African Vision and Eye Health
ISSN: (Online) 2410-1516, (Print) 2413-3183

Retinopathy of prematurity screening in Johannesburg, South Africa: A comparative study

Authors:
Teboho Seobi[1,2]
Innocent Maposa[3,4]
Mokokomadi A. Makgotloe[1,5]

Affiliations:
[1]Department of Ophthalmology, Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa

[2]Department of Ophthalmology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

[3]Health Science Research Office, Johannesburg, South Africa

[4]Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

[5]Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Corresponding author:
Mokokomadi Makgotloe, aubrey.makgotloe@wits.ac.za

Dates:
Received: 02 May 2022
Accepted: 07 July 2022
Published: 23 Sept. 2022

Background: Timeous screening of retinopathy of prematurity (ROP) is an important predictor of ROP screening outcomes, and hospitals at different levels of care might have different access to ROP screening by ophthalmologists, resulting in different ROP screening outcomes.

Objective: To compare ROP screening outcomes between premature babies from a neonatal facility at a central hospital to those from regional hospitals in Johannesburg.

Setting: Retinopathy of prematurity screening in babies born at central and non-central hospitals in Johannesburg, South Africa, between 01 January 2015 and 31 June 2020.

Methods: A cross-sectional study describing clinical findings in babies referred for ROP screening at a central Johannesburg hospital.

Results: A total of 2035 ROP screening records were included in the study. The babies screened from the central hospital and regional hospitals were 1081 (53.1%) and 954 (46.9%), respectively. The proportion of babies with ROP were 125 (11.6%) and 121 (12.7%) in the central hospital and regional hospitals, respectively, and this difference was not statistically significant, $p = 0.435$. There was a significant association between gestational age (GA) categories and birth weight (BW) with the hospital of birth, with proportionately more babies with GA < 28 weeks, 212 (19.6%) versus 158 (16.6%) $p < 0.001$, and BW < 1500 g, 894 (82.7%) versus 737 (77.3%) $p = 0.001$, being referred by the central hospital compared to regional hospitals.

Conclusion: The prevalence of ROP in regional hospitals does not seem to differ from that found in central hospitals.

Keywords: prematurity; retinopathy; African; gestational age; birth weight.

Introduction

Retinopathy of prematurity (ROP) is a major cause of visual impairment and blindness in surviving premature babies, and more importantly, it is a preventable cause of blindness in middle-income countries.[1,2,3] The advancement of neonatal care has resulted in an increase of the survival rates of extremely premature infants, which has resulted in an increase in the prevalence of ROP.[3]

A ROP third epidemic is described as a phenomenon seen mostly in middle-income countries such as South Africa. This is because of improved survival of premature babies with an accompanying lack of adequate monitoring of oxygen therapy in neonatal high care units.[2,4] These low- and middle-income countries often have limited resources in neonatal intensive care facilities, resulting in lack of continuous monitoring of all babies on supplemental oxygen and inadequate nursing care for numerous babies simultaneously.[4]

It is estimated that worldwide, approximately 50 000 children are blind because of ROP.[2,4] In developed countries, with an infant mortality of less than 10 per 1000 live births, ROP is estimated to account for 6% – 18% of childhood blindness.[5] In South Africa, ROP accounted for 10.6% of cases of blindness in schools of the blind in 1995.[6] An estimated 16 000 infants are at risk of ROP in South Africa.[1]

How to cite this article: Seobi T, Maposa I, Makgotloe, MA. Retinopathy of prematurity screening in Johannesburg, South Africa: A comparative study. Afr Vision Eye Health. 2022;81(1), a771. https://doi.org/10.4102/aveh.v81i1.771

The key strategy in the prevention of ROP is a successful screening programme, as this will result in timeous management of appropriate stages of the condition and ultimately prevent progression of the disease to irreversible blindness.[1,2] Retinopathy of prematurity can be treated with anti-vascular endothelial growth factor or laser.[5]

