ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

PREVALENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY AMONG INFANTS IN MINILK II HOSPITAL: A RETROSPECTIVE STUDY, ADDIS ABEBA, ETHIOPIA, 2020

BY: HANA ENDALE

ADVISER: YOSIEF TSIGE (ASSISTANT PROFESSOR)

CO-ADVISER: EMEBET BERHANE (LECTURER)

A THESIS SUBMITTED TO POSTGRADUATE STUDIES IN ADDIS ABEBA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY, DEPARTMENT OF NURSING FOR PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER'S IN NEONATAL NURSING

JUNE, 2020
ADDIS ABABA
ETHIOPIA

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

PREVALENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY AMONG INFANTS IN MINILK II HOSPITAL: A RETROSPECTIVE STUDY, ADDIS ABEBA, ETHIOPIA, 2020

BY: HANA ENDALE

ADVISER: YOSIEF TSIGE (ASSISTANT PROFESSOR)

CO-ADVISER: EMEBET BERHANE (LECTURER)

A THESIS SUBMITTED TO POSTGRADUATE STUDIES IN ADDIS ABEBA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY, DEPARTMENT OF NURSING FOR PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER'S IN NEONATAL NURSING

JUNE, 2020
ADDIS ABABA
ETHIOPIA

ACKNOWLEDGEMENT

First, I would like to thank my al mighty God and His mother saint Virgin Mary for helping me to do this thesis work.

Next, I would like to express my gratitude to my advisors Mr. Yosief Tsige and Sr. Emebet Berhane for their unreserved support and guide, without their support this thesis is not been real.

I have a gratitude to Dr Misrak Tadesse (Neonatologist) who is volunteered assigned by Vermont Oxford Network which supports our Neonatal MSC track, for her fruitful suggestion forward to my thesis work.

I would like thank to Dr Sadik Taju (ophthalmologist) for his unreserved knowledge sharing on screening of retinopathy of prematurity.

My deepest appreciation also goes to Tikur Anbessa Specialized Hospital for giving me this golden opportunity especially for Dr Asrat Demetse (Neonatologist) who straggled to start this program for the first time.

Finally, I would like to thank my family and my friend those giving me support and enormous encouragement throughout my work.

Table of Contents

ACRONYMS AND ABRREVIATION

AAP	American Academic of Pediatrics
AAPOS	American Association for Pediatric Ophthalmology and Strabismus
AP-ROP	Aggressive Posterior Retinopathy of Prematurity
BIO	Binocular Indirect Ophthalmoscope
CA	Chronological Age
CSROP	Clinically Significant Retinopathy of Prematurity
GA	Gestational Age
ETROP	Early Treatment of ROP
IGF-1	Insulin-like growth factor-1
IVH	Intra Ventricular Hemorrhage
LMICs	Low-and Middle- Income Countries
NICU	Neonatal Intensive Care Unit
PMA	Post Menstrual Age
RDS	Respiratory Distress
ROP	Retinopathy of Prematurity
SGA	Small for Gestational Age
SPSS	Statistical Package for Social Science
T1ROP	Type one Retinopathy of Prematurity
VEGF	Vascular Endothelial Growth Factor
VLBW	Very Low Birth Weight

LIST OF TABLES

LIST OF FIGURES

Abstract

Introduction: Retinopathy of prematurity is the growth of abnormal retinal vessels secondary to deficient vascularization of the retinal tissue as a result of hyperoxia causing reduces a regulation of vascular endothelial growth factor and death of endothelial cells. In developing countries, heavier and term infant develop ROP since there is inadequate awareness of the risk factors of the disease development. There are many risk factors of ROP; the major risk factors are low birth weight (BW), small gestational age (GA), and long term oxygen therapy.

Objective: To assess the prevalence and risk factors of retinopathy of prematurity among infants in Minilik II Hospital, Addis Ababa, Ethiopia, 2020.

Methodology: An institutional based retrospective cross sectional study was conducted from March to April 2020 at Minilik II hospital pediatrics outpatient referral eye clinic. A sample size (301) was determined by using single population proportion formula. And study subjects were selected using systematic random sampling method. Data was collected from medical records of all infants from January 2018 - December 2019 with a structured check list. The collected data was entered and cleaned using Epi data 6.4.2.0 and then exported & analyzed using SPSS version 25. Bivariate and multivariate analysis was used to recognize the associated factors.

