Original Article

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Incidence and Screening of Retinopathy of Prematurity in Africa: A Systematic Review

Ophthalmology Section

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ABSTRACT

Introduction: Retinopathy of Prematurity (ROP) significantly contributes to the statistics of blindness among babies born prematurely. Population-based studies of the disease in Africa is scanty with many African countries lacking screening guidelines.

Aim: To review the current statistics of ROP in Africa and present a summary of the incidence as well as the disease screening criteria within Africa.

Materials and Methods: An in-depth literature search was done on various databases following the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist for systematic review protocols. Some keywords guiding the search were "ROP," "Retinopathy," and "screening." The International Prospective Register of Systematic Reviews (PROSPERO) registration (522296) was done, and databases were screened from inception up to December 2023 via African Journals Online (AJOL), Science Direct, Embase, Web of Science, Cumulated Index to Nursing and Allied Health Literature (CINAHL), PubMed, Ovid, and Medline. The inclusion criteria were English language studies about disease screening published from inception up to December 2023. Studies that did not include the number of babies screened or ROP screening criteria used, case studies, and duplicated studies were excluded. The Anatomical Quality Assessment tool (AQUA) was applied to confirm any bias and for reporting study results.

Results: A total of 15 articles were included, with sample sizes ranging from 33 to 424 participants. Two countries (Kenya and South Africa) have national screening guidelines, while for the rest of the countries in Africa, ROP is screened as per on the agreement of the ophthalmologists at each hospital.

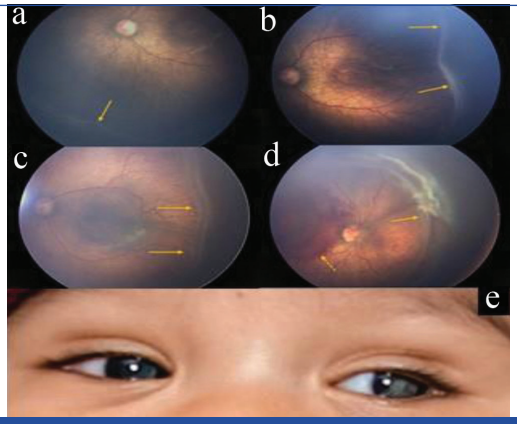
Conclusion: The present review highlights the fact that ROP is the leading cause of blindness globally, yet there is little research being done on the statistics and screening of the disease. Many countries in Africa do not have national screening guidelines for the disease, which is a great challenge.

Keywords: Birth weight, Gestational age, Prevalence, Screening guideline

INTRODUCTION

The Retinopathy of Prematurity (ROP) disease affects babies born before week 28 or weighing 1500 g [1]. Screening and treatment for the disease are conducted in many urban hospitals. However, many babies born in rural settlements are not screened, and much is not known about the statistics [2]. Retinal vessels begin to form as early as week 16, and by week 39, they are completely developed [1,2]. Babies born before term face challenges with their retinal vessels not being fully developed, and in most cases, the vessels stop growing and then rapidly start growing in the wrong direction, causing retinal traction [3].

As shown in [Table/Fig-1], ROP progression occurs in five stages. Stages one and two have mild symptoms, and sometimes babies recover without any medical support. However, when the disease reaches stage III, there is a need for diagnosis and treatment [4,5]. Stages four and five are severe and irreversible. The present seeks to summarise studies on ROP incidents in countries in Africa, focusing on disease screening, severity, and stages. This will help create awareness of the disease and assist in identifying regions where the disease is highly prevalent for establishing the necessary support.



[Table/Fig-1]: ROP stage 1 (image a), stage 2 (image b), stage 3 (image c), stage 4 (image d), stage 5 (image e),

MATERIALS AND METHODS

The protocol was registered in PROSPERO, an internationally recognised register for systematic reviews under ID-CRD42024522296, on 16 February 2024. PRISMA guidelines were adopted while conducting the review. The two key questions guiding the study were: 'What are the current ROP statistics within Africa?' and 'Which African countries have national screening guidelines for ROP disease?'