In South Africa, approximately 80% or more of the 1 million live births per annum babies occur in the public health sector.[6,7] Approximately half of these babies are born in district hospitals.[1] In facilities with specialist-run services, 32% are born in regional hospitals and 20% in tertiary or central hospitals.[1] Most of the district and regional hospitals do not have easy access to ophthalmologists or ROP screening facilities, in contrast to tertiary or central level institutions which do.[7]

The 2012 consensus ROP screening guidelines were developed by the paediatricians, neonatologists and ophthalmologists in the South African public and private practices and endorsed by the United South African Neonatal Association, the Ophthalmological Society of South Africa and the South African Vitreoretinal Society.

The guidelines stipulate that screening must be done on all neonates born before the gestational age (GA) of 32 weeks or birth weight (BW) of less than 1500 g (very low birth weight [VLBW] and extremely low birth weight [ELBW]). Preterm neonates between 1500 g and 2000 g should only be screened if they have a family history of ROP and/or have medical indications for such screening.[1] Such screening must be performed when the baby is 4–6 weeks chronological age or 31–33 weeks post conceptual age, whichever comes later. All babies requiring screening must be screened before 37 weeks postconception.[1]

Many neonatal intensive care unit facilities in South Africa do not have ophthalmology services onsite, which often results in these babies being referred to a central hospital.[1] Mayet et al. reported that at Chris Hani Baragwanath Hospital, a central hospital in Johannesburg, the incidence of ROP was 17%.[8] At Tygerberg Hospital, a central hospital in Cape Town, they reported that the prevalence of ROP was 31.1%.[7] These all indicate the combined prevalence of ROP in central and referring district/regional hospitals.

The ophthalmology unit at a central hospital in Johannesburg (Charlotte Maxeke Johannesburg Academic Hospital [CMJAH]) perform ROP screening in babies referred from CMJAH (central hospital) as well as those referred from its regional hospitals (non-CMJAH Hospitals).

Because timeous screening of ROP is an important predictor of ROP screening outcomes, and hospitals at different levels of care might have different access to ROP screening by ophthalmologists, resulting in different ROP screening outcomes, it was decided to study the ROP screening outcomes of babies from a central hospital and compared them to those from regional hospitals.

Study objective

The aim of this study was to compare ROP screening outcomes between premature babies from a neonatal facility at a central hospital to those referred from regional hospitals in Johannesburg.

Methods

This was a cross-sectional study of all babies referred for ROP screening at a central hospital's ophthalmology department, between 01 January 2015 and 31 June 2020.

This screening included babies referred by the neonatology unit based at this central hospital and units based at referring regional hospitals. These regional hospitals did not have ophthalmologists who could screen for ROP during the period studied.

Babies were screened either as inpatients, central hospital patients only, or as outpatients, central and regional hospitals' patients, by ophthalmology senior registrars trained in performing this procedure, assisted by a consultant ophthalmologist who reviewed the babies with the registrar if there were any concerns. All the patients were screened using an indirect ophthalmoscope. The fundoscopic clinical findings and treatment were recorded on the Redcap (Research Electronic Data Capture) programme, which is hosted by the University of the Witwatersrand. The information for this study was obtained from this database. All babies screened for ROP between 01 January 2015 and 31 June 2020 were included in this study, and babies screened for retinopathy not caused by ROP were excluded from this study.

Statistical analysis

Descriptive statistics such as frequencies or proportions were used with categorical data, while means or medians and standard deviations or interquartile ranges (IQRs) were used with continuous data as appropriate. Differences in proportions between study groups were compared using a chi-square test or Fisher's exact test. To compare averages between groups, an unpaired *t*-test or Mann–Whitney *U* test was used, depending on the distribution of the data. To determine association between children's characteristics and screening outcome, the multivariable logistic regression model was utilised. A *p*-value less than 0.05 was considered significant.

Ethical considerations

Ethics approval was obtained from the Human Research Ethical Committee of the University of the Witwatersrand, Johannesburg (ref. no. M190276).

