OUTCOMES AND ASSOCIATED FACTORS OF RETINOPATHY OF PREMATURITY TREATMENT AT MUHIMBILI NATIONAL HOSPITAL DAR ES SALAAM, TANZANIA.

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A Dissertation submitted in partial fulfillment of the requirements for the Degree of Master in Medicine (Mmed Ophthalmology) at Muhimbili University of Health and Allied Sciences

October, 2024

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF OPHTHALMOLOGY

Outcomes and Associated Factors of Retinopathy of Prematurity Treatment at Muhimbili National Hospital Dar Es Salaam, Tanzania.

By

Warda Khalef

A Dissertation submitted in partial fulfillment of the requirements for the Degree of Master in Medicine (Mmed Ophthalmology) at

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Science a dissertation entitled: **"*Outcomes and associated factors of retinopathy of prematurity treatment at Muhimbili National Hospital Dar es Salaam, Tanzania*",** in (partial) fulfillment of the requirement for the degree of Master of Medicine (Ophthalmology) of the Muhimbili University of Health and Allied Science.

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Date_____

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Dr. Suzan Mosenene

(Co-supervisor)

Date_____

DECLARATION AND COPYRIGHT

I, **Dr. Warda Khalef**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature..... Date.....

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ACKNOWLEDGEMENT

Firstly, I am deeply grateful to the Almighty God for blessing me with good health and the capability to undertake this work. Without divine guidance and strength, this achievement would not have been possible.

Secondly, my sincere gratitude to my supervisors, Dr. Celina Mhina and Dr. Suzan Mosenene, for their tireless efforts and invaluable guidance throughout the entire process of preparing and finalizing this dissertation. Their unwavering dedication has been instrumental in shaping the outcome of my research, and I am deeply thankful for their support.

Thirdly, I am grateful to Dr Paul Nyaluke, the former head of the Department of Ophthalmology at Muhimbili National Hospital (MNH), for granting me permission to collect data during the study period. Also, I would like to thank Miss Restituta Mworia and Mr. Wilfred Mgaya (Optometrists at MNH) for their assistance to confirm refraction results during the data collection process. Their expertise and assistance have significantly contributed to the overall quality of the study.

Furthermore, I want to acknowledge and thank my family for their sacrifice, patience, and unwavering support throughout this demanding period. Their understanding and encouragement have been essential in helping me overcome the challenges and complete this research.

DEDICATION

To my parents Khalef Mohamed and Mtumwa Saleh for their endless love and support throughout my life and my education.

ABSTRACT

Background: Retinopathy of prematurity (ROP) is a potentially blinding disease caused by abnormal growth of retinal blood vessels in premature infants, leading to scarring, retinal detachment, and vision loss. It accounts for about 10% of childhood blindness worldwide. Despite the advancements in medical interventions, treatment outcomes for ROP remain highly variable with some infants responding well to treatment while others continue to experience disease progression, complications such as vitreous hemorrhage, or tractional retinal detachment, ultimately leading to blindness. Additionally, visual development may still be impaired despite treatment. The inconsistency in the treatment results and the lack of conclusive data on contributing factors underscore the need for this investigation, which seeks to provide evidence that may guide clinical decision-making and enhance care for premature infants at risk of blindness.

Aim: To assess outcomes and associated factors of ROP treatment at Muhimbili National Hospital.

Methodology: A hospital-based analytical cross-sectional study that consecutively recruited 40 children who had ROP and had received treatment from 2019 to 2022 was conducted. The study was conducted for a period of six months, from August 2022 to January 2023. Participants were assessed for structural findings, visual status, and refractive errors. Data were analyzed using SPSS version 24. Frequencies and percentages were used to show the structural, visual status and refraction status. while Fisher's Exact Test was used to show relationship between type of treatment with presenting visual acuity and refraction status. Multiple linear regression analysis was used to show association between factors and presenting visual acuity. Univariate and multivariate logistic regression was used to show association between factors and refractive error. A p-value less than 0.05 considered to be statistically significant.

Results: Seventy-nine eyes of 40 patients were analyzed. Majority of the study participants were females (65.0%), and the mean age was 11.50 (*±5.60SD*) months. The majority of eyes (71.3%) had stage 3 ROP. ROP regression was seen in all eyes. Normal vision was observed in 79.7% of eyes. Most (65.3%) of eyes had refractive error and of them, majority had myopia. Birth

weight, gestational age (GA), PMA at treatment, and disease severity showed no association with structural outcome, visual and refractive status.

Conclusion: All eyes showed ROP regression. Normal vision was observed in majority of eyes. Majority of eyes had refractive error and myopia was the common. PMA at treatment, birth weight, and disease stage showed no association with treatment outcomes.

Recommendations: Efforts to screen, detect and treat children with ROP at MNH must continue in order to maintain a good outcome. Children who had undergone ROP treatment should be closely followed up to early identify, correct refractive error on time, and improve their quality of life. To encourage scaling up of ROP screening and treatment throughout the country.

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LIST OF ABBREVIATIONS

Acronym	Abbreviations
AP-ROP	Aggressive Posterior-Retinopathy of prematurity
Bwt	Birth weight
GA	Gestational age
ICROP	International Classification of Retinopathy of Prematurity
MMed	Masters of medicine
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
NPL	No perception of light
PMA	Post menstrual age
PNA	Postnatal age
PL	Perception of light
ROP	Retinopathy of prematurity
VEGF	Vascular endothelial growth factor
WHO	World Health Organization

DEFINITION OF KEY TERMS

Gestation age (GA): It is the time elapsed between the first day of the last normal menstrual period and birth measured in weeks(2).

Premature newborn: Is a live baby born before the completion of 37 weeks of gestation(3).

Retina: a layer in the back of the eyeball that contains light-sensitive cells which generate nerve impulses that travel to the brain via the optic nerve and form a visual image(4).

Retinopathy of Prematurity: This is an eye disorder affecting premature babies characterized by abnormal blood vessel development in the retina(5).

Post menstrual age (PMA): It is the time elapsed from the first day of the last normal menstrual period and birth to the time elapsed after birth, expressed in weeks(6).

Visual acuity: Sharpness of vision, measured by the ability of an eye to discern letters or numbers at a given distance according to a fixed standard(7).

Anti VEGF agents: they are medications that blocks the vascular endothelial growth factor (VEGF), thereby slow or stop damage from the abnormal vessels in the retina (33).

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND

Retinopathy of prematurity (ROP) is a potentially blinding disease caused by abnormal growth of retinal blood vessels in premature infants. It occurs in premature infants who are born before the retinal vessels complete their normal growth. The prevalence of premature delivery remains significant, approximately 13.4% worldwide (2)(37). ROP accounts for about 10% of childhood blindness worldwide (5)(10). Advances in obstetric and neonatal care, have allowed even extremely premature infant to survive, which has contributed to an increase in number of cases of ROP. Lower gestational age, low birth weight, and prolonged exposure to unregulated oxygen contribute to the emergence of ROP as a serious problem (3). The estimated incidence of ROP ranges from 5% o 29%, and about 8.8% to 26.8% of those affected require treatment (3)(38).

In cases of retinopathy of prematurity (ROP), the underdeveloped retina may lack retinal vessels in certain areas, causing retinal ischemia. This leads to the release of growth factors that stimulate abnormal vascular growth. The normal process of vascular growth is disrupted, and new blood vessels proliferate into the vitreous cavity at the junction between the vascular and avascular retina. As the disease advances, complications such as vitreous hemorrhage and tractional retinal detachment may occur, and eventually leading to blindness. Other complications that affect the visual development may occur. Myopia being the most common refractive error in children born premature whether treated or not treated for ROP. There is also increased incidence of strabismus, anisometropia (different in refractive power between the two eyes) and amblyopia (poor vision due to abnormal visual experience early in life) (12).