Result: Out of 301 infants enrolled in the study, 39(13%) developed ROP. Of these more than half (56.4%) of them who had ROP were on Zone II + Stage 1 followed by Zone II + stage 5 (12.8%) and Stage 5(10.2%). From those infants who had ROP, 16(41%) infants were regressed spontaneously with follow up. Univariate analysis showed that gestational age, birth weight, oxygen therapy, preeclampsia, apnea, RDS, anemia, blood transfusion and sepsis were a significant variable. But, birth weight, oxygen therapy and sepsis remained a significant factor in multivariate analysis.

Conclusion and recommendation: The prevalence of ROP in this study was 13%. Birth weight, oxygen therapy and sepsis were a significant factor for the development of ROP. Preventing risk factors of ROP that are underweight at birth, sepsis and long term oxygen therapy are very important to reduce childhood blindness.

Keywords: Retinopathy of prematurity, Retina, Premature

CHAPTER ONE

1. INTRODUCTION

1.1. Background

Retinopathy of prematurity (ROP) is defined as a vasoproliferative retinal disorder persists as the main cause of avoidable childhood blindness universally (1). The growth of abnormal retinal vessels secondary to incomplete vascularization of the retinal tissue as a result of hyperoxia causing reduce a regulation of vascular endothelial growth factor(VEGF) and death of endothelial cells is the characteristics of it. For this reason, neonates who have ROP are prone to increase visual complications, both structural and functional in extended terms. Structural complication contain refractive errors and strabismus while functional complications consist of visual impairment from mild to severe, even absolute blindness, decrease contrast sensitivity, visual field defects and irregular color vision and perception(2, 3).

In human embryos, there are two stages which are retina vascularized. These are vasculogenesis and angiogenesis. During the early stage of retinal vascularization that is from 12 weeks to 21 weeks of gestational age in which endothelial progenitor cells differentiate into endothelial cells to form blood vessels is called vasculogenesis stage. In the later stage of retinal vascularization which is the superficial plexuses that are accountable for the central hemal arch form is an angiogenesis stage. At beginning of 16 weeks of gestational age the blood vessels progressively develop to surround the retina from the optic disk. At 32 weeks reaching the nasal retina and the temporal retina is develop from 36 to 40 weeks of gestational age(4). In premature babies the retinal blood vessels is incomplete however the vessels possibly grow and branch unusually with a lot of factors. Abnormal blood vessels may grow and bleed inside the eye from the plane of the retina when the blood and abnormal vessels are reabsorbed, it may give rise to numerous bands resembling membranes, which can pull up the retina, causing detachment of the retina and finally blindness prior to 6 months occurred (5).

Retinopathy of prematurity (ROP) is now rising as a significant cause of ocular morbidity in low and middle income countries(6). Furthermore, it is important to note that affected infants in developing countries are usually larger and of older gestational age than infants in the developed countries.

The initial examination time is based on postmenstrual age (PMA) and chronological age (CA) and it is undertaken to detect 99% of infants at risk of a poor visual outcome. Between four and nine weeks CA the first examination is carried out depending on PMA at birth. Subsequent studies have confirmed that the efficacy of conducting the first examination at four weeks CA in more mature infants(7). If ROP is detected on time, its blindness is largely preventable and has gained public importance in countries (8). And then the examination may discontinue at post-menstrual age of 50 weeks if no pre threshold disease (or worse ROP) is present. Finally, their caregivers should have to be well-informed about ROP prior to their baby's discharge from the neonatal intensive care unit, as it is not uncommon for infants to be sent home from the hospital before their ROP has resolved or before their retinal vasculature is mature. These infants require continued screening exams on an outpatient basis (9).

1.2. Statement of the problem

Globally, ROP is estimated that about five million children lost their vision permanently each year (10). Nevertheless it is a primary cause of avoidable blindness in both developed and developing countries(2). The prevalence and causes of childhood blindness vary extensively wide-reaching reflecting socio-economic development, coverage of specific control measures, and access to high quality eye care but up to 40% of blindness in children is potentially avoidable (11).