Results

Between 01 January 2015 and 31 June 2020, 2853 records were identified from the ROP screening database for possible

inclusion in the study. A total of 725 records were excluded from the study because they were identified as duplicate records, and 93 were removed because they did not have a hospital recorded. A total of 2035 records thus were included in the study (see Figure 1).

Table 1 summarises the demographic and clinical features of babies screened by location of birth. A majority of babies, 1081 (53.1%), were referred from the central hospital's neonatal service and 954 (46.9%) from regional hospitals. A total of 1048 (51.5%) of the babies were female. The proportion of babies with ROP from the central hospital was 11.6% (n = 125) while among those referred from regional hospitals was 12.7% (n = 121), and this difference was not statistically significant. Results also show a significant association between GA categories and BW with location of birth, with proportionately more babies with GA < 28 weeks and BW < 1500 g being referred by the central hospital.

Retinopathy of prematurity prevalence

The prevalence of ROP was 246 (12.1%). The group-specific prevalence was 125 (11.6%) and 121 (12.7%) in the central hospital and regional hospitals' groups, respectively; this difference was not statistically different: $p = 0.435$.

Chronological age at screening

There were 176 (8.6%) babies who were younger than three weeks chronological age at screening. The central hospital had proportionately more of these babies than regional hospitals, 109 (10.1%) and 67 (7.0%), respectively. Of these 176 babies, 16 (9.1%) had ROP at the time of screening.

Table 2 shows that there is no significant association between hospital of reference with ROP individually or adjusted (univariate odds ratio [OR] = 1.11, 95% confidence interval [CI]: 0.85–1.45, $p = 0.435$; multivariate OR = 1.25, 95% CI: 0.94–1.65, $p = 0.122$). There are, however, significant associations between GA and ROP with those born between 28–32 weeks and lower than 28 weeks having higher odds (multivariate OR = 2.53, 95% CI: 1.56–4.11, $p < 0.001$) and (multivariate OR = 4.20, 95% CI: 2.49–7.08, $p < 0.001$), respectively, compared to those born more than 32 weeks. Birth weight category was also significantly associated with ROP individually and adjusted, with those born with less than 1500 g having higher odds of presenting with ROP (multivariate OR = 3.55, 95% CI: 1.83–6.89, $p < 0.001$) compared to those born with 1500 g or more.

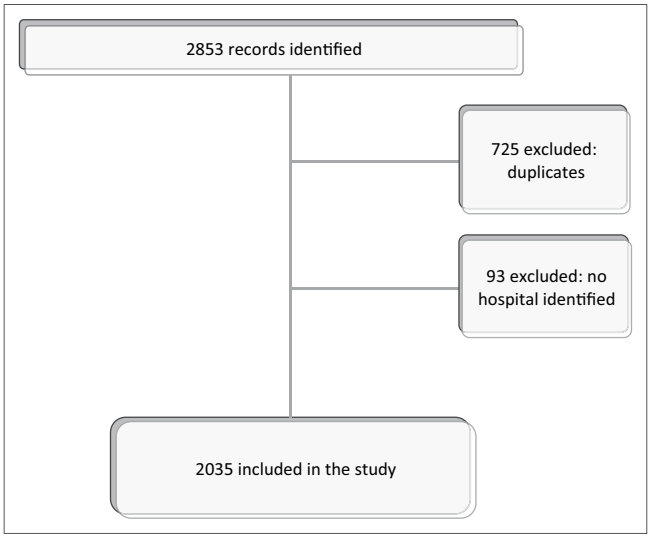

FIGURE 1: A flow chart of study participants.