Inclusion criteria:

- Studies conducted in Africa
- Population-based studies
- Research dissertations with available data
- Studies with documented ROP screening criteria
- Studies published in English, covering the years from database inception to December 2023

Exclusion criteria:

- Studies that do not include the number of babies screened
- Studies that do not include the ROP screening criteria used
- Case reports
- Duplicated studies

Information Sources and Search Strategy

To extract the required literature, an in-depth search was done for the period between the inception of these databases and December 2023. Data were obtained from the following databases: African Journals Online (AJOL), Science Direct, Embase, Web of Science,

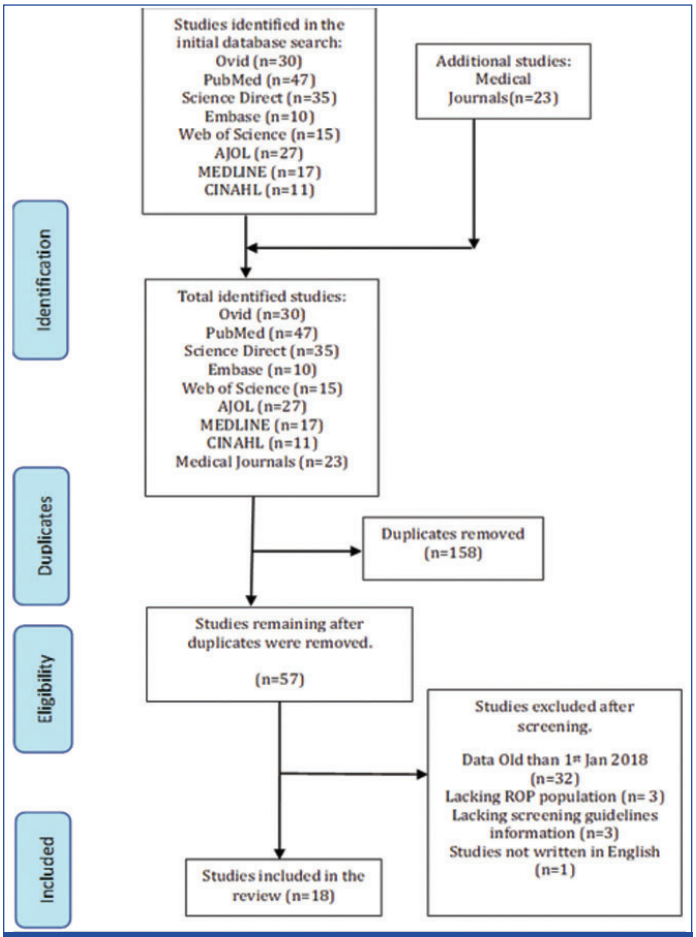
CINAHL, PubMed, Ovid, and Medline. The search terms used were: 'Retinopathy'(MESH) OR 'ROP'{Medical Subject Headings (MeSH)} OR 'retinopathy screening guidelines' {Title/Abstract (TIAB)} OR 'Birth weight'(TIAB), 'Gestational age'(TIAB), 'Preterm' (TIAB), OR 'Pathogenesis of ROP'(TIAB) OR 'ROP in Sub-Saharan Africa'(TIAB) OR 'third global pandemic'(TIAB), 'ROP statistics'(TIAB).

Assessment of Bias Across Studies

The AQUA risk assessment tool [6] was used to check for any bias. Two authors worked independently to review the articles and summarise their findings to determine the availability of the following important sections: Aim of the study, study design, methodology, and results reporting. This was summarised using a yes or no output to set questions. Judgement was done using either low, high, or unclear. For example, if all criteria were marked yes, the study output was considered at low risk of bias, and vice versa for No. The unclear rating was used when data and information were insufficient to make an accurate judgment. In cases where there were variations in the ratings by the two reviewers, a third opinion was sought from an additional reviewer.

Collection and Analysis of Data

Two reviewers assessed the quality of the articles based on their titles and results. Articles that did not include information about the results in the abstract were discarded. The authors went through all selected articles to confirm that they passed the set inclusion criteria. The initial database search gathered 192 papers. An additional 23 papers were obtained from medical journals, making the total number of identified studies to 215. A total of 192 duplicates were removed, together with eight articles were excluded because they did not meet the criteria. This led to a total of 15 studies, as shown in [Table/Fig-2] [7-20].



[Table/Fig-2]: Search strategy PRISMA flowchart [7-20].