About 60% of the world's preterm births occur in sub-Saharan Africa and Asia. The enhancements of neonatal systems in developing countries have increased the survival rates for premature infants. Among the survived infants, many of them grow with disabilities, including visual complications. For this reason, the improvement of the standards in neonatal intensive care units (NICU) and prenatal care has increased the survival rate for the premature babies over the last decades. Furthermore, in regions of the world where resources are limited, there is an increasing incidence of ROP corresponding to neonatal interventions to treat premature infants who would not previously have survived. Consequently, the occurrence of ROP has increased in equivalent. In such cases, there is a difference between saving premature infants and successfully diagnosing and managing their ROP (3, 12, 13).

When ROP severe be able to effect in everlasting visual disability, it is also a cause of economic burden for the community and the individual. In developing countries, heavier and term infant can also develop ROP. Since there is inadequate awareness of the risk factors of the disease development, a lack of skilled professionals and/or a scarcity of resource to care for infant, guidelines have been prepared in some countries to enhance early identification and on time treatment of babies with ROP(14, 15). Over the previous two decades many low and middle income countries (LMICs) have developed programs for ROP control although many have incomplete coverage and poor coordination (16).

In developing countries the screening criteria for ROP should be modified though the development of screening guidelines that are appropriate for all institutions in a middle-income country is challenging(12, 17). Screening criteria and risk factors that are recognized in one country do not necessarily apply in another country where available prenatal care may not be comparable. The criterions are also dependent on NICU quality of care and this varies widely between units. For this reason, recognizing and treating ROP in a timely fashion is critical for achieving the best visual outcome. ROP can cause problems throughout a patient's life; therefore, long-term monitoring by an ophthalmologist is very important(18, 19).

There are massive impacts of blindness and life time vision impairment which caused by ROP on the quality of life of affected infants (20). Hence, prevention is desired to keep the value of their life. Prevention of ROP includes improved care in the NICU. The consequence of improved care is reduced morbidities and risk factors that put a neonate at-risk for developing ROP. It is also responsibility of pediatricians, medical officers, resident doctors and neonatal nurses who are involved in the care of affected infants. Any intervention to improve quality care of a newborn can contribute to reducing the occurrence of ROP in developing countries(21).

There is a variable risk for the incidence of ROP among different countries in the world. For example, the incidence of ROP among developing countries was 47.2% in Nigeria(22), 33.9% in India(23) and 26.1% in Iran(24). There are many risk factors of ROP,low birth weight (BW), small gestational age (GA) and long term oxygen therapy are the major ROP risk factors(25). ROP is a multi-factorial disease and the major risk factors are preterm delivery, mainly before the 32 week of gestation and birth weight less than 1500 g(26), various maternal factors-mode of delivery, diabetes, preeclampsia,(27) neonatal risk factors such as respiratory disorders, infection, increased oxygen (O_2) consumption, phototherapy, blood transfusion and amount of received oxygen(28).

Studies on prevalence and risk factors of ROP in Ethiopia are scarce. Therefore, the purpose of this study is to evaluate the prevalence and risk factors of ROP among infants in Minilik II hospital.

1.3. Significance of the Study

This study will contribute as baseline data on ROP prevalence rate and risk factors to federal ministry of health of Ethiopia and sub-Saharan Africa. And it will help to prepare screening guideline of ROP in Ethiopia. In addition, this study will support health professionals who are working in NICU and prenatal care to improve their quality of care. Furthermore, it will create awareness for NICU nurses about the prevalence of ROP and the efforts toward ROP prevention. And it will provide base line information for researchers to use it for further study and supports policy makers to see where the gap is and to take measure.

CHAPTER TWO

2. LITERATURE REVIEW

2.1. Retinopathy of prematurity

ROP involve the complete retina though abnormalities particularly striking at the connection of the posterior vascularized retina and anterior avascular retina. The degree of Retinopathy described in terms of stage, location and extent.

Retinopathy in terms of stage is described in to five stages. These are:-

Stage 1 ROP: In this stage, a flat line of demarcation occurs between the vascular and a vascular retina.