To ascertain the association between ROP and hospital of birth (either the central hospital or regional hospitals) as exposure, stratifying by BW as an effect modifier, we did a separate analysis using the Mantel–Haenszel method. We noted elevated odds of ROP for babies who were born at regional hospitals compared to the central hospital for both categories of weight, although the effects were not significant (multivariate OR = 3.38, 95% CI: 0.70–16.30, $p = 0.106$) (Multivariate OR = 1.13, 95% CI: 0.86–1.49, $p = 0.386$) respectively for 1500 g or more and less than 1500 g groups. Stratifying by GA categories showed similar results, with elevated insignificant odds for babies born in regional hospitals for those in age category less than 28 weeks (multivariate OR = 1.35, 95% CI: 0.81–2.25, $p = 0.243$), between 28 and 32 weeks (multivariate OR = 1.28, 95% CI: 0.89–1.82, $p = 0.174$) and reduced odds for babies born more than 32 weeks (multivariate OR = 0.70, 95% CI: 0.29–1.68, $p = 0.425$).

Gestational age

Proportionately more babies with a GA of less than 28 weeks were referred from the central hospital compared to regional hospitals, 211 (19.6%) and 155 (16.4%), respectively. In the

TABLE 1: A summary of demographic and clinical features of babies screened.

Variables	Central hospital		Regional hospitals		Total	p
	n	%	n	%		
All patients	1081	53.1	954	46.9	2035	-
Gender						0.318
Male	519	48.0	438	45.9	957	-
Female	545	50.4	503	52.7	1048	-
Missing	17	1.6	13	1.4	30	-
ROP						0.435
ROP absent	949	87.8	826	86.6	1775	-
ROP present	125	11.6	121	12.7	246	-
Missing	7	0.6	7	0.7	14	-
ROP requiring treatment	43	4.0	52	5.5	95	-
GA						< 0.001
Less than 28 weeks	212	19.6	158	16.6	370	-
Between 28 and 31 weeks	631	58.4	497	52.1	1128	-
More than 31 weeks	220	20.4	281	29.5	501	-
GA unrecorded	18	1.6	18	1.8	36	-
BW category						0.001
BW < 1500 g	894	82.7	737	77.3	1631	-
BW 1500 g – 2000 g	137	12.7	169	17.7	306	-
BW > 2000 g	19	1.8	21	2.2	40	-
BW: Not recorded	31	2.8	27	2.8	58	-

ROP, retinopathy of prematurity; GA, gestational age; BW, birth weight; n, number.

TABLE 2: Univariate and multivariable logistic regression to determine factors associated with retinopathy of prematurity.

Characteristics	Univariate logistic regression							Multivariable logistic regression		
	ROP		No ROP		OR	95% CI	*p*	OR	95% CI	*p*
	n	%	*n*	%						
HC facility										
Central hospital	125	11.6	949	88.4	1.00	ref	-	1.00	ref	-
Regional hospitals	121	12.8	826	87.2	1.11	0.85–1.45	0.435	1.25	0.94–1.65	0.122
Gender										
Female	122	11.7	919	88.3	1.00	ref		1.00	ref	
Male	119	12.5	832	87.5	1.08	0.82–1.41	0.588	1.15	0.87–1.53	0.314
Gestational age										
> 32 weeks	21	4.2	480	95.8	1.00	ref	-	1.00	ref	-
28–32 weeks	142	12.7	976	87.3	3.33	2.08–5.33	< 0.001	2.53	1.56–4.11	< 0.001
< 28 weeks	76	20.7	291	79.3	5.97	3.60–9.88	< 0.001	4.20	2.49–7.08	< 0.001
Birth weight										
≥ 1500 g	10	2.9	334	97.1	1.00	ref	-	1.00	ref	-
< 1500 g	232	14.3	1389	85.7	5.58	2.93–10.62	< 0.001	3.55	1.83–6.89	< 0.001

HC, healthcare; CI, confidence interval; ROP, retinopathy of prematurity; OR, odds ratio.

category of babies born between 28 and 32 weeks, there were 628 (58.4%) babies from the central hospital compared to 493 (52.1%) from regional hospitals. In the category of babies born more than 32 weeks, there were more babies from regional hospitals, 280 (29.6%) compared to central hospital, 219 (20.4%).