ROP is classified according to international classification of ROP (ICROP) depending on the anatomical zones I-III, the extent of the disease, stages 1-5, and the state of the vessels in the posterior pole (plus disease- vessel tortuosity and dilation). Aggressive posterior ROP (AP-ROP) is usually considered to be a separate condition and it is characterized by several signs

indicating significant vascular anomalies in the posterior pole(8)(12)(13). Different treatment modalities are used in the treatment of ROP. These include intravitreal anti- vascular endothelial growth factor (anti-VEGF) injection, laser photocoagulation therapy, cryotherapy, scleral buckling, and vitrectomy. Intravitreal anti-VEGF include Bevacizumab, Ranibizumab and Aflibercept are currently used in the treatment for type 1 ROP (zone I any stage with plus disease, zone I stage 3 without plus disease or zone II or III stage 3 with plus disease) and aggressive posterior ROP (APROP). For stage 4A which is characterized by partial retinal detachment extra fovea, laser photocoagulation therapy can be used (14).

Cryotherapy though less commonly used in treatment for severe ROP has a significant reduction in disease progression and improvement in visual development. In comparison between laser photocoagulation and cryotherapy, myopia reported to be less severe in the eyes treated with laser as compared to those treated with cryotherapy (14).

Scleral buckling is usually performed in stage 4 and 5 which are characterized by partial retinal detachment and complete retinal detachment respectively. This procedure makes the retina to flatten back onto the wall of the eyeball. Vitrectomy is performed in stage 5 ROP in which the vitreous is removed and replaced by saline solution allowing the retina to relax and lay back against the eyewall (15).

The above-mentioned treatment modalities have been reported to have some structural effect on the retina. Cryotherapy since it is applied to the peripheral retina, it can result in reduction of peripheral vision, but also associated with high myopia (14). Intravitreal anti-VEGF injection have been reported to have less damage to the retinal tissue as well as preservation pf peripheral vision (35).

The structural outcomes of the treatment vary depending on several factors like birth weight, GA at birth, PMA, and gender. Most commonly, babies born with very low birth weight and more premature are reported to have a poor outcome (9)(11)(16)(17). The disease stage as well as aggressiveness of a disease affects the outcomes of treatment. The most advanced stage of ROP has a poor outcome after treatment (14)(16)(18). Although few studies have found a link

between the aforementioned factors and treatment outcomes, the effect of those factors on treatment outcomes remain inconclusive.

Infants who have type 1 ROP, stage 4 and stage 5 disease are reported to have poor visual acuity ranging from 6/60 or worse even after having an adequate treatment for their condition. Myopia has been found to be the common refractive error in babies with ROP whether the disease resolve spontaneously without treatment or with treatment. The presence of refractive error is associated with development of amblyopia and eventually strabismus in affected children. Visual acuity assessment, refraction and strabismus assessment are essential during the follow up of these babies.

ROP screening and treatment was initiated in 2019 at Muhimbili national Hospital (MNH). Screening is performed on infants born at a gestational age of less or equal to 34 weeks at 4 weeks post-delivery with a birth weight of less than or equal to 2000grams, or with a birth weight of more than 2000grams but with other risk factors such as multiple blood transfusions, or prolonged supplemental oxygen therapy. Those infants who are diagnosed with ROP and require treatment receive either intravitreal Bevacizumab injection or laser photocoagulation, depending on the severity of the disease at the time of screening. The outcomes of these treatment are not yet known. Therefore, it was important to conduct a study on outcomes and associated factors of retinopathy of prematurity treatment at MNH.

1.2 PROBLEM STATEMENT

Globally, ROP is the leading cause of visual impairment in children, and remains the leading cause of blindness in about 10% of infants worldwide (10)(12)(15). Estimated incidence rate of premature births estimated to be 5% worldwide. In Tanzania, the estimated preterm birth rate is 11.4% (36). Due to Improved obstetric and neonatal care allow even a very premature infant to survive adding to the magnitude of ROP (22). A blind child is a burden to the family, community and country emotionally, socially and economically. Also, a blind child faces difficulties in learning, social dependency as well as reduced productivity in adulthood. ROP can only be detected through screening of premature infants. Early detection of infants with ROP is very crucial for timely treatment and prevention of blindness.

Several previous studies have examined the outcomes of different treatment approaches for ROP, but their findings have been inconsistent. Some studies have found that laser photocoagulation therapy cause more myopia than intravitreal anti-VEGF injection (31). Moreover, while some studies have identified factors such as birth weight and gestational age as predictors of ROP treatment outcomes, others have found no significant associations (11)(14)(20)(21).

For the past three years at MNH, all infants who are diagnosed with ROP and required treatment received either intravitreal Bevacizumab of laser photocoagulation depending on the disease presentation at time of diagnosis.

However, there are no available data on treatment outcome on children treated for ROP. Therefore, this study aimed at finding out treatment outcomes and associated factors influencing outcomes in ROP treated cases at MNH.

1.3 CONCEPTUAL FRAMEWORK

Several studies have discussed several treatment strategies based on the severity of ROP and how certain factors influence treatment outcome. (11)(14)(16)(18).

This study revealed the structural, visual and refractive outcome after treatment in babies who had ROP requiring treatment and factors influencing their outcomes at MNH.

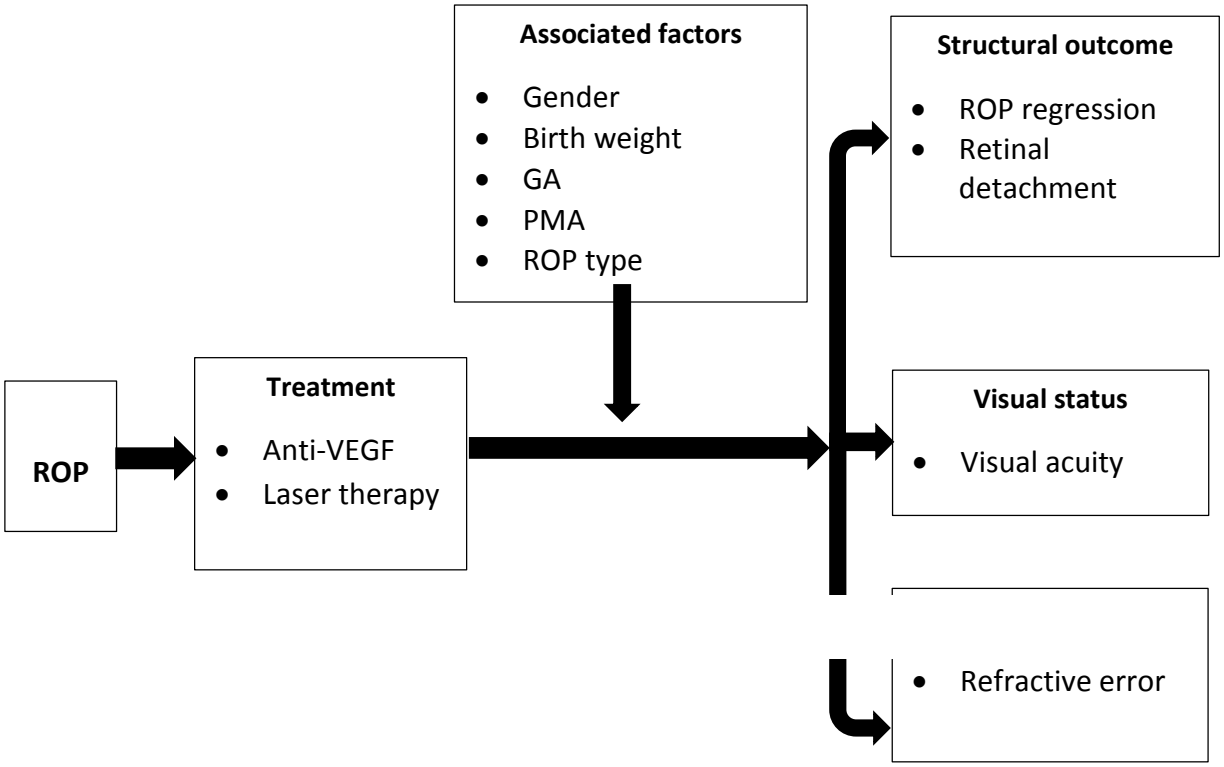


Figure 1: **Describes the relationship between independent variables and their possible outcomes**.

