



Demographics and Clinical Patterns of Retinopathy of Prematurity at the University of Teaching Hospitals, Women and Newborn Hospital

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Retinopathy of prematurity (ROP) is a disorder of the developing retina of very low birth weight (VLBW) preterm infants. It is an important cause of childhood blindness and is listed as one of the causes of avoidable blindness in the vision 2020 - "The Right to Sight" Programme.

ROP is more prevalent in highly developed countries where neonatal services' availability, access and outcomes are good. The survival rates of Very low Birth Weight (VLBW) infant and low gestational age (GA) at the University Teaching Hospital (UTH), Women and Newborn Hospital (WNH) Neonatal Intensive Care Unit has improved.

Aims: To estimate the prevalence of ROP at UTH, WNH, NICU.

Study Design: Hospital-based cross-sectional study.

Place and Duration: Neonatal Intensive Care Unit, Women and Newborn hospital at the University Teaching Hospital, in Lusaka, Zambia between November 2021 to April 2022.

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Methodology: We included 110 (54.5% males and 45.5% females) infants either born at <32 weeks GA or weighed <1500g. Dilated fundus examinations were done at 4 to 6 weeks chronological age or 31 to 33 weeks GA. Medical records were reviewed to identify associated factors.

Results: Mean gestational age at birth was 30.6±2 weeks ranging from 27 to 34 weeks, mean birth weight was 1422.7±334.3 g ranging from 900g to 2200 g, mean Apgar score at 1 minute was 7±1.3, at 5 minutes the mean was 7.8±0.9, and at 10 minutes the mean was 8.4±0.7. Twenty-six (23.6%) were products of multiple gestations. Hyaline membrane disease was observed in 14 (12.7%), neonatal sepsis in 48 (43.6%), necrotising enterocolitis in 6 (5.5%), patent ductus arteriosus in one (0.9%), and hyperglycaemia in 56 (50.9%) cases.

Conclusion: Our study found no participant with retinopathy of prematurity at UTH NICU. Further, the study could not make associations between suggested risk factors to the development of ROP. However, being a novel study on this topic in the country, it highlights the importance of setting up screening protocols and their attendant equipment in Special Care Baby Units at UTH and improving neonatal care services.

Keywords: preterm infant; retina; retinopathy of prematurity; risk factor; screening.

1. INTRODUCTION

Retinopathy of prematurity (ROP) is an important cause of avoidable blindness [1]. ROP is a disorder of the developing retina of very low birth weight (VLBW) preterm infants who may have tractional retinal detachment (American Academy of paediatrics, 2012).

Factors that have shown significant and consistent association with ROP are low gestational age, low birth weight and prolonged exposure to supplementary oxygen following delivery. Other risk factors include intraventricular haemorrhage, surfactant therapy, anaemia and frequent blood transfusions, apnoea, mechanical ventilation and sepsis [2].

The proportion of children who are blind due to ROP is influenced by the availability, access and outcomes of neonatal care services. It is more prevalent in highly developed countries due to the availability of high levels of neonatal care [3]. The annual global incidence of blindness and visual impairment from ROP was estimated to be 32,300 with sub-Saharan Africa reporting the lowest incidence [4].

Zambia's neonatal care services are expanding and are capable of looking after VLBW preterm infants. The prevalence of blindness in Zambia ranges between 2.2% (339,000 people) and 4.4% (678,000 people) [5]. A study done by Mutati [6] which assessed the causes and distribution of blindness in 3 schools for the blind in Zambia found that the retina accounted for 30% of the anatomical site for visual loss. There is scanty data on the prevalence of ROP in

Zambia. This study sought to raise awareness of ROP and inform the formulation of a screening program and treatment protocols.

1.1 Statement of the Problem

There is an increased risk of neonates developing ROP due to increased survival of VLBW (ZDHS, 2018) preterm infants at the University Teaching Hospital (UTH), Women and Newborn Hospital(WNH) Neonatal Intensive Care Unit (NICU). NICU has no screening program and the demographics and clinical patterns of ROP are not known.