Birth weight

Proportionately more babies from the central hospital had a BW less than 1500 g, 888 (81.6%), compared to babies from regional hospitals, 729 (77.1%). Regional hospitals had more babies in the BW range of 1500 g – 2000 g than central hospital's babies, 170 (18.0%) and 138 (12.8%), respectively.

There were 113 (50.47%) babies referred from regional hospitals with a weight more than 1500 g as compared to the central hospital referrals, having 111 (49.55%) babies. A total of 66 (3.1%) babies screened had a BW greater than 2000 g, referred by both the central hospital and regional hospitals.

Discussion

The central hospital studied here has both ophthalmological and neonatal services. It receives referrals for ROP screening from neighbouring regional hospitals. These hospitals offer secondary-level care, which includes neonatal care but does not include managing babies with ROP. Such babies are referred to the central hospital for screening and management.

In this study, babies referred from the central hospital's neonatology unit were slightly more than those from regional hospitals (53.1% vs 46.9%), even though regional hospitals collectively treat more babies. This might reflect the fact that there could be more VLBW babies managed at central hospital's neonatology unit compared regional hospitals' units, because it is a highly specialised facility, or alternatively that qualifying babies from these referring hospitals are lost to follow-up before their scheduled screening appointment at the central hospital. These babies are usually discharged from their hospital and given instructions to book their ROP screening visit at the central hospital.

The recommended postnatal age at screening in South Africa is four weeks or older. Visser et al. reported in a study conducted in Tygerberg that the median postnatal age of the infants at the first screening examination was five weeks (IQR: 4–7).[7] In our study, there were 176 (8.6%) babies who were younger than three weeks chronological age at the time of screening, and 16 (9.1%) of these had ROP at the time of screening. This means that a significant number of ROP babies would have been missed, had the four-week cut-off recommendation been adhered to. This study's results suggest that an earlier screening might be useful in some settings, particularly in hospitals which have ROP screening services available on site.

A trend to screen earlier has been reported in other hospitals in South Africa. Jacoby et al., in Port Elizabeth at Dora Nginza Hospital, reported that in 2009 all infants in their hospital were referred after 6 weeks. They noted that this proportion had decreased to 7.9% in 2014. They attributed this change to an increase in the number of ophthalmologists screening for ROP and referrals by paediatricians treating these ROP babies.[9]

Delayed screening remains a challenge, even in other centres around the world. Chen et al. conducted a retrospective study to understand the status of ROP screening in Northern China at the Provincial Screening Centre of Hebei province. The patients in their study were referred by doctors from various levels of other hospitals. The mean postnatal age of the first screening was 7.38 weeks. Only 38.34% of patients were screened at 4–6 weeks postnatal.[10] Their study also highlighted the lack of understanding of ROP by parents and staff members, and the importance of raising awareness in staff members and parents about ROP.

A majority of the babies being referred from both central hospital and regional hospitals were VLBW babies, with

BW < 28 weeks. The number of VLBW babies from the central hospital was significantly higher than those referred from regional hospitals (82.7% and 77.3%, respectively, $p = 0.001$). Similarly, more babies who were < 28 weeks GA were referred from the central hospital (19.6%) when compared to regional hospitals (16.6%, $p < 0.001$) babies. This is most likely due to the central hospital's specialised neonatal care, resulting in the survival of these VLBW babies. It is also likely that babies with ELBW < 1000 g are being referred from the regional hospitals to the central hospital's neonatal units soon after birth. In their study in South Africa, Visser et al. reported that the median GA at birth was 28 weeks (IQR: 27–29, range: 24–37).[7]

The prevalence of ROP in our study patients was 11.5% and 12.6% in the central hospital and regional hospitals respectively, and this difference was not statistically significant. A previous study by Dadoo et al. reported a prevalence of 15.6% at a central hospital, which is similar to this study.[2] Overall, there was no statistical difference in the number of babies with ROP between these hospitals.