1.4 RATIONALE

The result of this study helped in ruling out factors associated with ROP treatment outcomes, this provides an evidence-based insight to healthcare providers such as neonatologists and ophthalmologists to improve their care for premature infants with ROP. Also, this study showed how factors such as birth weight, postmenstrual age, gestational age, and type of treatment received influence the outcomes of ROP treatment hence will help healthcare providers refine their management strategies, ultimately enhancing overall treatment efficacy and improving outcomes for infants affected by ROP.

1.5 RESEARCH QUESTIONS

1. What are the structural outcomes among patients treated for ROP at MNH during the study period?

2. What is the visual status among patients treated for ROP at MNH during the study period?

3. What is the refractive status among patients treated for ROP at MNH during the study period?

4. What are the associated factors that determine the outcome of treatment of patients treated for ROP at MNH during the study period?

1.6 OBJECTIVES

1.6.1 Broad Objective

To assess outcomes and associated factors of children treated for ROP at Muhimbili National Hospital.

1.6.2 Specific objectives

1. To determine structural outcomes among children treated for ROP at MNH during a study period.
2. To determine the visual status among children treated for ROP at MNH during a study period.
3. To determine refractive status among children treated for ROP at MNH during a study period.
4. To determine associated factors influencing treatment outcomes among children treated for ROP at MNH during a study period.

1.7 LITERATURE REVIEW

Retinopathy of prematurity (ROP) is a preventable cause of childhood blindness. Due to advancements in neonatal care, there is an increase in the number of premature children who survive, hence the risk of developing ROP increases (22). The incidence of children with ROP requiring treatment range from 4% to 44.8% (23)(34). To gather information on the treatment outcomes, a comprehensive literature search was conducted. The search included the keywords like “Retinopathy of Prematurity”, “ROP treatment outcomes”.

Additionally, the literature review highlighted that treatment outcomes and influencing factors for ROP are unknown in many African countries, including Tanzania, due to the recent establishment or absence of screening and treatment programs (24). This highlights a critical gap in knowledge and underscores the need for further research in these regions.

1.7.1 Structural outcomes of ROP treatment

There are different treatment modalities that are employed in the treatment of ROP which include cryotherapy, laser photocoagulation, intravitreal anti-VEGF, and surgeries which are vitrectomy and scleral buckling. These treatments have different structural outcomes ranging from disease regression to retinal detachment.

1.7.1.1 Structural treatment outcomes for Intravitreal anti-VEGF agents

Different structural outcomes following intravitreal anti-VEGF agents have been reported by several reports. In a study done by Quijing Huang et al. in China where premature children received intravitreal Ranibizumab, 94% had disease regression (16). Similar findings seen in Romania by Simona Nicoara et al., where ROP regression was seen in 85.1% (18).Another study which was done in China by Tong et al. 2018, about 65.6% of children who received intravitreal Bevacizumab had disease regression (25). In Africa, a study done in South Africa by Kana H et al. found that 95.3% of cases which received Intravitreal Bevacizumab had complete regression of ROP (26).

1.7.1.2 Structural treatment outcomes for Laser photocoagulation therapy

Laser photocoagulation in children with ROP requiring treatment has promising results in terms of structural outcome. A study done in Phillipines by David Francis Fullon et al. has shown about 60% of infants had ROP regression. Similar findings were observed in a study done by Andres Kychetal et al. (64.6%) (11)(27). A study done by Yothin Titawattanakul et al. in Thailand and in Iran by Homeira Bigdeli. et al about 88.46% and 84% had disease regression respectively (9)(20). Other studies done by Sudha Chaundary et al. in India and by William V Good et al. have found that only 9% of children with ROP who received laser therapy had a disease progression (20)(28).

1.7.1.3 Structural treatment outcomes for surgical treatment

Surgeries in the treatment of children with ROP are employed in cases of advanced stages of a disease, stage 4 and stage 5 with the successful structural outcome. Vitrectomy and scleral buckling are widely performed if initial treatment fails or the disease is in its advanced stage. This was observed in a study done by Yothin Titawattanakul et al. in Thailand, in which both vitrectomy and scleral buckling were employed in the treatment had retinal reattachment in about 75% of ROP treated cases (28). Also, another study done by Andres Kychetal et al. found about 87% had a successful structural outcome (27).

1.7.2 Visual status after ROP treatment

The visual status is determined by the visual acuity assessed using different techniques depending on age of a child. Visual acuity varies among children who receive ROP treatment depending on modality of treatment received.

1.7.2.1 Visual status after Intravitreal anti-VEGF

Visual status in children who received intravitreal anti-VEGF seems to be good. A study done in Romania by Simona Delia Nicoara et al. in Romania, they study on outcomes and prognostic factors of intravitreal Bevacizumab found that about 94.4% had VA within normal limits (18).

1.7.2.2 Visual status after Laser photocoagulation therapy

In laser treated children, the VA is good with only 14.3% having unfavorable VA which is NLP, LP and low vision. This was found in a study done by William V good et al. which was about final result on Early Treatment of ROP (ETROP), where they assessed grating VA by Teller acuity cards (28).

1.7.3 Refractive status after ROP treatment

The prevalence of refractive error in children who received treatment for ROP varies depending on the type of treatment given. Most studies reported high prevalence of myopia in children who received treatment.

1.7.3.1 Refractive status after Intravitreal anti-VEGF

A study done in Houston by Mintz-Hittner et al. about treatment outcomes following Bevacizumab therapy compared with conventional therapy found the prevalence of low myopia was3.8% while 1.7% had high myopia (29).

Another study done in China by Chen YH et al., which assessed the prevalence of refractive error in children with ROP treated with intravitreal Bevacizumab after 2years. The study found that 47.5% of cases had low myopia, while 10% had high myopia. (19).

1.7.3.2 Refractive status after Laser photocoagulation therapy

A study done in Vietnam by Phuoc Huu Nguyen et al., found the prevalence of refractive error was as high as 80% of which 59% was myopia and 21% was hyperopia. Same study, found the prevalence of astigmatism was about 79%, while 49% had high astigmatism and 6% had esotropia while 4% had exotropia (17). Similarly, a study done by Mintz-Hittner et al. found that, high myopia was about 51.4% and 36.4% in zone II and Zone II respectively (29). However, a study done in China by Chen YH et al. showed that the prevalence of myopia was as high as 82.4% (19).

1.7.4 Associated factors for outcomes of treatment

Some of the risk factors for developing ROP which are patient based are linked to have an effect on the outcomes of treatment. Factors like very low birth weight, greater prematurity expressed in GA, older PMA and more advanced ROP stage have been linked to having poor structural as well as visual outcomes.

1.7.4.1 ROP severity

Different stages and severity of a disease influence the outcomes of treatment. A study done in China by Quijing Huang et al. assessed anatomical outcome following ROP treatment with intravitreal Ranibizumab and factors influencing it, found that those with zone II have lower risk of disease reactivation as compared with more severe forms which was about 80% (16).

A study done by Simon Delia Nicoara et al. in Romania 2015 has shown that success rate in regression of ROP occurs more in infants with a less severe form of ROP who were treated with Intravitreal Bevacizumab. Disease regression was 100% in zone 1 stage 3+ while 85.13% had disease regression in babies who had aggressive posterior ROP (18).

Children treated with laser also show different outcomes depending on presentation of a disease at time of treatment. A study done by Andres Kychental et al. showed babies who had anterior zone 1 ROP had disease regression 64.6%, and the remaining with posterior zone 1 disease had disease progression (27).

Surgery which involves vitrectomy and scleral buckling as modalities of treatment in stage 4A, 4B and 5 ROP, have different anatomical outcomes. A study done in India by PK Shah et al., the structural success result for stage 4A was 90%, stage 4B 44.4% and stage 5 14.3% (14).

Another study done by Andres Kychental et al. on clinical characteristic and treatment outcomes following laser and surgery of babies with ROP, in a surgically treated group 74% of stage 4 had good structural while only 13% in stage 5 had good structural outcome (27).

Visual outcome after treatment can also be affected by ROP stage. This was shown in a study done by PK Shah et al. in India, babies who had ROP stage 4B and 5 had poor visual outcome

with VA of PL about 21.4%, the rest had NPL while those with stage 4A had central fixation (14).