1.2 Justification for Study

The study sought to determine the prevalence and clinical patterns of ROP in VLBW (< 1500 g) and preterm Infants (< 32 weeks gestation) at UTH, WNH, NICU.

1.3 Research Question

What are the Demographics and clinical patterns of retinopathy of prematurity at UTH, WNH Neonatal unit in Lusaka, Zambia?

1.4 Study Aim

To establish the demographics and clinical patterns of Retinopathy of prematurity at UTH, WNH neonatal unit in Lusaka.

1.5 Specific Objectives

1. To estimate the prevalence of Retinopathy of prematurity at UTH, WNH neonatal unit in Lusaka.

2. To determine the factors associated with ROP at UTH, WNH neonatal unit in Lusaka.
3. To establish common clinical patterns of ROP at UTH, WNH neonatal unit in Lusaka.

2. LITERATURE REVIEW

2.1 Overview of Retinopathy of Prematurity

Retinopathy of prematurity is a proliferative retinopathy that affects very low birth weight (<1500g) premature (<32 weeks gestation) infants [7]. It was first described as a retrolental fibroplasia occurring in 12 percent of infants weighing less than 3lbs (1360 g) or less at birth by Terry in [8,9]. The prevalence of ROP has been increasing despite and partly due to the advances in neonatal care in developing countries. Gilbert et al. [3] referred to the current surge as the third epidemic of ROP. The first epidemic occurred in the 1940s-1950s and the second in the 1970s in industrialised countries due to the use of unmonitored supplemental oxygen.

2.2 Risk factors for Retinopathy of Prematurity

Risk factors for developing ROP are very low birth weight (<1500g) and low gestational age (<32 weeks gestation) and prolonged exposure to supplemental oxygen following delivery. According to the cryotherapy of retinopathy of prematurity (CRO-ROP) study, > 81.6 % of infants that weighed less than 1000g at birth developed ROP [10].

Several studies have linked supplemental oxygen, oxygen concentration and prolonged mechanical ventilation to ROP. Maintaining lower saturations of oxygen in infants of 24 to 28 weeks gestation age reduces the incidence of ROP and chronic lung disease [11]. The supplemental therapeutic Oxygen for pre-threshold retinopathy of prematurity (STOP ROP) trial compared the effects of oxygen saturation of 89-94% and 96-99%, and found no significant difference in ROP incidence [12]. The surfactant, positive pressure, Pulse Oximetry Randomized Trial (SUPPORT) and Benefits of Oxygen saturation targeting study II (BOOST-II) compared oxygen saturations of 85-89% and 91-95% and found lower ROP incidence rates with lower oxygen saturations. However, the mortality rate was higher in the lower oxygen saturation groups.

Celebi et al. [13] also demonstrated various systemic risk factors such as culture-proven sepsis, blood transfusion, artificial ventilation for more than 7 days, surfactant therapy, phototherapy for neonatal jaundice and maternal pre-eclampsia. Other risk factors include hyaline membrane disease, intraventricular haemorrhage, prenatal steroids for lung maturation, patent ductus arteriosus, necrotising enterocolitis and postnatal glucocorticoids.

A study by Higgins et al [14] showed that infants whose mothers received antenatal dexamethasone developed less ROP that was stage 2 or higher than infants without history of antenatal dexamethasone. The association of postnatal steroids with ROP is not clear. A study by Cuculich et al. [15] which looked at whether postnatal dexamethasone treatment for bronchopulmonary dysplasia increases the risk of ROP in very low birth-weight neonates was not certain.

Anaemia during the first postnatal week is an a risk factor for developing ROP which is caused by an immature hematopoietic system, inadequate erythropoietin production and iatrogenic blood loss [16].

Some studies have suggested a racial variation in incidence and severity of ROP. The CRO-ROP study found black infants to have lower incidence of threshold ROP compared to white infants. Aralikatti et al. [17] found black infants to have a higher incidence of severe ROP than white infants. The racial variation suggests a genetic predisposition to ROP.