Elevated odds of ROP were noted for babies who were born at regional hospitals compared to the central hospital, for both categories of weight, that is, 1500 g or more and less than 1500 g groups, although the effects were not significant. Regional hospitals do not have ophthalmologists who can screen babies for ROP, resulting in delayed screening as babies await discharge before they can be referred to central hospitals for screening. Delayed referral of premature babies has been reported to result in the development of severe ROP. Chen et al. reported that of the babies who had severe disease on first presentation in their cohort, 0.46% had presented on time and 1.53% had delayed screening. Our study did not specifically describe the severity of ROP between these hospitals.

Conclusion

To our knowledge, this is the first study to compare the ROP screening patterns between a central hospital with ROP screening ophthalmologists and a group of regional hospitals without this service.

The conclusion from this study is that more babies with VLBW are referred from a central hospital and that the odds of developing ROP for a given GA and BW are not significantly different between these hospitals, even when screening for ROP is delayed.

Limitations

The major limitations of this study is its retrospective nature, which makes the data collection nonsystematic, resulting in some data missing.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

T.S.'s contribution includes project conceptualisation and design, data collection and analysis and write-up of the manuscript. I.M.'s contribution includes project conceptualisation and design, data collection and analysis and write-up of the manuscript. M.A.M.'s contribution includes project conceptualisation and design, data analysis, review of the manuscript, supervision of the project and funding acquisition.

Funding information

This research received no specific grant from a funding agency in the public, commercial or not-for-profit sectors.

Data availability

Raw data of this research is available on request from the corresponding author, M.A.M.

Disclaimer

The views and opinions expressed in this article are those of the authors, and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. Visser L, Singh R, Young M, Lewis H, McKerrow N. Guidelines for the prevention, screening and treatment of retinopathy of prematurity (ROP). S Afr Med J. 2012;103(2):116. https://doi.org/10.7196/SAMJ.6305
2. Dadoo Z, Ballot DE. An evaluation of the screening for retinopathy of prematurity in very-low-birth-weight babies at a tertiary hospital in Johannesburg, South Africa. S Afr J Child Health. 2016;10(1):79. https://doi.org/10.7196/SAJCH.2016.v10i1.1099
3. Afarid M, Hosseini H, Abtahi B. Screening for retinopathy of prematurity in South of Iran. Middle East Afr J Ophthalmol. 2012;19(3):277. https://doi.org/10.4103/0974-9233.97922
4. Gilbert C. Retinopathy of prematurity: A global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev. 2008;84(2):77–82. https://doi.org/10.1016/j.earlhumdev.2007.11.009
5. Trivli A, Polychronaki M, Matalliotaki C, et al. The severity of retinopathy in the extremely premature infants. Int Sch Res Notices. 2017;2017:1–4. https://doi.org/10.1155/2017/4781279
6. Varughese S, Gilbert C, Pieper C, Cook C. Retinopathy of prematurity in South Africa: An assessment of needs, resources and requirements for screening programmes. Br J Ophthalmol. 2008;92(7):879–882. https://doi.org/10.1136/bjo.2008.137588
7. Visser Kift E, Freeman N, Cook C, Myer L. Retinopathy of prematurity screening criteria and workload implications at Tygerberg Children's Hospital, South Africa: A cross-sectional study. S Afr Med J. 2016;106(6):602. https://doi.org/10.7196/SAMJ.2016.v106i6.10358
8. Mayet I, Cockinos C. Retinopathy of prematurity in South Africans at a tertiary hospital: A prospective study. Eye. 2006;20(1):29–31. https://doi.org/10.1038/sj.eye.6701779
9. Jacoby MR, Du Toit L. Screening for retinopathy of prematurity in a provincial hospital in Port Elizabeth, South Africa. S Afr Med J. 2016;106(6):598. https://doi.org/10.7196/SAMJ.2016.v106i6.10663
10. Chen L, Su M, Ren S, Hua H, Wang J, Zheng W. Analysis of current status and strategies of retinopathy of prematurity screening during 6 years in local regions of China: Implication and caution. J Ophthalmol. 2014;2014:1–6. https://doi.org/10.1155/2014/756059