RESULTS

This section presents a detailed summary of the results of the identified studies [7-21] as well as the output of the risk bias assessment for the included studies. A summary of the number of identified studies, those excluded, and those included is shown in [Table/Fig-2].

Data Collection, Summary Measures and Synthesis of Results

A summary of the included studies, year of publication, country, number of ROP cases, and the screening guideline adopted is provided in [Table/Fig-3] [7-20].

Authors/years	Country	Population size	Screening criteria	ROP statistics
Onyango O et al., 2018 [7]	Kenya	43	GA<29.9±2.2, BW<= 1280.1±333.0	9 ROP stage III, the rest ROP stage I and II
Sitati SM et al., 2018 [8]	Kenya	130	GA<32, BW<1500	3 had ROP, 2 Stage I, 1 ROP stage II
Metho AA 2018 [9]	Kenya	228	GA<32	ROP cases were at 53.6% for GA < 30 weeks and 20% for GA between 31- 32 weeks
Smedt SKD 2018 [10]	Rwanda	424	GA<35, BW<1800	6 had ROP, 3 had severe ROP
Mutangana F et al., 2020 [11]	Rwanda	154	GA<30, BW<1500	31 babies had ROP, out of which 13 had severe ROP
Uwizihiwe F 2016 [12]	Rwanda	148	GA<30	22 had ROP, 9 having ROP stage one, 12 stage two and one ROP stage three
Melesse MA et al., 2020 [13]	Ethiopia	33	GA<29, BW<1186	21 with severe ROP, 2 with aggressive ROP, 12 with ROP stage five and blind
Sherief ST et al., 2023 [14]	Ethiopia	202	GA<32, BW<1500	65 had ROP with 13 having ROP stage one and 13 with severe ROP
Ndyabawe I et al., 2023 [15]	Uganda	331	GA<29, BW<1170	19 had ROP of any stage
Ademola-Popoola D et al., 2020 [16]	Nigeria	723	GA <34, BW ≤2000 g	128 had ROP of any stage
Mohamed N et al., 2022 [17]	Egypt	240	GA <34 weeks or BW <2000 g	82 had ROP of any stage
Braimah Z et al., 2019 [18]	Ghana	401	GA<37, BW<2kg	55 had ROP of any stage
Seobi T et al., 2022 [19]	South Africa	1081	GA<28, BW<1500	263 had ROP of any stage
Epee J et al., 2022 [20]	Cameroon	5640	GA<22-37	835 had ROP of any stage

[Table/Fig-3]: ROP statistics in Africa [7-20].

ROP Incidences and National Screening Guidelines in Africa

A population-based study done by Onyango O et al., at Nairobi Hospital had 103 babies admitted for screening, all with a gestational age of less than 29.9 weeks and a birth weight of less than 1280.1 grams [7]. Out of the 103 babies, 43 were diagnosed with ROP disease, representing 42% of the total. The majority of these cases had ROP stage one and ROP stage two in Zone II, which healed after several screening reviews. A total of 9 babies were diagnosed with ROP stage three and/or pre-plus ROP disease, representing 21% of the cases. Sitati SM et al., conducted a study in the western part of Kenya at Jaramogi Oginga Odinga Teaching and Referral Hospital between March 2015 and April 2016 [8]. The screening criteria included a gestational age of less than 32 weeks and/or a birth weight of less than 1500 grams. Screening was repeated after one or two weeks to identify ROP in Zone III. A total

of 130 babies were screened with a gestational age of 30.64±3.6 weeks and a birth weight of 1478±414.08 grams. Three babies were diagnosed with ROP, two with stage one ROP in Zone II and one with ROP stage two in Zone II. All cases healed without the need for medical treatment.

Metho AA conducted a study to determine the factors associated with the development of ROP disease, collecting data from three major hospitals in Nairobi: Aga Khan Hospital, Mater Hospital, and Nairobi Hospital [9]. The study, published in 2018, was conducted between January 2010 and December 2017. The three hospitals used the same ROP screening guidelines, screening babies born before 32 weeks. A total of 228 babies were screened for ROP, with 99 from Aga Khan Hospital, 83 from Nairobi Hospital, and 46 from Mater Hospital. ROP cases were observed in 53.6% of babies born before reaching 30 weeks and 20% of babies born before 32 weeks. The study did not investigate ROP stages or severe ROP cases.