2.3 Retinopathy of Prematurity in Africa

Africa is the world's second largest and second most populous continent after Asia with an estimated population of 1.216 billion people. Vision 2020- the right to sight initiative of the World Health Organisation (WHO) recognised ROP as a major cause of avoidable blindness in babies. However, the disease is neglected in most blindness prevention programs in Africa. ROP was believed to be rare in Africa due to the non-survival of preterm babies because of inadequate neonatal care facilities (Popoola, 2017).

Very few studies on the prevalence of ROP have been done in Africa. The prevalence of ROP from literature ranges from 5% to 47%. Some studies from Egypt, South Africa, Nigeria, Kenya and Zimbabwe are shown in Table 1.

Table 1. Incidence of ROP in African countries

Study	Study year	No of preterm babies	Any stage of ROP	Treatable stage in babies screened ROP cases
Nigeria				
Adio et al. [18]	2012	53	25(47.2%)	1(7.5%)
Fajolu et al. [19]	2011-2014	80	12(15%)	6(50%)
Oluleye et al.	2016	29	7(24.6%)	2(8.9%)
Egypt				
Hakeem et al. [20]	2009-2010	172	33(19.2%)	6(18.2%)
Hadi and Hamdy [21]	2010-2012	152	52(34.4%)	15(28.6%)
South Africa				
Mayet [22]	2003-2006	514	84(16.3%)	
Jacoby and du toit [23]	2009-2014	919	245(26.7%)	22(8.9%)
Zimbabwe				
Mataswa [24]	2015-2016	121	6(5%)	None
Kenya				
Onyango et al. [25]	2010-2015	103	43(41.7%)	9(20.9%)
Wanjala et al. [26]	2003-2004	120	20(16.7%)	6(5%)

In the study done by Mayet and Cockinos [22] where 514 infants were screened at a hospital in South Africa, Johannesburg over a two- and half-year period, the incidence of ROP was reported to be 16.3% with ROP needing treatment at 1.6%.

In a hospital retrospective review of records of premature infants in Kenya at a hospital with advanced neonatal care by Onyango et al. [25], the prevalence rate of ROP was reported to be 41.7%. A low prevalence rate was reported at a hospital study in Zimbabwe by Mataswa [24]. In this study, 141 preterm and VLBW infants were enrolled and they reported a prevalence of 5%. Sixty percent (60%) of all preterm births are in sub-Saharan Africa and of those, 15% are born before 32 weeks gestational age. In Zambia, there are 84000 preterm births each year (<37 weeks gestational age) and 4000 of those are born before 28 weeks gestation (everypremie.org, 2019).

Mulindwa [27] et al reported VLBW infants (<1500g) accounted for 600-500 (20%) of total admissions at UTH NICU in 2011. The 2019 neonatal ward recorded reported 4740 admissions. The majority of the admissions were due to prematurity. However, the admission data was not aggregated according to weight. The 2019 neonatal ward mortality was 28.9% which was lower than the 2017 mortality rate of 35%. There is not much documentation about the determinants of preterm deaths for babies sent to UTH Neonatal Intensive Care Unit. There is

scanty data on the prevalence of retinopathy of prematurity at UTH WNH NICU and in Zambia in general.

3. MATERIALS AND METHODS

3.1 Study Design

A hospital-based cross-sectional study was conducted on preterm babies born at <32 weeks gestational age and very low birth weight infants (<1500 g) admitted to UTH, WNH neonatal unit.

3.2 Study Setting

The study was done at UTH, WNH Neonatal Intensive Care unit (NICU). NICU is a referral unit that receives patients from different clinics and hospitals around Lusaka city and the country at large. This unit designed for 40 to 60 babies accommodates at least 100 babies per day. Fifty percent (50%) of all admitted babies are preterm whose gestational age may not be certain, as most women do not have a formal antenatal scan for correct dates at 18 to 22 weeks.

