decrease the incidence of ROP is regulating oxygen administration.[7,8] Many countries experienced an ROP epidemic prior to instituting oxygen monitoring and regulation.[9] Better oxygen delivery management could immediately reduce the morbidity for preterm infants across sub-Saharan Africa; however, most neonatal units responding to our survey lacked the in-wall oxygen and air lines required for oxygen blenders.

Aside from lack of funding and advocacy, the proliferation of local neonatal intensive care units has likely contributed to the paucity of oxygen management equipment in sub-Saharan Africa. In 2009, the "White Paper for the Transformation of the Public Health System in South Africa" advocated the decentralization of services to improve access to healthcare (http://www.doh.gov.za/docs/policy/white paper/healthsys97_01.htm). The recommendation resulted in more premature infants being treated in small, district-level centers without neonatologists and ophthalmologists trained to manage ROP.

From 1990 to 2017, the infant mortality rate in sub-Saharan Africa decreased from 46 to 28 per 1,000 births.[10] With the increased survival rate of premature babies came an increased incidence of ROP.[11] It is imperative that neonatal intensive care units in sub-Saharan Africa incorporate the regulation of oxygen and ROP screening and treatment to prevent another ROP epidemic.

Both gestational age and birth weight are used for ROP screening criteria by ophthalmologists in most of the countries we surveyed; however, specific guidelines vary widely (Table 3). The most appropriate screening criteria for units in sub-Saharan Africa will likely vary depending on their use of oxygen-regulating equipment. In the United States, there are widely accepted guidelines for ROP screening that are updated periodically as needed.[12-14] The most appropriate ROP guidelines for sub-Saharan Africa may differ from those used in the United States because of differences in how oxygen is administered.

There is marked variability in the reported number of infants treated for ROP each month at different units in sub-Saharan Africa, with a median of 2. Many neonatologists and ophthalmologists reported concern that they did not have access to the equipment needed to regulate oxygen intake for ROP treatment. A possible solution is for countries to invest in larger, centralized neonatal intensive care units. However, this would create the logistical problem of transporting infants from small units to tertiary care centers for treatment. Another possible approach would be to incorporate telemedicine into the ROP screening process. This could allow infants in smaller units to be screened more effectively.[15] Most of the units responding to our survey indicated that they did not participate in telemedicine: inconsistent access to electricity, power outages, and slow upload speeds remain barriers to telemedicine.

Treatment modalities for ROP have expanded, from cryotherapy to laser therapy to intravitreal injection of anti-VEGF drugs.[16] Although many ophthalmologists in sub-Saharan Africa indicated that they did not have access to lasers, most had access to anti-VEGF drugs. The standard of care in the United States for treating type 1 ROP in zone II is laser photocoagulation. However, the cost of acquiring a laser and its subsequent maintenance is likely prohibitive for most units in sub-Saharan Africa.[17] Despite the prevalence of anti-VEGF agents to treat ROP in sub-Saharan Africa, there are concerns about its long-term use.[18] However, anti-VEGF agents may have fewer systemic side effects when administered to babies in sub-Saharan Africa, who are generally larger than babies treated for ROP in high income countries.

Limitations to this study include a lack of responses from many sub-Saharan countries. We attempted to contact every neonatologist and ophthalmologist involved in the care of infants with ROP. Our goal was not only to survey current practice but also to lay the foundation for future interactions with these sites, with the ultimate aim of helping to reduce the incidence of blindness secondary to ROP. Because we were planning to contact these neonatologists and ophthalmologists again in the future, the survey was not anonymous, and this might have affected respondents' openness and willingness to participate. That our survey was only available in English was a major shortcoming of this study and was certainly a factor in the low response rate in francophone countries. There was also a disproportionate number of responses from Nigeria, which has a large population and a relatively more advanced medical system than many other sub-Saharan countries. Our low overall response rate of 36% may reflect the lack of discretionary time available to physicians in low-income

countries to respond to online surveys. Additionally, because many of the surveys were sent to contacts and associates of contacts that attended the IPOSC conference in South Africa, it is likely that survey responses were biased toward a more informed group of physicians. It is also likely that some of the responses we received were incorrect. For example, ophthalmologists reported that only 2 babies in their unit became blind from ROP each year. This is likely an underestimate due to the low follow-up rate after hospital discharge.

We do not know how many total units are operating and caring for premature infants at risk for ROP in sub-Saharan Africa; thus, we do not know what proportion of units we surveyed. Many of the responses we received were from ophthalmologists and neonatologists practicing in major cities. It is likely that units that did not respond to our survey would have similar, if not greater, needs.

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