A study done by Smedt SKD in Rwanda, via a program developed for screening ROP, screened 424 babies with data collected from September 1, 2015, to July 2017 [10]. Babies with a gestational age of less than 35 weeks and/or a birth weight of less than 1800 grams were screened, investigating all ROP stages and zones. Six babies were diagnosed with ROP, with gestational age greater than 30 weeks and birth weight greater than 1500 grams, out of which three had severe ROP and were treated. Mutangana F et al., investigated the risk factors of ROP using data collected from multiple health centers in Rwanda [11]. A total of 154 babies were screened for ROP, with 31 babies diagnosed with ROP, 13 of whom required treatment. Six babies born after week 30 with a birth weight greater than 1500 grams had ROP. Uwizihiwe F conducted a study at the Muhima Baby's Clinic for babies born between weeks 30 and 37, from September 2015 to March 2016 [12]. A total of 148 babies were screened, with 22 babies diagnosed with ROP: nine with ROP stage one, 12 with ROP stage two, and one with ROP stage three.

Melesse MA et al., conducted a study in Ethiopia regarding ROP screening for babies at the WGGA Eye Screening Centre [13]. The study period was from June 1, 2016, to December 31, 2019. Of the babies screened, a total of 33 had ROP, with 21 having severe ROP, two having aggressive ROP, and 12 having ROP stage five leading to blindness. Screening was done for babies born before week 29 or with a birth weight less than 1186 grams. The study by Sherief ST et al., aimed to determine ROP risk factors for neonates admitted to two Neonatal Intensive Care Unit (NICU) centres, Menelik II and TASH, in Addis Ababa, Ethiopia [14]. Data was collected between June 2019 and June 2020, with screening criteria targeting all babies born before week 32 or weighing less than 1500 grams. A total of 202 babies were screened, with 65 diagnosed with ROP, including 13 with ROP stage one and 13 with severe ROP.

A study was done in Uganda by Ndyabawe I et al., within two tertiary clinics screened 331 babies [15]. A total of 19 babies had ROP, with 18 from Mulago Specialised Women and Neonatal Hospital and one from Kawempe National Referral Hospital. Out of the 331 babies, half were male and half were female. The screening criteria targeted babies with a gestational age below 29 weeks or a birth weight less than 1170 grams. In a study by Ademola-Popoola D et al., in Nigeria between the years 2017 and 2018, a population of 723 babies was screened for ROP under the criteria of gestational age less than 32 weeks or birth weight less than 2000 grams, with 17.6% of the screened population having ROP disease [16].

In Ethiopia, a study by Melesse MA between June 2016 and August 2019, involving a population of 66 babies, revealed that 42.4% of babies had ROP, all screened based on criteria targeting babies with a gestational age less than 28 weeks or a birth weight less than 1172 grams [13]. Mohamed N et al., conducted a study in Egypt between October 1 and October 31, 2020, involving 240 infants, with ROP cases at 34.1%. The screening criteria were gestational age less than 34 weeks or a birth weight of less than or equal to 2000 grams [17]. Braimah Z et al., conducted a study in Ghana for a period of nine months (June 2018-February 2019), where 401 babies were screened for ROP, resulting in ROP incidents at 13.7%, with all babies screened having a birth weight of less than 1600 grams and/or a gestational age of less than 37 weeks [18]. Seobi T et al., conducted a study in South Africa between January 1, 2015, and June 31, 2020, with a population of 1081, revealing an ROP percentage of 24.3% under the criteria of gestational age less than 28 weeks or a birth weight less than 1500 grams [19]. A study by Epee J et al., conducted in Cameroon with a population of 5640 resulted in data collection from three hospitals, resulting in an ROP percentage of 14.8% under the screening criteria of gestational age between 22 to 37 weeks [20]. A detailed summary of the ROP incidences in East Africa is shown in [Table/Fig-3].