The unit is divided according to severity of illness with a 4-ventilator neonatal intensive care unit (NICU), a step-down high dependency unit offering surfactant and Continuous Positive Airway Pressure (CPAP) to premature babies. There is a step-down feeders and growers section for premature babies awaiting admission to the 26 bed Kangaroo Mother Care (KMC) where babies get discharged with a weight of at

least 1400 grams. Preterm babies spend an average of 3 to 6 weeks in the department. Discharged babies are reviewed in the outpatient department weekly depending on the weight at discharge and the confidence of the mother.

3.3 Target Population

Infants who were admitted to UTH, WNH NICU unit in Lusaka, Zambia.

3.4 Study Population

Infants who were admitted at UTH, WNH NICU born at < 32 weeks gestational age and/or preterm infants with birth weight of less than 1500g (<32weeks and/or <1500Kg).

3.5 Inclusion criteria

1. Neonates born prior to 32 weeks gestation
2. Preterm neonates weighing <1500 g

3.6 Exclusion Criteria

1. Critically ill neonates
2. Unilateral or bilateral retinal or choroidal disease other than ROP
3. Obstructed fundal view
4. Lack of consent from the parent/guardian

3.7 Sampling

Sample size = 109 neonates

3.7.1 Sampling technique

Simple random sampling of patients who met the inclusion criterion was employed in the study.

3.8 Data collection procedure

Infants that met the inclusion criteria were enrolled into the study after obtaining informed consent from the parents or caregivers. Patient information of birth date, birth weight, Apgar score, mode of delivery, sex, multiple births, HIV exposure, history of exposure to oxygen, blood transfusion, postnatal steroids and diagnosis of hyaline membrane disease, neonatal sepsis, patent ductus arteriosus, necrotizing enterocolitis was obtained from the medical record. Maternal

information of age, Last menstrual period, history of pre-eclampsia were obtained by reviewing medical records. Anterior segment and posterior segment examinations were done at 4-6 weeks chronological age or 31-33 weeks gestational age (Visser, 2013) in the presence of neonatologist and critical care nurse. Neonates who died or lost to follow up were excluded from the study.

3.9 Data Analysis

A database was created in Microsoft Excel and was transferred to Statistical Package for the Social Sciences software (SPSS version 25.0) which was used in statistical analysis. The average, standard deviation, percentage, minimum and maximum values of the data were calculated. Chi-square test was used in the analysis of categorical data. The normal distribution of data was calculated using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean \pm standard deviation (SD), and categorical variables as frequencies and percentages.

4. RESULTS

4.1 Background Characteristics

The study period was from November 2021 to April 2022. 160 preterm babies met the inclusion criteria and were enrolled into the study. 110 (68.8%) preterm babies were examined, 37 (23.1%) died and 13 (8.1%) were lost to follow up. Of those examined, 60 (54.5%) were females and 50 (45.5%) male. Mean gestational age at birth was 30.6 ± 2 weeks ranging from 27 to 34 weeks. The mean birth weight was 1422.7 ± 334.3 g ranging from 900g to 2200g. The mean Apgar score at 1 minute was 7 ± 1.3 , at 5 minutes the mean was 7.8 ± 0.9 , and at 10 minutes the mean was 8.4 ± 0.7 . Majority (82.7%) of the babies were delivered through SVD while 19 (17.3%) were delivered by caesarean section. Twenty-six (23.6%) were products of multiple gestations and 3 (2.7%) were exposed to HIV. A combination of low birth weight and low gestation (42.7%) was the most common indication for ROP screening followed by low gestation (32.8%) and low birth weight (24.5%).