Type of ROP influence the structural outcome which later defines the visual status of a child. This was reported in a study done Simon Delia Nicoara et al. in Romania, found that children who had good structural outcome which was influenced by type of ROP about 94.4% had normal VA (18).

1.7.4.2 Gestation Age (GA)

Higher GA associated with good outcome, while the lower the GA associated with poor outcome of treatment. A study done in China by Quijing Huang et al. reported that children who had GA of less than 29.5weeks had ROP regression in about 38.4%, while those who had GA greater than 29.5weeks had disease regression in about 70.4% after initial treatment with intravitreal Ranibizumab (16).

A study done in Phillipines by David Fullon et al. assessed anatomical outcome following laser photocoagulation therapy, children who had median GA of 28wks had good structural outcome which is disease regression (11). This was similar to a study done by Homeira Bigdeli et al. which had a P value of 0.021 (9).

In contrary to the above studies, a study done in Romania by Simona Delia Nicoara et al. showed that GA had no influence on the structural outcome following treatment with intravitreal Bevacizumab (18).

A study done by Phuoc Huu Nguyen et al in Vietnam looked on refractive outcome after laser treatment, reported that the proportion of myopia was higher in children who had GA 28weeks and below compared to those who had GA 29weeks or higher (17).

1.7.4.3 Birth weight

The lower the birth weight affects the treatment outcome. A study done by Qiujing Huang et al. reported that, children with lower birth weight have poor structural outcome after treatment with Intravitreal Ranibizumab (16). In contrary to the study done by Simona Delia Nicoara et al.

reported that birth weight had no influence on the structural outcome after treated with intravitreal Bevacizumab (18).

Another study done by David Francis Fullon Chan et al. in Phillipines 2019, reported that median birth weight of 1112.86g associated with good outcome of treatment after receiving laser photocoagulation therapy although was statistically not significant (11)(5). However, a study done in Iran 2017 by Homeira Bigdeli et al. reported that lower birth weight associated with poor structural outcome (9).

Other factors like PMA, PNA at first examination have been reported in some studies to have influence on the treatment outcome. A study done by Homeira Bigdeli et al. in Iran 2017 and Davis Fullon Chan et al. 2019 where older PMA and PNA associated with poor outcome (9). However, Simona Delia Nicoara et al. reported factors like PMA and PNA were statistically not significant (18).

CHAPTER TWO

2. METHODOLOGY

2.1 Study design

The study design was a hospital based analytical cross-sectional study.

2.2 Study Area

This study was conducted at Muhimbili National Hospital (MNH) which is a national referral hospital, and used as a teaching hospital for MUHAS, located at Upanga in Ilala district, Dar es Salaam, Tanzania. The rate of preterm baby admissions averages at 280 newborns per month and about 50% of them are extreme low birth weight (<1000g).

The study was conducted specifically at the ROP screening clinic and pediatric eye clinic at Muhimbili National Hospital (MNH). ROP clinic at MNH is conducted every Monday. Children who meet the criteria for screening in the premature ward and neonatal ICU ward are given an appointment for screening. Those found with a disease requiring treatment are scheduled for treatment which is done in the operating theatre and children who have been discharged from ROP clinic are being attended at the pediatric eye clinic which is done two times per week, Mondays and Fridays.

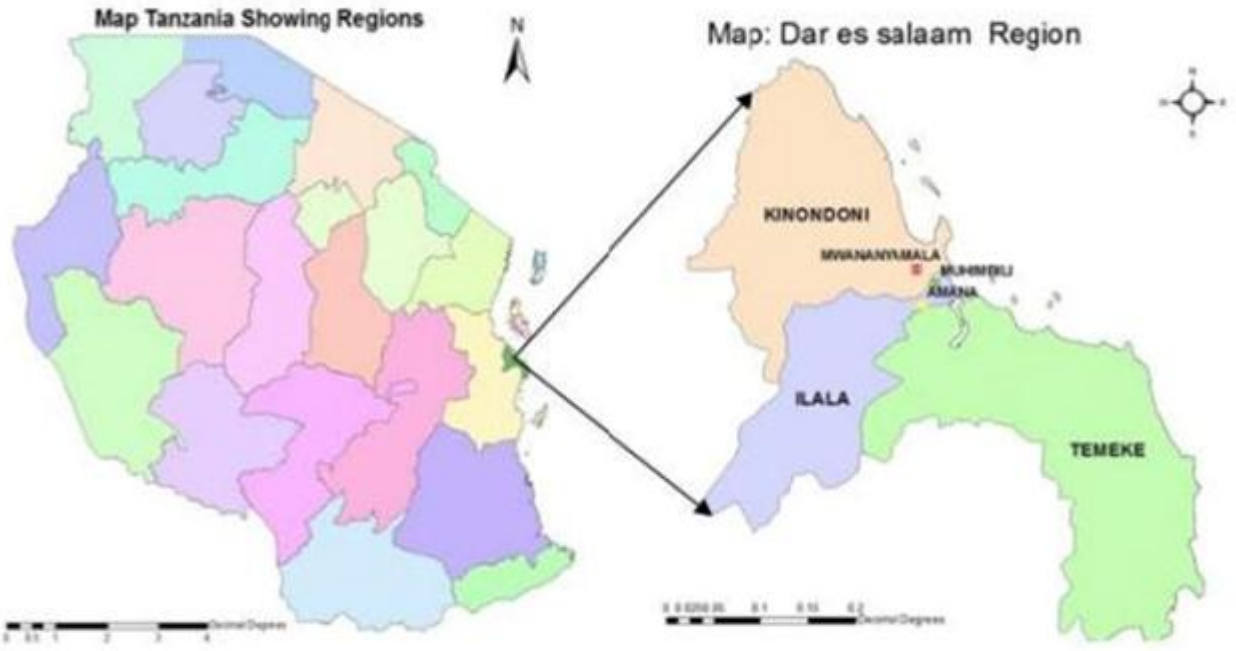


Figure 2: Map of Dar es Salaam city.

2.3 Study Period

This study was conducted for a period of six months, from August 2022 to January 2023.

2.4 Study Population

All children who received treatment for Retinopathy of Prematurity (ROP) from July 2019 to December 2021.

2.5 Inclusion criteria

Children who were diagnosed with type 1 ROP (Zone 1 any stage with plus disease, zone I stage 3 without plus disease and zone II or III stage 3 with plus disease), stage 4A (partial retinal detachment extrafoveal) and aggressive posterior ROP (APROP) and received treatment either with intravitreal Bevacizumab injection or laser photocoagulation from July 2019 to December 2021 or both and have completed 6 months after receiving treatment.

2.6 Exclusion criteria

Children with any ocular congenital disease that affect visual and refractive status, making fundus examination impossible.

2.7 Sample size calculation

The sample size has been calculated using the modified Cochran's formula due to the finite population as follows:

$$n = \frac{Nz^2\, p\,(100 - p)]}{e^2(N-1) + z^2p(100-p)}$$

Where;

n = The number of participants required in the study

z= Confidence interval (95% of C.I. =1.96) expressed as a percentage point of the normal distribution

e= Maximum error expected in the study, 5%

p = expected proportion in the population (8.8% is a proportion of the children who received treatment in a study done by Yusta et al at Dar es salaam, Tanzania)

N= total number of patients who received treatment for retinopathy of prematurity (ROP) from July 2019 to December 2021

$$n = \frac{[76(1.96)^2 \times 8.8 \times (100 - 8.8)]}{5^2(76-1) + (1.96)^2\, 8.8(100-8.8)}$$

n= 47

The sample size required was 47 children who received treatment for ROP, but 40 children were available and included in the study.

2.8 Sampling method

The consecutive sampling technique was used. All children who met inclusion criteria were recruited for the study during the study period.

2.9 Data collection tools

A well-structured questionnaire was used to fill in participants' information obtained during data collection. The questionnaire consisted of four parts. The first part collected participant's demographic data. The second part collected information regarding structural findings and the third part collected information on visual status and refraction status. The fourth part collected participants' information concerning birth weight, GA, PMA at first screening, diagnosis and treatment given and PMA during treatment.