Stage 2 ROP: In this stage, the line of demarcation acquires volume in order to become a ridge. On the posterior edge of the ridge tuft of new vessels may appear however these vessels still are within the retina.

Stage 3 ROP: Neo vascularization can be seen within the ridge, and extra retinal vascularization extends out of the retina.

Stage 4 ROP: Partial retinal detachment occurs, which may be extra foveal or foveal.

Stage5 ROP: Eventually total retinal detachment may occur (with resulting complete blindness).

Retinopathy is also described into three zones based on the location

Zone I: refers to most posterior, consists of a circle with a radius of twice the distance from the optic disc to the center of the macula, centered on the optic disc.

Zone II: refers to the area that extends from zone I forward to the anterior edge of the retina (oraserrata) on the nasal side of the eye, centered on the optic disc. The oraserrata is closer to the optic disc on the nasal side than on the temporal side of the eye.

Zone III: refers to anterior part of the retina to zone II (only appears on the temporal side) (29).

ROP is a disease relating to many factors, and its exact etiology is not known. There are different studies conducted on prevalence of ROP worldwide. A study done in Kenya indicate that the incidence of ROP was 41.7% and 20.9% of premature infants with ROP required treatment(27).

Adio et al in Nigeria also verified a similar picture, with an ROP prevalence of 47.2%(22). Another study done in South Africa on screening criteria of ROP, of 1104 eligible infants, 33.4% had ROP clinically significant ROP (CSROP) 9.1%, type one prethreshold (T1ROP) 2.5%). All T1ROP infants received laser therapy. Screening infants with a GA of ≤28 weeks or a BW of <1000gm would have detected all infants with T1ROP but missed two outliers with CSROP. These outliers would only have been detected GA of ≤32 weeks or a BW <1 500 g(30).

A study conducted in India shows that out of 78 babies who fulfilled the inclusion criteria were screened and 15 babies had developed ROP and with a prevalence of 19.2%(31). According to the screening guideline of ROP in China, the occurrence of ROP in different area of the country is 6–18%(32). Another study conducted in China has shown that 31.65% of severely premature infants treated in the NICU at Guangzhou First People's Hospital developed ROP(33). A study conducted in Switzerland shows that the prevalence of ROP was 9.3%. and 1.2% of the premature infants with ROP required treatment(34).

2.2. Infant characteristics

Age and Gender

Age of presentation is one factor for the development of ROP. The Indian eastern Madhya Pradesh study identified that age of presentation had a significant association on sever ROP(35). A prospective study on timely screening versus delayed presentation showed of sight threatening ROP in timely presenting was 1.2% where as in delayed presenting was increased to 8.0%. It was also showed that with increased post conception age (Gestational age plus chronological age) the severity of ROP significantly increases. Probability of severe ROP increased from 2.1% at a post conception age of 29 weeks to 5.2% at a post conception age of 39 weeks and 12.4% at a post conception age of 49 weeks (36). Another study done in India showed that a larger proportion of males were screened in private hospitals compared to the government centers female (private, male: female= 1.32) vs.(government, male: female 1.00) $P < 0.001$)(37).

2.3. Major risk factors

GA, BW and oxygen therapy

Infants with a low birth weight or small gestational age or who require extended long term oxygen therapy have an increased occurrence of ROP (38). In a Palestine study only 6.3% of infants who had a gestational age more than 30 weeks developed ROP (37). Guidelines available by the American Academy of Pediatrics (AAP) and American Association for Pediatric Ophthalmology and Strabismus (AAPOS) for ROP screening says that infants whose weight less than1500 g or GA $\leq$ 30 weeks, and infants whose weight between 1500 and 2000 g or gestational above 30 weeks with an unstable clinical course should examined for ROP (39). Although, a Palestine study showed that two infants had a birth weight higher than 1500gm which is over as the recent AAP and AAPOS guidelines recommended for weight screening (40).

In addition to this a population study done by Holmström G and Larsson E say, 20% to 50% of very low birth weight (VLBW, birth weight <1500 g)4% to 19% infants will develop severe ROP consequently it is primarily affect neonates born at <32 weeks gestational age as result of this the risk and severity of ROP increasing with decreasing gestational age (41). A meta-analysis study in Iran shows that small gestational age ($p < 0.001$), low birth weight ($p < 0.001$) and oxygen therapy have significant risk factors for ROP ($p<0.05$)(42).