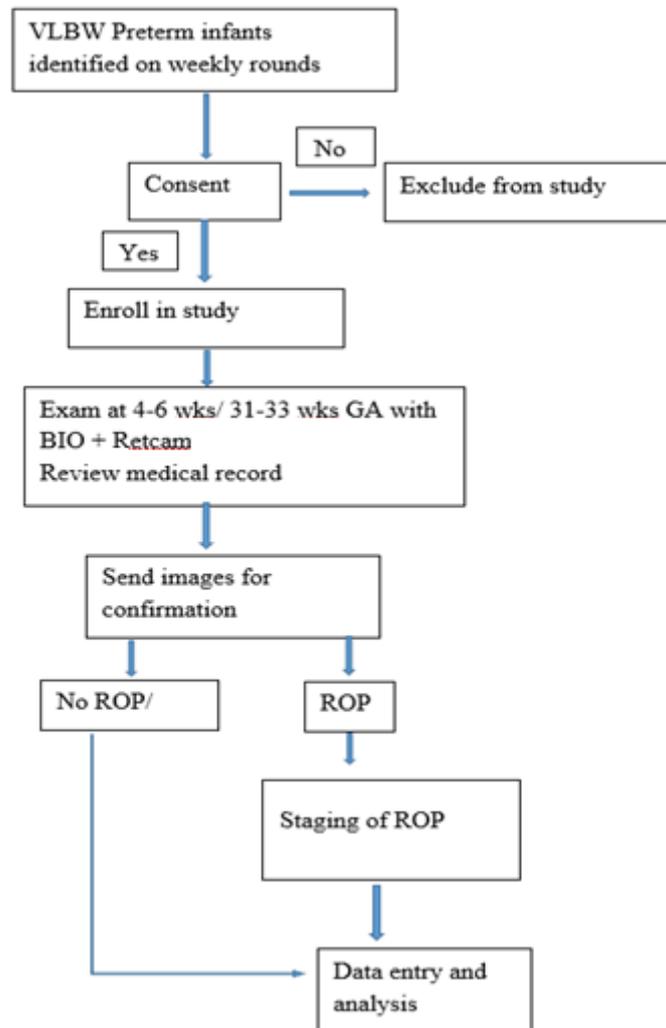


Chart 1. Flow chart showing data collection procedure

Table 2. Demographic characteristics of study subjects

Variables	Total (n = 110)
Sex	
Male	50 (45.5)
Female	60 (54.5)
Mode of delivery	
SVD	91 (82.7)
Caesarean	19 (17.3)
Multiple births	
Yes	26 (23.6)
No	84 (76.4)
HIV exposure	
Yes	3 (2.7)
No	107 (97.3)
Indication for ROP screening	
Weight < 1500g	27 (24.5)
Gestational age < 32 weeks	36 (32.8)
Both	47 (42.7)