ROP National Screening Guidelines in Africa

As shown in [Table/Fig-4] [7-21], screening for ROP in Kenya follows national guidelines. Babies with a gestational age of ≤32 weeks and/or a birth weight of ≤1500 grams are screened [21-22]. Babies with pre-existing medical conditions that do not fit into this screening age and weight criteria are also screened. Rwanda does not have national screening guidelines; however, the criteria for ROP screening is a gestational age less than or equal to 30 weeks and/or a birth weight less than 1199 grams [22]. Egypt does not have national screening guidelines for ROP [23]. However, two recent studies by Twafik et al., [24] screened ROP at 32 Neonatal Intensive Care Units (NICUs) located in rural settlements with a GA <=34 and/or BW <=2000, finding ROP cases to be 47.4% for the population examined. A study by Abdel et al., [25] in Egypt adopted a screening criteria of GA <=33.4±2.6 weeks and/or BW <=1842.3 ±570.1 grams.

A study by Visser et al., [25] showed that South Africa has national ROP screening guidelines. Babies born before week 32 and/or weighing less than 1500 grams are screened for ROP. Those

Domain / Studies	Domain 1 Objective(s) and subject characteristics	Domain 2 Study design	Domain 3 methodology characterisation	Domain 4 descriptive anatomy	Domain 5 reporting of results
Onyango O et al., 2018 [7]	High	High	High	High	High
Sitati SM et al., 2018 [8]	High	High	High	Low	High
Metho AA 2018 [9]	High	High	High	Low	High
Smedt SKD 2018 [10]	High	Low	Unclear	Low	Low
Mutangana F et al., 2020 [11]	High	High	High	Unclear	High
Uwizihiwe F 2016 [12]	Low	Unclear	High	High	Low
Melesse MA et al., 2020 [13]	High	High	Low	High	High
Sherief ST et al., 2023 [14]	High	Low	High	Low	High
Ndyabawe I et al., 2023 [15]	High	High	High	High	High
Ademola-Popoola D et al., 2020 [16]	Low	Low	High	Low	Low
Mohamed N et al., 2022 [17]	High	High	Low	Low	High

Braimah Z et al., 2019 [18]	High	Low	High	High	Low
Seobi T et al., 2022 [19]	High	Low	Unclear	Low	High
Epee J et al., 2022 [20]	High	High	High	Low	High

[Table/Fig-4]: Interpretation of each domain based on AQUA tool [7-20].

weighing between 1500-2000 grams are also screened if the family has a history of ROP, cardiac diseases, the mother has had more than two blood transfusions, or if their oxygen levels have not been optimal. Nigeria does not have national screening guidelines for ROP; however, two studies by Ademola-Popoola D et al., [16] used a screening criterion for GA < 34 or BW <=2000, and Adio A et al., [26] conducted ROP screening for GA < 27 weeks or BW < 913. A detailed summary of the ROP national screening guidelines in Africa is shown in [Table/Fig-4].

The results of the risk of bias assessment using the AQUA tool and its interpretation presented in [Table/Fig-2]. Based on the interpretation obtained, two studies [7,15] had a high-risk bias, with all items in their domains marked as high. Thirteen studies [8-14,16-20] had some of their domain outputs as low or unclear.

DISCUSSION

The Retinopathy of Prematurity (ROP) is the highest cause of blindness among children born preterm, with babies born with underlying medical conditions also at risk of contracting the disease. The diagnosis of the disease remains an economic burden for many African countries that lack an adequate number of ophthalmologists for disease diagnosis, and many countries also lack screening guidelines. The present review aimed to review the current statistics of ROP in Africa and present a summary of the incidence rates as well as the disease screening criteria within the continent. It was found that only two countries, South Africa [21] and Kenya [22], have national screening guidelines for ROP disease screening.

Three studies [7-9] were conducted in Kenya, and there is a noticeable adherence to the provided screening guidelines. In South Africa, one study [19] was conducted according to the provided guidelines. Rwanda does not have screening guidelines, and three studies [10,11,14] showed variations in the choice of screening criteria based on birth weight and gestational age.

In Ethiopia, the authors identified three studies [13-14], and for all the studies, there were variations in the choice of screening criteria for gestational age and birth weight. Other countries like Uganda, Nigeria, Egypt, Ghana, and Cameroon had one study [15,16,17,18,20] each, respectively, which indicated that they do not have national screening guidelines for ROP disease. Screening for ROP in Kenya is done following national guidelines. Babies with a gestational age of ≤32 weeks and/or a birth weight of ≤1500 grams are screened [22]. Babies with pre-existing medical conditions that do not fit into this screening age and weight criteria are also screened. Rwanda does not have national screening guidelines; however, the criteria for ROP screening is a gestational age less than or equal to 30 weeks and/or a birth weight less than 1199 grams [23].