Arjumand et.al identified ROP in 10.5% of neonates at first eye examination. A32 weeks GA and 1500 g BW infant were observed and has a significant association between ROP and GA. They also had concern to serial follow-up of neonates at risk for ROP is important when making a final diagnosis (43). The Vermont Oxford Network database, which gather data from more than 1000 NICUs worldwide, showed that an incidence of 33.2% of ROP in neonates with birth weight less than 1500 g in 2010(44).

Supplemental oxygen is also a major risk factor for ROP. The boost II unit kingdom and New Zealand Collaborative Groups evidenced that prior of 34weeks of postmenstrual age maintaining oxygen saturation at lower level be able to decrease the incidence of ROP. However, it is unclear whether this benefit justifies the systemic risks to preterm infants(45).

R Nikhil studies showed, out of 78 babies screened, 51 were given oxygen and 15 (29.41%) babies developed ROP (p <0.001). None of the babies for whom oxygen was not given developed ROP. Subsequently oxygen supplementation was an independent factor for the development the incidence of ROP. Along with the regular screening, each neonatal unit ought to have a policy on oxygen administration and Pulse-ox meters and blended oxygen should have to use in delivery rooms and neonatal units to guide oxygen therapy. All babies who receive oxygen should be monitored closely to target oxygen saturation of 90-95% with proper use of oxygen blenders(31).

2.4. Maternal related risk factors

Maternal age, mode of delivery, maternal preeclampsia/eclampsia and maternal diabetes mellitus

Advanced maternal age has relationship with different adverse outcomes including preterm births, intrauterine growth restriction, miscarriage, low birth weight and chromosomal abnormalities(46). And preeclampsia is often associated with prenatal morbidities, other than also known to be associated with higher levels of anti-antigenic factors such as sFlt-1 (soluble fms-like tyrosine kinase-1), placental growth factor and an antagonist of vascular endothelial growth factor (VEGF)(47, 48). Several studies showed that preeclampsia /eclampsia to be an independent risk factor for development ROP.(48, 49)

A study conducted in Nigeria described that mode of delivery and other factors also had association with ROP, Delivery by caesarian section (χ2= 4.22; P=0.04, receiving supplemental oxygen (χ2= 6.17; P = 0.01), presence of sepsis (χ2= 7.47; P = 0.006) and multiple blood transfusions (χ2= 5.11;P = 0.02), and were important risk factors for the development of ROP(22). And Diabetes also has impact on ROP development. It may have both direct(elevated retinal VEGF by hyperglycemia) and indirect which has (relation with respiratory distress syndrome) impact on ROP development(50).

2.5. Infant co morbidities

Apnea, Respiratory distress syndrome (RDS), anemia and infection

Premature infant who have apnea are more likely to need mechanical ventilation and oxygen administration, and may be more vulnerable to develop ROP(51) and RDS is caused by a surfactant deficiency in the preterm neonate. With RDS, the newborn may develop hypoxic and need mechanical ventilation (Prolonged mechanical ventilation (PMA), often defined as >7 days of ventilator dependence), and oxygen therapy, both of which are associated with increased rate of ROP. Therefore, RDS is associated with increased risk of developing ROP(52). Freitas on his study showed that impaired lung function as shown by the incidence of pneumonia, hyaline membrane disease, or bronchopulmonary dysplasia, is an independent risk factor for ROP and a determinant element of increased risk of developing type 1 prethreshold ROP(23).

Akter S, on his study found that lower average hemoglobin level in newborn was found to be an independent risk factors for the development of ROP in univariate analysis and those without ROP, the lowest hemoglobin level before the date of first examination was found to have an average of 8.4 ± 1.4 g/dl, whereas in the affected group it was 7.8 ± 1.5 g/dl (P = 0.038). Akter on his study also found that on the first logistic regression that blood transfusion had a significant association for ROP development(53).