SVD: spontaneous vaginal delivery

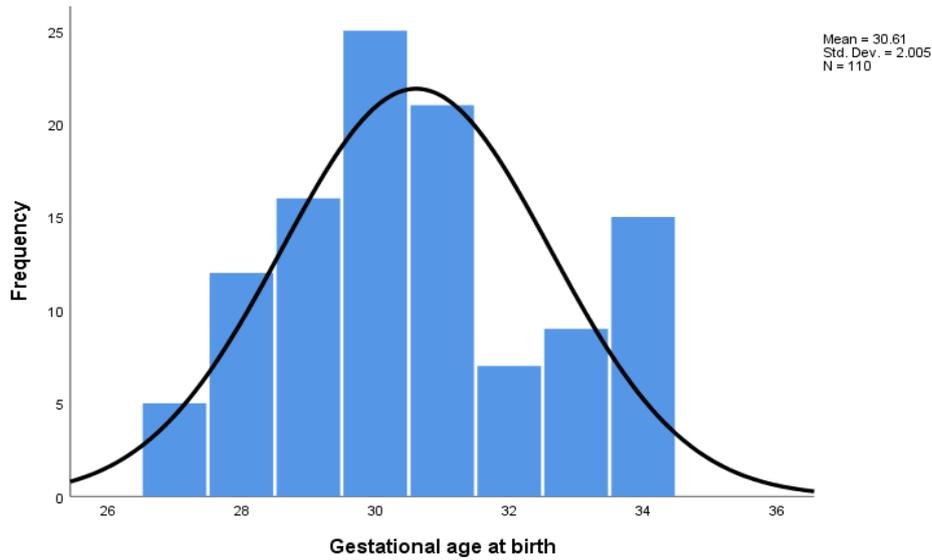


Fig. 1. Graphic representation of gestational age at birth among study subjects

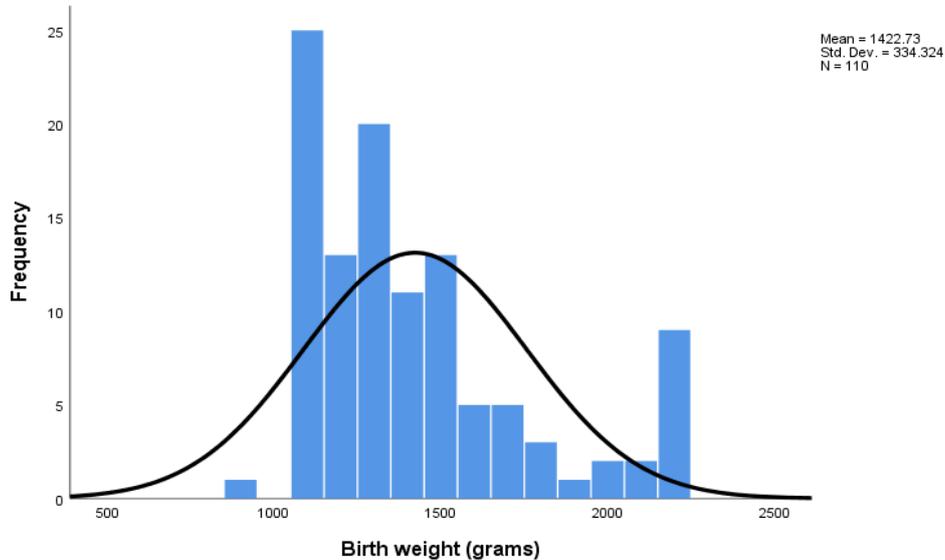


Fig. 2. Graphic representation of birth weight among study subject

4.2 Maternal Characteristics of Study Subjects

Table 3 shows the maternal characteristics of study subjects.

Majority (41.4%) of the preterm babies had their mothers aged between 24 to 30 years while 23 (32.9%) babies' mothers were aged over 31 years and the remaining 18 (25.7%) mothers were aged below 23 years. Three-quarters (75.7%) of the mothers received steroids to

facilitate lung maturity prior to delivery, and only 17 (24.3%) mothers were diagnosed with pre-eclampsia during pregnancy.

4.3 Associated Systemic Conditions and Interventions

Hyaline membrane disease was observed in 14 (12.7%), neonatal sepsis in 48 (43.6%), necrotising enterocolitis in 6 (5.5%), patent ductus arteriosus in one (0.9%), and hyperglycaemia in 56 (50.9%) cases (Table 4).

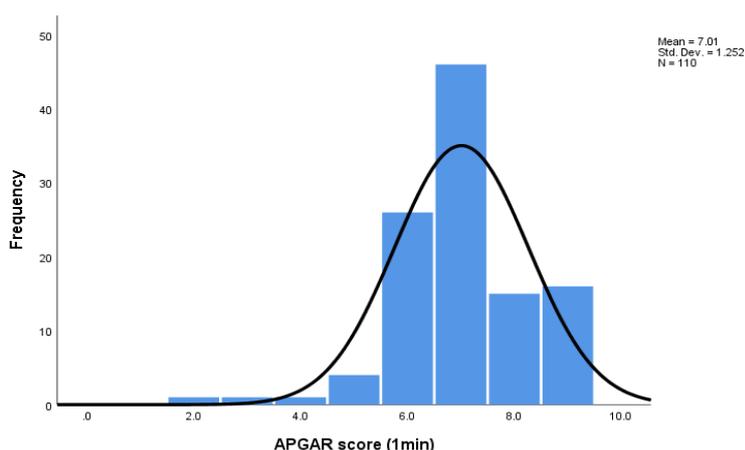


Fig. 3. Graphic representation of APGAR score at 1 minute of birth among study subjects