2.10 Data collection procedure

All children who attended ROP screening clinic and pediatric eye clinic and met the inclusion criteria were included in the study. Those children who were not attending the clinic, phone numbers of their parents were traced from the ROP record book and called to participate in the study. Data was collected twice per week, Mondays and Fridays. Parents or caretakers were given a consent form to sign for confirmation of agreeing to participate in the study.

Medical records were reviewed to provide information on ROP-related factors such as zone of ROP and circumferential extent of extraretinal proliferation, gestational age at birth in weeks, birth weight in grams, the eye whether right or left or both, and type of treatment given.

The visual status of each child was checked using age specific test. For those who were 6months to 18months old, VA was tested using a Teller acuity and Cardiff card at a 50cm distance. For those who were 2 to 3years old, Kay pictures was used in testing the visual acuity. The VA readings obtained graded according to WHO visual acuity ranges and categories which are; normal vision when VA is 6/18 or better, moderate visual impairment when VA is less than 6/18 to 6/60, severe visual impairment when VA is worse than 6/60 to 3/60, and blindness when VA is worse than 3/60. Then, VA of 6/18 and better was considered a good visual outcome and VA of less than 6/18 was considered to be a poor visual outcome.

Refraction status was obtained by doing cycloplegic refraction in which cyclopentolate eye drop 1% was used. Objective refraction was done by one experienced optometrist with experience in doing pediatric refraction using a streak retinoscope (Riester Ri-scope L2 Xenon, 3.5V), and trial lenses. The refraction obtained and was graded as follows; low myopia is when the refractive error was equal or less than -3D, moderate myopia when a refractive error was between -3D to -6 D and high myopia is when a refractive error was equal or greater than -6D. Low hyperopia is when a refractive error was equal or less than +2D, moderate hyperopia is when a refractive error was between +2D to +5D (however, in children of less than 3years of age a hyperopia of +3.5D or less in considered to be normal), and high hyperopia is when refractive error is greater than +5D. Also, astigmatism and high astigmatism was defined as cylinder of 1 D and 2 D respectively.

Complete ocular examination was done using pen torch and slit lamp examination. Retinal examination was done by using binocular indirect ophthalmoscope (AAO wireless Appasamy Associates), scleral depressor and 20 Diopter Volk condensing lens. Media clarity checked followed by retinal examination of both eyes. Visualization of peripheral retina aided by scleral depressor, taking care not to put too much pressure on the globe.

Then the ROP specialist reviewed again all children for consistency of the findings obtained from the fundus examination before making the final diagnosis.

2.11. Study Variables

2.11.1 Dependent Variables

ROP regression, retinal detachment, visual status, and refractive status.

2.11.2 Independent Variables

PMA, GA, birth weight, disease severity and type of treatment.

2.12 Data Analysis

Data entry and analysis was performed using Statistical Package for Social Sciences (SPSS) version 24. Description of demographic data of participants who received treatment for ROP was done using frequencies and percentages. Frequencies and percentages were also used to determine the treatment outcomes of ROP in the study population. Fisher's Exact Test was used to show association between type of treatment received with visual status and refraction status.

Multiple linear regression analysis was used to check for the association of visual acuity and influencing factors like PMA, GA, birth-weight, and zone of a disease. Univariate and Multivariate logistic regression analysis was done to test for the strength of association between factors and likelihood of refractive error. Variables that showed statistical significance in univariate analysis were transferred to multivariate analysis to control for confounders. Confidence level was set at 95% and p-value of less than 0.05 was considered to be statistically significant.

2.13 Ethical Consideration

Ethical approval

Ethical clearance was requested from MUHAS Institutional Review Board (IRB). Permission to conduct the study was sought from the executive director of Muhimbili National Hospital (MNH).

Written informed consent was obtained from the parents and guardians of all children who met inclusion criteria prior to enrolment in the study. Parents or caretakers of the study participants had the right to withdraw from the study. Every parent or caretaker were informed about his/her child's VA, refractive status, and retinal findings after the examination. They were also informed of any abnormality that was picked during the examination of a baby as well as treatment options that are available. This study did not cause any harm to the participants or any other participant who in one way or another were involved in the study.

Confidentiality

The information on the data collection tool was only accessible to the investigator and involved research team. All information collected on the participant was considered confidential and treated as such. All personally identifiable information was kept private in the questionnaire.

2.14 Dissemination Plan

Findings from this study was presented to the ophthalmology department as well as at the Tanzania Ophthalmology Society (TOS) conference. The report of this study will be submitted as a dissertation to Muhimbili University of Health and Allied Sciences as a partial fulfillment for the award of Degree of Masters of Medicine in Ophthalmology. A copy of a study report submitted to the department of Ophthalmology MUHAS, MUHAS library, and to a reputable peer-reviewed journal for publication.

CHAPTER THREE

3.0 RESULTS

A total of 933 were screened for retinopathy of prematurity from 2019 to June 2022, and among them 8.1% received treatment for ROP with the response rate of 52.6%.

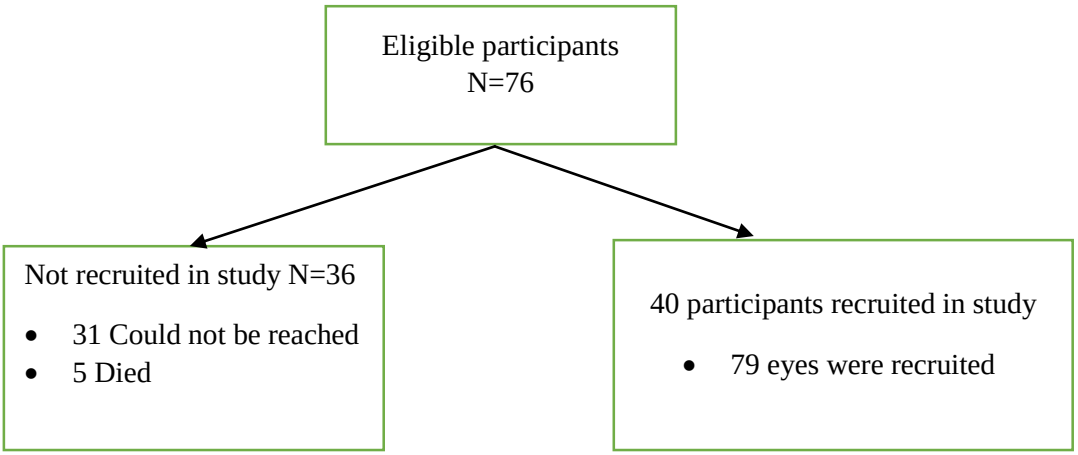


Figure 3: Flow chart showing recruitment of the study participants

A total of 40 participants (79 eyes) were recruited and analyzed. One eye had a total retinal detachment and the patient was referred to a vitreoretinal surgeon after completing treatment of the other eye. Of the 40 participants 26 (65.0%) were females. Majority were aged between 7months to 12months with the mean age of 11.50 months. Most of the participants were coming from Temeke district (Table 1).

Table 1: Demographic characteristics of the study participants, N=40

Characteristic	**Frequency**	
	n	**(%)**
Sex		
Male	14	35.0
Female	26	65.0
Age (*months)*		
7 – 12	29	72.5
13 – 18	06	15.0
19 – 24	03	7.5
> 24	02	5.0
Mean 11.50 (±*5.60SD*)		
Residence		
Kinondoni	07	17.5
Ilala	06	15.0
Ubungo	06	15.0
Temeke	16	40.0
Kigamboni	01	02.5
Others*	04	10.0
Total	40	100

Others: 1-Pwani, 1-Songea, 1-Lindi, 1-Mtwara

Table 2: Distribution of clinical characteristics among the study participants, N=40

Characteristic	Frequency	
	n	%
Birth weight (*grams)*		
600-800	13	32.5
801-1000	11	27.5
1001-1200	08	20.0
1201-1400	06	15.0
1401-1600	02	5.0
Mean 995.06 (±*253.70SD*)		
GA (*weeks*)		
26-27	09	22.5
28-29	16	40.0
30-31	11	27.5
32-33	04	10.0
Mean 28.88 (±*5.60SD*)		
PMA at treatment (*weeks*)		
30-32	13	32.5
33-35	19	47.5
36-38	07	17.5
39-41	01	2.5
Mean 33.63 (±*2.40SD*)		
Total	40	100.0

One third of the participants had birth weights between 600-800 grams and most had gestational age between 28-29 weeks (40.0%) (Table 2).