Neonatal sepsis is the most frequently identified risk factors for any ROP. Hakeem on his study suggest that small gestational age, oxygen therapy, sepsis and frequency of blood transfusions are independent risk factors in the development of ROP (54). A study conducted in Turkey also showed that a lower BW, smaller GA, late-onset sepsis, frequency of red blood cell, total days on oxygen and relative weight gain were recognized as important risk factors for severe ROP (55).

A meta-analysis study in Iran also showed that septicemia, respiratory distress syndrome, continuous positive pressure ventilation, saturation above 50%, apnea, frequency and duration of blood transfusion has significant association with ROP(42).

2.6. Other factors

Blood transfusion and Length of hospital stay

Blood transfusions, recombinant EPO to treat or prevent anemia, Since EPO, regulated by oxygen in both kidney and retina, is a significant proangiogenic factor and has been associated with retinal vascular stability in a mouse model of ROP, Transfusion of RBCs had risk factor for the advance of ROP. In a study conducted in Italy, of 421 infants examined 265 (62.9%) developed ROP and 102 (24.2%) P-ROP. Following the multivariate analysis erythropoietin-therapy ($p < 0.0001$) and Intraventricular hemorrhage (IVH)($p = 0.003$) were independently associated with ROP(56).

Hakeem also, mentioned on his study, frequency of blood transfusions have independent factors for ROP development(54). Length of initial hospital stay has been associated with higher occurrence of ROP and a number of other rarely studied factors containdopamine, phototherapy, inhaled nitric oxide use, sildenafil treatment, fresh-frozen plasma transfusion, twin-twin transfusion syndrome, myocardial injury after birth, elevated mean platelet volume and serum neutrophil-to-lymphocyte ratio (46).

Yunxia Leng et al, on their studies indicated that, out of 436 premature infants who were consecutively screened for ROP, 138 (31.65%) were developed ROP. In univariate analysis, ROP had association with birth weight, multiple births, mechanical ventilation, and gestational age, the number of operations, intravascular hemolysis and blood culture results. Multivariate analysis also showed that gestational age; birth weight, daily weight gain, mechanical ventilation and minimum SaO2 were important risk factors for ROP incident(33).

Currently, there are well organized private and governmental neonatal intensive care units in Ethiopia. These NICU have done lots of effort on premature care. As different literature mentioned that risk factors and prevention start from NICU care, awareness should be created for health professional who works in NICU about the risk factors of ROP. Therefore the purpose of this study will be to assess the prevalence and risk factors of ROP in Minilik II hospital in Ethiopia.

2.7. Conceptual frame work

Conceptual frame work of retinopathy prematurity in Minilk II hospital Addis Ababa, Ethiopia 2020 was represented below (figure1). Factors that were infant characteristics, major risk factors, maternal related risk factors, infant comorbidities and other factors had relation to retinopathy of prematurity.