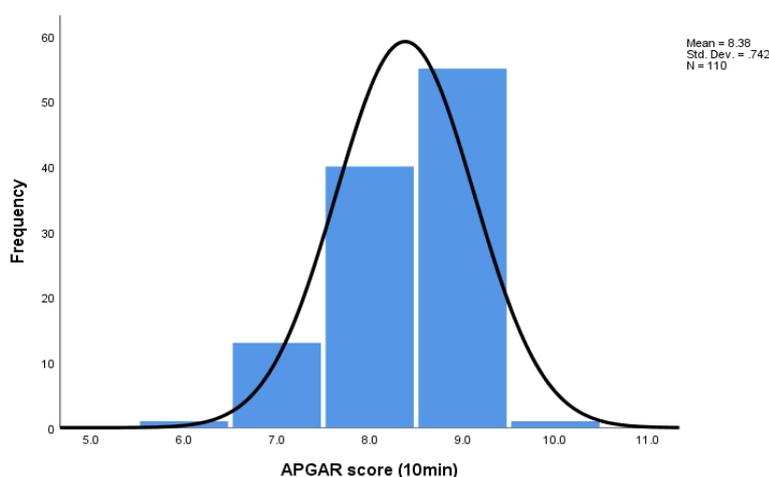


Fig. 4. Graphic representation of APGAR score at 10 minutes of birth among study subjects

Table 3. Distribution of maternal factors among study subjects

Variables	Total (n =110)
Maternal age (years)	
≤ 23	18 (25.7)
24 – 30	29 (41.4)
≥ 31	23 (32.9)
Antenatal steroids	
Yes	17 (24.3)
No	53 (75.7)
Pre-eclampsia	
Yes	17 (24.3)
No	53 (75.7)

Twelve (10.9%) babies received phototherapy, seven (6.4%) babies received surfactant therapy, and postnatal steroids were administered in seven (6.4%) babies. Blood transfusion was performed in six (5.5%) babies, and Sixty-six

(60%) babies received supplemental oxygen most commonly delivered through CPAP in 45 (68.2%) babies while the other 21 (31.8%) babies received oxygen through nasal prongs (Table 4).

Table 4. Distribution of associated systemic conditions and interventions

Variables	Total (n =110)
Exposure to oxygen	
Yes	66 (60)
No	44 (40)
Mode of oxygen delivery	
Nasal prong	21 (31.8)
CPAP	45 (68.2)
Hyaline membrane disease	
Yes	14 (12.7)
No	96 (87.3)
Neonatal sepsis	
Yes	48 (43.6)
No	62 (56.4)
Necrotising enterocolitis	
Yes	6 (5.5)
No	104 (94.5)
Patent ductus arteriosus	
Yes	1 (0.9)
No	109 (99.1)
Blood transfusion	
Yes	6 (5.5)
No	104 (94.5)
Phototherapy	
Yes	12 (10.9)
No	98 (89.1)
Surfactant therapy	
Yes	7 (6.4)
No	103 (93.6)
Postnatal steroids	
Yes	7 (6.4)
No	103 (93.4)
Hyperglycaemia	
Yes	56 (50.9)
No	54 (49.1)

4.4 The Ocular Features of the Study subjects

The anterior segment was within normal limits in all 110 babies screened. All of the 110 babies also had immature retinæ.

All the study infants showed various stages of immature retina on funduscopy examination and on the photos taken by the RetCam

5. DISCUSSION

From 1942 when Terry described ROP, it has continued to be a significant complication in preterm neonates and an important cause of potentially preventable blindness worldwide. Since the diagnosis and treatment of ROP requires serious clinical experience, it poses

certain difficulties for ophthalmologists [28-31]. Today, ROP is detected before the serious stages with the increasing awareness of pediatricians and parents and in cases where treatment is required, intervention is made without delay (Sen et al. 2018); [32-34].