Egypt does not have national screening guidelines for ROP [24]. However, two recent studies by Twafik S et al., screened ROP at 32 Neonatal Intensive Care Units (NICUs) located in rural settlements with a GA <=34 and/or BW <=2000, finding ROP cases to be 47.4% for the population examined [23]. A study by Abdel I et al., in Egypt adopted a screening criteria of GA <=33.4 ± 2.6 weeks and/or BW <=1842.3 ± 570.1 grams [25]. Adio A et al., conducted ROP screening for GA < 27 weeks or BW < 913 [26]. The ROP screening guidelines in Africa is illustrated in [Table/Fig-5] [11,16,21,22,23,25,26].

The findings of the present review revealed that in regions where ophthalmologists are few and/or in low-resource regions with few or no ophthalmologists, clinicians capture retina images and send them to hospitals with ophthalmologists for assistance in disease

Authors/years	Country	Gestational age	Birth weight	ROP National screening guideline
Mutangana F et al., 2020 [11]	Rwanda	GA<= 30.1(SD 2.4, range of 25-36) weeks for babies with ROP and 31.7 (SD 2.2, range of 24-37) weeks for all babies	BW<1199g (SD 303.3 for a range of 685-1800) for babies with ROP and BW<1479g(SD 360.1 for range of 650-2800)	None
Ademola-Popoola D et al., 2021 [16]	Nigeria	GA< 34	BW<=2000	None
Visser L et al., 2012 [21]	South Africa	GA< 32	BW< 1500 or between 1500-2000	Yes
Sitati S et al., 2018 [22]	Kenya	GA<=32	BW<= 1500	Yes
Tawfik S et al., 2021 [23]	Egypt	GA<=34	BW<= 2000	None
Abdel-Aziz I et al., 2022 [25]	Egypt	GA<=33.4±2.6	BW<= 1842.3±570.1	None
Adio A et al., 2021 [26]	Nigeria	GA <27	BW<913	None

[Table/Fig-5]: ROP screening in Africa [11,16,21,22,23,25,26].

diagnosis. Irrespective of the fact that the disease is a global pandemic [27], there are few population-based studies showing the statistics in Africa as well as screening criteria in the region, as depicted in [Table/Fig-3,5]. The present review also identified remarkable work by ophthalmologists in Kenya [7] who have been supporting their Ministry of Health and ensuring that ROP images are stored in a privately owned database for research purposes. As shown in [Table/Fig-4], the ophthalmologists developed an ROP screening flowchart to track the procedure for diagnosing and treating babies born preterm.

South Africa has national ROP screening guidelines developed in 2012, and screening is done for babies with GA < 32 and/or BW<1500. As shown in [Table/Fig-5], only four countries-Kenya, Rwanda, Ethiopia, and Uganda-have conducted population-done studies from January 2018 to December 30, 2023. This highlights the need for more research as well as publications on the disease statistics and treatment within the region.

Limitation(s)

The included studies were only those that met the study objectives and the present findings revealed a challenge: there are few recent ROP population-based studies published. The present review also excluded important information on treatment procedures for babies diagnosed with ROP; hence, the authors recommend future extensions to compare the methodologies of ROP treatment among different countries.

CONCLUSION(S)

The present paper aimed to review the statistics of ROP disease and the screening guidelines in Africa. Gestational age and birth weight are two parameters for ROP screening. For countries without national screening guidelines, ophthalmologists agree on those parameters to be followed for screening, which may vary from one group of ophthalmologists to another, posing a prevailing issue. Additionally, the process of capturing and transmitting retina images by clinicians to ophthalmologists to assist in diagnosis is a concern due to image quality distortion,

confidentiality breaches, as well as privacy issues. With the prevailing issues regarding ROP disease diagnosis, the authors additionally recommend that more population-based studies on ROP incidents should be published, and governments should work to ensure the development of national screening guidelines for countries that do not have them.

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