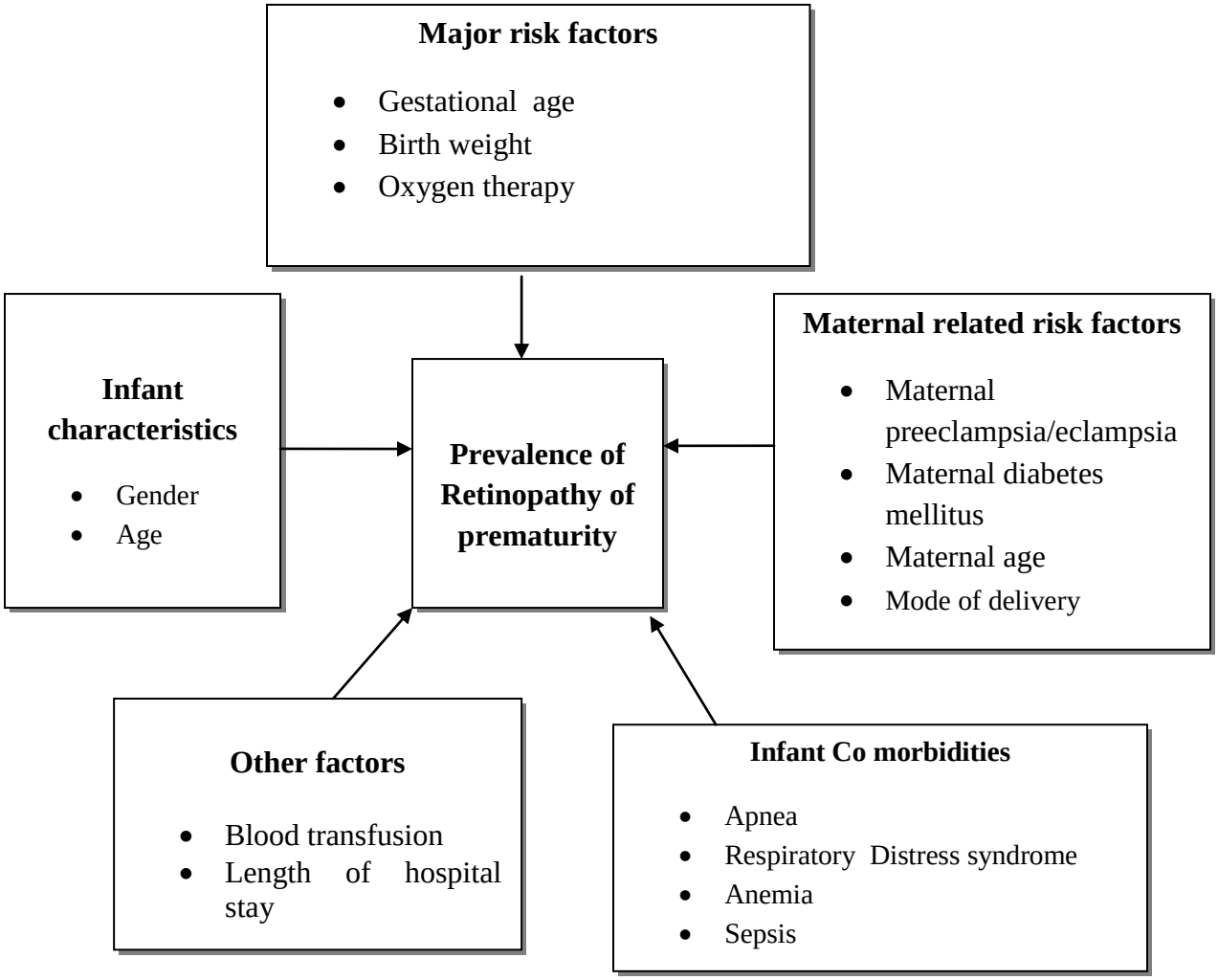

Figure 1: Conceptual framework

Adapted from Clinical Models and Algorithms for the Prediction of Retinopathy of Prematurity(57)

CHAPTER THREE

3. OBJECTIVES

3.1. General Objective

- To assess the prevalence and risk factors of retinopathy of prematurity among infants in Minilik II Hospital, Addis Ababa, Ethiopia, 2020.

3.2. Specific Objectives

- To evaluate the prevalence of Retinopathy of prematurity among infants in Minilik II Hospital, Addis Ababa, Ethiopia, 2020.
- To identify the relationship between Retinopathy of prematurity and its risk factors among infants in Minilik II Hospital, Addis Ababa, Ethiopia, 2020.
- To describe risk factors of ROP among infants in Minilik II Hospital, Addis Ababa, Ethiopia, 2020.

CHAPTER FOUR

4. METHODS AND MATERIALS

4.1. Study Area

The study was carried out in Addis Ababa which is the capital city of Ethiopia. It is located at the center of the country with the area of about 540 square kilo meters, it is the biggest city in the country having 10 sub cities and 116 weredas, with a total population size of 3,273,001 with annual growth rate of 2.1(58).

Minilik II Referral Hospital is found in the north eastern part of Addis Ababa, In Guleli sub city Kebele 06. It was established in 1896 following the defeat of the Italian military force at the battle of 'Adwa' and the settlement of the Ethiopian patriots in Janmeda, Addis Ababa. After conducting minimum study, a 6,194.6m^2 area holding the drainage of Kebena river was selected and tents were planted and started temporary service inside the tents. The area was selected strategically in order to give medical treatment for the injured patriots by washing wounds by the Kebena river water. At that time the name of the area become "Hakim Seffer" or "Hakim meda" means doctor's village and the Russian medical doctors gave treatment in the area. Later on, the hospital was established by emperor Minilik II in 1902 E.C and started national service as the first hospital of Ethiopia. Currently, the hospital is administered by the Ministry of Health (MOH) and provides more than ten Medical services. Of these medical services the department of ophthalmology of the hospital is a tertiary referral center providing general and subspecialty services and training. Pediatrics outpatient eye clinic provides service for all referral cases. From that around 480 infants seen per year that is 40 infants per month.