5.1 The Prevalence of Retinopathy of Prematurity

This study aimed at establishing the prevalence of ROP at UTH WNH NICU. There was no case of ROP reported during the course of this study. This is significantly lower than the reported prevalence rates across the globe which ranges from 5% in Zimbabwe [24] to 47.2% in Nigeria [18]. This may be because these studies had larger sample sizes.

The incidence of ROP is known to be higher with increased survival of neonates with lower birth weight and lower gestational age. The low prevalence rate of ROP can be attributed to the high mortality rate among preterm neonates in the unit. A high mortality (>60%) was reported by a study that modelled mortality within 28 days among preterm infants at UTH's WNH [35]. Most of the deaths occur within the first week of life with sepsis being the most prevalent cause of death [36].

5.2 Screening for Retinopathy of Prematurity

The present study used gestational age of less than 32 weeks and birth weight of less than 1500g as the criteria for screening babies for ROP. This was similar to most guidelines available like the American Academy of Pediatrics, American Academy of Ophthalmology and American Association for Pediatric Ophthalmology and Strabismus which stipulate that all infants ≤ 30 weeks GA or ≤ 1500 g BW should be screened for ROP [32].

In the present study, the gestational age was calculated based on the reported last menstrual period. This could have contributed to the low prevalence of ROP. A study by Price et al. [37] at UTH WNH that quantified bias of gestational age based on reported last menstrual period and ultrasonography found that reported last menstrual period based gestational age over estimated preterm births by 50% compared to ultrasonography based gestational age estimates. This could have contributed to the low prevalence reported as some of the neonates enrolled in the study may have had a higher gestational age.

Current screening guidelines recommend for follow up screening based on the retina findings, gestational age and chronological age [32]. Our study design was a cohort study and follow up examinations were not done. This was different to the studies conducted around the region which had follow up examinations. This may have contributed to the low prevalence as some neonates that developed ROP may have been missed.

5.3 Risk Factors of Retinopathy of Prematurity

The current study could not establish the factors associated with ROP because no case of ROP

was reported. The risk factors that were examined include gestational age, birthweight, multiple pregnancy, Apgar score, mode of delivery, supplemental oxygen, maternal age, hypertensive disorders of pregnancy, respiratory distress syndrome, blood transfusions, patent ductus arteriosus, necrotizing enterocolitis, sepsis and hyperglycaemia.

5.4 Study Limitation

The study had limitations that may have affected the presentation and generalization of results. Firstly, the study was a cross-sectional study which could have resulted in failure to capture cases which might have developed later. Some of the neonates that were enrolled did not survive and some infants were missed on the date of the examination.

6. CONCLUSION

Our study found no participant with retinopathy of prematurity at UTH NICU. Further, the study could not make associations of suggested risk factors to the development of ROP. The study highlights the need for improvement of care in the NICU. However, being a novel study on this topic in the country, it highlights the importance of setting up screening protocols and its attendant equipment in Special Care Baby Units at UTH

7. RECOMMENDATIONS

There is need to set up screening protocols and its attendant equipment in our Special Care Baby Unit (SCBU) and the outpatient paediatric clinics to be able to examine infants and children for vision-threatening diseases. We also recommend further studies be conducted with a prospective study design based on ultrasound gestational age estimate with a larger sample size.

ETHICAL APPROVAL AND CONSENT

Ethical clearance for the study was obtained from UNZABREC and National Health Research Authority. Institution Permission to conduct the study was obtained from WNH and UTH's Eye Hospital. Informed consent was obtained from the caregivers. Tenets of the Declaration of Helsinki were followed in this study. Informed consent was obtained from the caregivers.

A coding system was used to ensure the confidentiality of patient details whilst ensuring all required data was captured for each patient.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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