Majority of the eyes (72.2%) had stage 3 disease

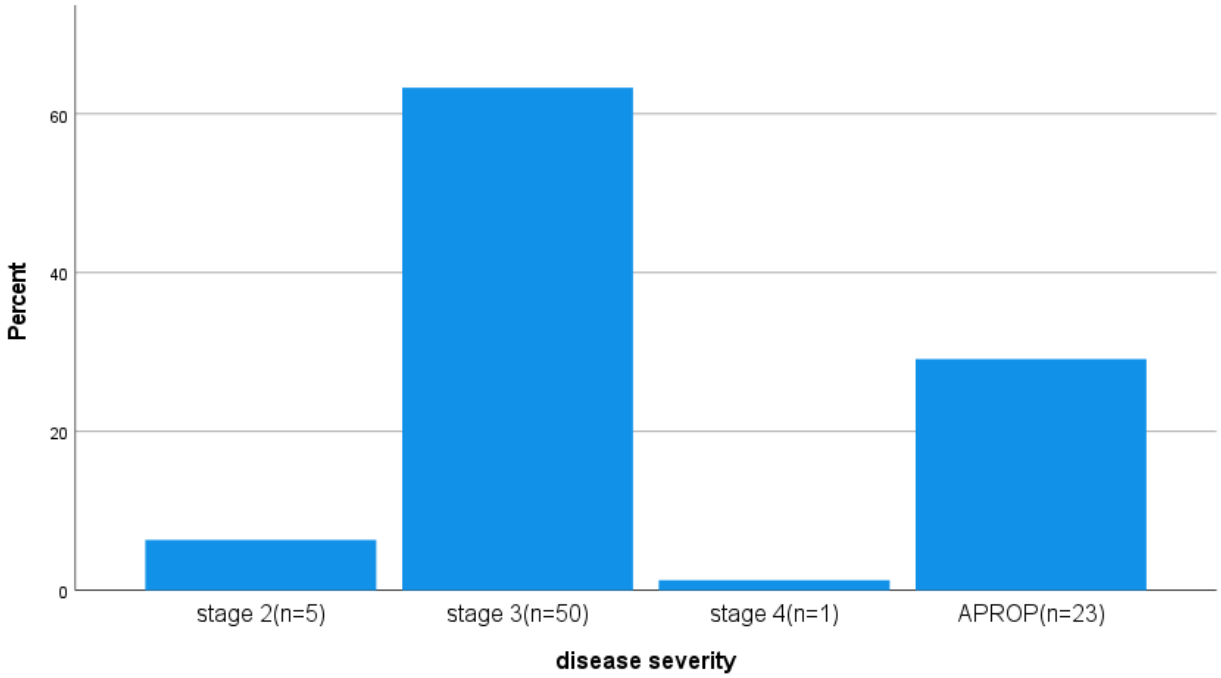


Figure 4: Distribution of disease severity among eyes which received treatment, N=79

Table 3: Zones and stages of ROP among eyes of study participants, N=79

Zone	ROP stage				Total
	Stage 2	Stage 3	Stage 4	APROP	
	n (%)	n (%)	n (%)	n (%)	n (%)
Zone I	0 (0.0)	29 (54.7) 26*	1 (1.9)*	23 (43.4)	53 (100.0)
Zone II	5 (19.2)*	21 (80.8)*	0 (0.0)	0 (0.0)	26 (100.0)
Total	5 (6.3)	50 (63.3)	1 (1.3)	23 (29.1)	79 (100.0)

**indicates "plus disease"*

Majority (96.7%) of eyes had zone I stage 3 disease. 53 eyes had plus disease and all with plus were either stage 2, stage 3 disease or APROP (Table 3).

Among 79 eyes which were treated, 87.3% received intravitreal Bevacizumab alone.

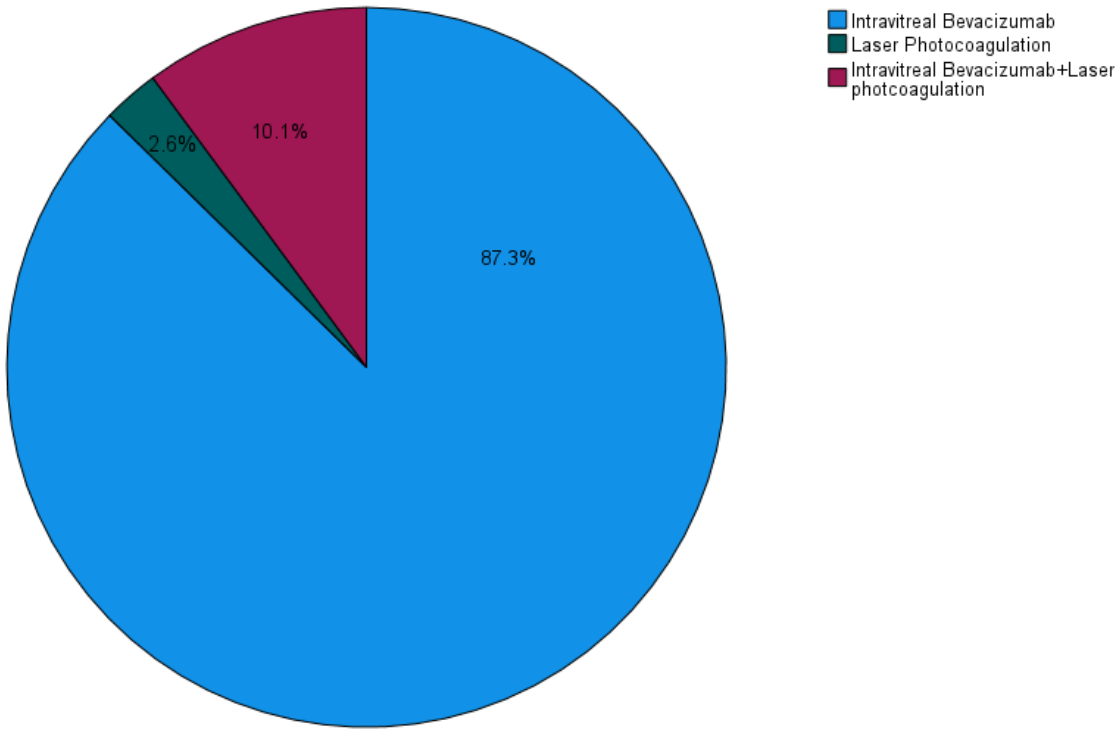


Figure 5: Type of treatment received among eyes of the study participants, N=79

Table 4: Distribution of structural outcomes among eyes with ROP three months and after 6months post-treatment, N=79 eyes

Structural outcomes	At 3 months	At 6 months
	n (%)	n (%)
ROP regression	78 (98.7)	79 (100)
ROP progression	01 (1.3)	0 (0.0)
Total	79 (100.0)	79 (100)

At three months only one eye had progressed, and at six months all eyes had disease regression (Table 4).

Table 5: Distribution of presenting visual status among eyes of the study participants, N= 79

Visual status (Visual acuity)	Frequency	
	N	%
Normal vision (6/6 - 6/18)	63	79.7
Moderate visual impairment (<6/18- 6/60)	14	17.7
Severe visual impairment (<6/60 - 3/60)	01	01.3
Blindness (<3/60)	01	01.3
Total	79	100.0

Majority (79.7%) of eyes had normal vision (Table 5).

Table 6: Distribution of refraction status among eyes of study participants, N= 79 eyes

Objective Refraction status	Frequency	
	N	%
Low hyperopia (≤ +2D)	29	36.7
High myopia (≥-6D)	11	13.9
Moderate myopia (>-3D to < -6 D)	20	25.3
Low myopia (≤ -3D)	14	17.7
Mixed astigmatism	5	6.3
Total	79	100.0

The majority of eyes had myopia (Table 6).

Table 7: Relationship between type of treatment received and presenting visual acuity, N=79 eyes

Type of treatment	Presenting visual acuity				p-value
	6/6-6/18 n (%)	<6/18-6/60 n (%)	<6/60-3/60 n (%)	<3/60 n (%)	
Avastin injection	65 (81.9)	13 (18.8)	0 (0.0)	0 (0.0)	
Laser photocoagulation	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.029
Avastin + laser photocoagulation	5 (62.5)	1 (12.5)	1 (12.5)	1 (12.5)	

Fisher's Exact Test used

Majority (81.9%) of eyes treated with Avastin injection only had normal vision (p-value= 0.029) (Table 7).

Table 8: Relationship between type of treatment received and refraction status, N=79 eyes

Type of treatment	Refraction status		p-value
	No refractive error n (%)	Refractive error n (%)	
Avastin injection	26 (37.7)	43 (62.3)	
Laser photocoagulation	2 (100.0)	0 (0.0)	0.073
Avastin + laser photocoagulation	1 (12.5)	7 (87.5)	

Fisher's Exact Test used

Type of treatment received has no relationship with the development of myopia (p-value= 0.073) (Table 8).

Table 9: Relationship between type of treatment received and refraction status, N=79 eyes

Gestational age (GA)	Refraction status		p-value
	No refractive error n (%)	Refractive error n (%)	
<28 weeks	3 (18.8)	13 (81.3)	0.081
28-32 weeks	26 (41.3)	37 (58.7)	

Majority of eyes of babies with GA less than 28 weeks had refractive error, however was significant (p-value= 0.081) (Table 9).

Table 10: Linear regression analysis between factors and presenting visual acuity among eyes of study participants, N=79 eyes

Factors	Coefficients Beta	T	p-value	95.0% CI	
				Lower limit	Upper limit
Birth weight	0.121	0.925	0.564	0.000	0.001
GA	-0.441	-1.876	0.063	-0.152	0.004
PMA at treatment	0.222	1.238	0.093	-0.007	0.088
Zone	-0.155	-1.151	0.255	-0.682	0.185

A 1% in GA, the presenting visual acuity decrease by about 0.441 logMAR. This suggest that increase in GA will increase the presenting visual acuity however, this was not statistically significant (p-value=0.063, 95%CI= -0.682-0.185) (table 9).

With each unit increase in Zone, the presenting visual acuity decrease by 0.155 logMAR, even though it was not statistically significant (p-value=0.255, 95%CI=-0.682-0.185) (Table 10).

Table 11: Logistic regression analysis of factors and refraction error among eyes of study participants, N=79 eyes

	Univariate Analysis			Multivariate Analysis		
Factors	**cOR**	**95%CI**	**p-Value**	**aOR**	**95%CI**	**p-value**
Birth weight	1.003	1.001-1.005	0.083	1.005	1.001-1.009	0.068
GA	1.210	0.921-1.589	0.172	0.653	0.348-1.225	0.184
PMA	1.183	0.931-1.503	0.183	1.130	0.714-1.789	0.714
Zone	1.355	0.512-3.585	0.541	-	-	-
Types of Treatment						
Avastin injection	0.222	0.026-1.908	0.170	0.130	0.013-1.263	0.079
Laser photocoagulation	0.000	0.0000	0.999	0.000	0.000	0.999
Avastin + laser photocoagulation (ref)				Ref		

Key: cOR: Crude Odds ratio, aOR: Adjusted Odds ratio, Ref: Reference category

Each additional gram in birth weight increases the likelihood of developing myopia by 0.5% (aOR= 1.005, 95% CI= 1.001-1.009, and p-value=0.068 (Table 11).

CHAPTER FOUR

4.0 DISCUSSION

Determining the anatomical, visual and refractive status of patients treated for Retinopathy of Prematurity (ROP) and the associations with contributing factors is very important for comprehensive monitoring, targeted intervention and personalized management plans. The mean age of study participants in this study was 11.50months with a range of 7 months to 29 months. In this study, the majority of participants (65.0%) were female, contrasting with findings by Parveen Sen et al., where most participants were male. This aligns with the 2022 Tanzania census, which also shows females as the majority (1)(32).

In our study, disease regression was seen in all eyes 6 months after treatment. This is similar to studies done by Huang et al. and Kana et al. that have reported high rates of disease regression about 94% and 95.3% respectively (16)(26). It was also observed that 87.3% of eyes had disease regression and complete retinal vascularization after only one injection of intravitreal Bevacizumab. This is consistent with the previous study done by Nicoara et al. where they reported 85.13% of ROP regression after one injection of intravitreal Bevacizumab (18). The higher rates of ROP regression could be due to timing of treatment after making diagnosis as treatment were initiated within 48hours. One eye progressed to stage 4A disease after one injection of intravitreal bevacizumab, however regression was achieved after laser photocoagulation therapy. In this case, the patient got lost to follow up, and came three months after treatment with partial retinal detachment. This highlights the importance of parents' compliance on proper follow up for their babies' clinic schedule. This difference can be due to type of treatment modality used, as in our study most of eyes were treated with intravitreal bevacizumab only while in their study, eyes were treated with either laser photocoagulation or cryotherapy.

In the present study, it was found that about 79.7% of eyes have normal vision. This is slightly lower compared to the study done by Nicoara et al. who reported normal vision of 94.44% in eyes with ROP which received treatment (18). The difference could be due to different visual

acuity testing method as in present study we used Teller acuity, Cardiff cards and Kay pictures while the previous study used Teller acuity only. Different modes of visual acuity (VA) testing in children can yield varying results, as each method engages different aspects of visual processing and assesses acuity at distinct levels of precision and complexity. In our study, only 2 (2.6%) eyes had severe visual impairment and blindness which is lower than a study done by William V Good et al. who reported that only 14.3% patients received treatment for ROP had LP and NLP (28). This difference can be due to type of treatment modality used, as in our study most of eyes were treated with intravitreal bevacizumab only while in their study, eyes were treated with either laser photocoagulation or cryotherapy.

In the present study, majority (63.3%) of eyes had refractive error with myopia being the most common. showed the most common refractive error is myopia. These findings are similar to the studies done by Chen YH et al. and Mints Hitlner et al. which reported a high prevalence of myopia in patients with ROP (19)(29). The prevalence of myopia in eyes treated for ROP could be due to the fact that bevacizumab and laser photocoagulation disrupt the local retinal and scleral growth signals for the development of anterior segment. Also, the prematurity itself causes steepening of the cornea, decreased depth of anterior chamber and increased thickness of the lens which might contribute to prevalence of myopia (30)(31). Further studies are needed to see the magnitude of refractive error in eyes which received treatment and those that did not receive treatment for ROP.

The present study showed that gestational age (GA), birth weight, PMA and disease severity have no association with presenting visual acuity following treatment. Similar findings were reported by other studies done by David Fullon Chan et al. and Simon Delia Nicoara et al. (11)(18). However, a study done by PK Shah et al. reported that disease severity affects the visual status following treatment for ROP (14). This discrepancy may be due to in this study most eyes had AP-ROP and stage 3 and received intravitreal bevacizumab injection while a study done by PK Shah et al. majority of eyes had stage 4 disease which received laser photocoagulation therapy which contribute to decrease in vision.

This current study also found that type of treatment received affects the presenting visual acuity. Those treated with intravitreal bevacizumab injection only, 81.9% had normal vision. This is similar to study done by Simon Delia Nicoara et al. and William V Good et al. (18)(28). This observation may be due to bevacizumab injection have less effect on the retina and sclera growth.

The refraction status among eyes treated for ROP was not found to be influenced by birth weight, GA, PMA at treatment, disease severity and type of treatment in the present study (p-value> 0.05). This finding is inconsistence with the study done by Chen YH et al. who reports that prevalence of myopia and high myopia significantly associated with ROP severity (19). The inconsistence can be because of disease presentation at the time of treatment most had stage 3 ROP while only one eye had stage 4A which is partial retinal detachment. Also, a study done by Wang JR et al. reported high prevalence of myopia in eyes treated with laser than in eyes which received intravitreal Bevacizumab injection (31). The difference could be in the present study only few eyes received laser photocoagulation therapy as compared to those who received intravitreal bevacizumab injection.

None of the treated eyes had complications associated with the intravitreal bevacizumab or laser photocoagulation therapy. Overall, the present study does not provide evidence to support the importance of GA, PMA and birth weight in predicting treatment outcomes in ROP. However, further studies with larger sample sizes, standardized treatment protocols, and extended follow-up periods are needed to confirm these findings and identify other potential factors that may influence treatment outcomes. this study does not find evidence that GA, PMA, and birth weight significantly predict treatment outcomes in ROP.

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATION

5.1 CONCLUSION

All eyes had regression of ROP following treatment at MNH. Normal vision is observed in majority of eyes. Majority of eyes had refractive errors with myopia being the most common. Factors like PMA, birth weight, and disease severity have no impact on treatment outcomes.

5.2 RECOMMENDATIONS

Efforts to screen, detect and treat children with ROP at MNH must continue in order to maintain the good outcome.

Close follow up of premature infants, especially those with lower gestational age to ensure timely detection and intervention.

Establish comprehensive post-treatment care plans that include regular eye examinations to identify and manage refractive errors.

To encourage conduction of multicenter studies to gather large sample size and more diverse populations, improving generalizability of findings.

5.3 STUDY LIMITATION AND MITIGATION

Limitation

The response rate was low as the study population is scattered and not in regular clinics due to the fact that some of the children received treatment three years ago.

Since the sample size of this study was from patients attending at MNH, then, the results obtained cannot be generalized to the general population of Tanzania.

Mitigation

Files were reviewed from the medical record to check for phone numbers and traced them. The response increased after counseling parents and caretakers on the importance of the study.

Muhimbili, being the National hospital, receiving patients referred from different parts of Tanzania, including from Tertiary hospitals in the country, then the results obtained can be generalized in MNH where treatment of ROP is done.

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APPENDIX I: Questionnaire English version

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

DIRECTORATE OF RESEARCH AND PUBLICATIONS

OUTCOMES AND ASSOCIATED FACTORS OF RETINOPATHY OF PREMATURITY TREATMENT AT MUHIMBILI NATIONAL HOSPITAL DAR ES SALAAM, TANZANIA.

S/N……

Phone number……

Hospital registration number……

Date of interview……

PART ONE: DEMOGRAPHIC DATA

1. Age……
2. Sex…….....
3. Residency……

PART TWO: ANATOMICAL OUTCOME

4. **Anterior Segment findings:** (Normal/Abnormal)
   (I) Right eye ……. (II) Left eye …….

If abnormal, specify the abnormality …….

5. **Posterior Segment findings:**
   (I) ROP regression: (Yes/No)
   RE…….. LE……
   (II) Retinal detachment (Yes/No)
   RE…..…. LE…….
   (III) Other findings ……

PART THREE: VISUAL AND REFRACTION STATUS

6. **Visual acuity test:**
   (I) Test type……..
   (II) Results: Right eye ……
   (III) Result: Left eye ……
7. **Refraction:**
   (I) Right eye ……..
   (II) Left eye ……
8. **Strabismus:** Present (Yes/No) ….....
   Type of strabismus if present……

PART FOUR: FACTORS ASSOCIATED WITH TREATMENT OUTCOMES

9. GA……
10. Birth weight……..
11. PMA at first screening…….
12. Diagnosis: (I) zone: RE…… LE…….....
    (II) Stage: RE…… LE…….
    (III) Plus disease (yes/no): RE……..... LE……..
    (IV) Other…….
13. PMA on treatment……

14. Treatment received RE LE

I). Intravitreal Bevaizumab…… ……

II). Laser photocoagulation……. ……

III). Intravitreal Bevacizumab and laser…… ...…….

IV). Surgery (Vitrectomy)…….. ……

15. How many times received treatment: RE…… LE…….

APPENDIX II: Ethical clearance letter

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR - RESEARCH AND PUBLICATIONS

Ref. No.DA.282/298/01.C/1371 Date: 22/09/2022

MUHAS-REC-09-2022-1371

Warda Khalef
MMed - Ophthalmology,
School of Medicine
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: OUTCOMES AND ASSOCIATED FACTORS OF RETINOPATHY OF PREMATURITY TREATMENT AT MUHIMBILI NATIONAL HOSPITAL DAR ES SALAAM, TANZANIA.

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 22/09/2022
EXPIRATION DATE OF APPROVAL: 21/09/2023

STUDY DESCRIPTION:

Purpose:
The purpose of this hospital-based analytical crossectional study is to assess outcomes and associated factors of Retinopathy of Prematurity treatment at Muhimbili National Hospital.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014155.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Muhimbili University of Health and Allied Sciences
DIRECTOR Research & Publications Box 65001

Prof. Bruno Sunguya
Chairman, MUHAS Research and Ethics Committee

Cc: Director of Postgraduate Studies

APPENDIX III: Introduction letter

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;

Ref. No. Ref. No. HD/MUH/T.180/2020 07th October, 2022

The Executive Director,
Muhimbili National Hospital,
P.O. Box 65000,
DAR ES SALAAM

Re: INTRODUCTION LETTER

The bearer of this letter is Warda Khalef, a student at Muhimbili University of Health and Allied Sciences (MUHAS) pursuing MMed. Ophthalmology.

As part of her studies she intends to do a study titled: **"Outcomes and Associated Factors of Retinopathy of Prematurity Treatment at Muhimbili National Hospital Dar es Salaam, Tanzania."**

The research has been approved by the Chairman of University Senate.

Kindly provide her the necessary assistance to facilitate the conduct of her research.

We thank you for your cooperation.

Ms. Victoria Mwaluko
For: DIRECTOR, POSTGRADUATE STUDIES

cc: Warda Khalef

9 United Nations Road, Upanga West, P.O. Box 65001, Dar Es Salaam; Tel. G/Line: +255-22-2150302/6; Ext. 1915;
Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz;Web https://www.muhas.ac.tz

APPENDIX IV: Permission letter

APPENDIX II: Ethical clearance letter

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR - RESEARCH AND PUBLICATIONS

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MUHAS-REC-09-2022-1371

Warda Khalef
MMed - Ophthalmology,
School of Medicine
MUHAS

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9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Muhimbili University of Health and Allied Sciences
DIRECTOR Research & Publications Box 65001

Prof. Bruno Sunguya
Chairman, MUHAS Research and Ethics Committee

Cc: Director of Postgraduate Studies

APPENDIX III: Introduction letter

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
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Kindly provide her the necessary assistance to facilitate the conduct of her research.

We thank you for your cooperation.

Ms. Victoria Mwaluko
For: DIRECTOR, POSTGRADUATE STUDIES

cc: Warda Khalef

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Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz;Web https://www.muhas.ac.tz

APPENDIX IV: Permission letter

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote:

Ref. No.: MNH/TRCU/Perm/2022/047 Date: 12th October, 2022

Head of Department
Pediatrics and Child Health
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH.

Name of student	**Walda Khalef**
Title	**"Outcomes and Associated Factors of Retinopathy of Prematurity Treatment at Muhimbili National Hospital Dar es Salaam Tanzania."**
Institution	**Muhimbili University of Health and Allied Sciences**
Supervisors	Dr. Celina Mhina
Co-Supervisor	Dr. Suzan Mosenene
Period	12th October, 2022, to 12th November, 2022

Approval has been granted to the above mentioned student to collect data at MNH.

Kindly ensure that the student abide to the ethical principles and other conditions of the research approval.

Sincerely,

Reid B. Mchome
Coordinator – TRCU
For: Head of Teaching, Research and Consultancy Unit

HEAD, TEACHING, RESEARCH & CONSULTANCY UNIT
P.O. Box 65000
DAR-ES-SALAAM
MUHIMBILI NATIONAL HOSPITAL

c.c DMS
c.c **Walda Khalef**

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