4.2. Study Design and Period

An institutional based retrospective cross-sectional study was conducted from March 1 to April 1, 2020.

4.3. Source of Population

Medical records of all children who visited pediatrics outpatient eye clinic of Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia.

4.3.1. Study Population

Medical records of all infants who visited pediatrics outpatient eye clinic of Minilik II hospital from January 2018 – December2019, Addis Ababa, Ethiopia.

4.4. Eligibility Criteria

4.4.1. Inclusion Criteria

Medical records of all infants with age of presentation were less than 12 months old and their gestational ages were less than 37weeks who visited pediatrics outpatient referral eye clinic of Minilik II hospital.

4.4.2. Exclusion Criteria

Medical records of infants who had congenital abnormality and congenital eye disease were excluded from the study.

4.5. Sample Size Determination

The sample size was determined by the assumption that 50% of prevalence of retinopathy of prematurity since there is no study conducted in Ethiopia concerning retinopathy of prematurity and with 5% marginal error, 95% confidence interval (CI) and 10% for contingency. Based on this assumption, the actual sample size for the study was determined using the formula for single population proportion.

When $n = \frac{(Z_{\alpha/2})^2\, p\,(1-p)}{d^2}$

n = sample size

z = z value for 95% C.L. = 1.96

p =expected prevalence = 50%q = (1-p)

d = Desired precision = 5%

Thus, $n = \frac{1.962 \times 0.5 \times 0.5}{(0.05)2} = 384$

By using adjustment formula

$n_{final} = \frac{n}{1+n/N}$

$n_{final} = \frac{384}{1+384/960}$

$n_{final} = \underline{\underline{274}}$

10% for contingency then it was 301

4.6. Study Variables

4.6.1. Dependent Variable

- Prevalence of Retinopathy of prematurity

4.6.2. Independent Variables

Infant characteristics

- Gender
- Age

Major risk factors

- Gestational age
- Birth Weight
- Oxygen therapy

Maternal related risk factors

- Maternal preeclampsia/eclampsia
- Maternal diabetes mellitus
- Maternal age
- Mode of delivery

Infant Co morbidities factors

- Apnea
- Respiratory distress syndrome (RDS)
- Anemia
- Sepsis

Other factors

- Blood transfusion
- Length of hospital stay

4.7. Operational Definition

Retinopathy of prematurity: is the developmental disorder of the retina in premature infants.

Prevalence of ROP: the proportion of individuals in a population having ROP.

Type 1 ROP: refers to retinal disease that occur at any stage in Zone I with plus disease and Stage 2-3 disease in zone II with plus disease received laser treatment within the neonatal unit within 48 hours of diagnosis.

Type 2 ROP: refers to retinal diseases that occur in stage 1-2 in zone I without plus disease and stage 2-3 in zone II without plus disease were kept on follow up every two weeks until regression of ROP or vascularization in zone-III was achieved.

Plus disease: refers to the presence of dilatation and tortuosity of the posterior retinal blood vessels.

Infant: is a young baby, from 28 days to12 months of age.

Gestational age: is extent of time that a fetus grows inside mother's uterus.

4.8. Sampling technique and procedure

Minilik II hospital was selected by purposive method which is the only referral hospital that has a dilated ROP eye exam. From pediatrics outpatient eye clinic HMIS registration book from January 2018-December 2019 a sampling frame was prepared for 301 infants of medical records. In order to prepare this sampling frame the infant medical records was selected from registration book based on the inclusive age of the infant that was less than 12 months old. Then, the study subject from the prepared sampling frame was selected using systematic random sampling method where every 3 infants were selected. Lottery method was used to identify the first unique number, as a starting point to select study subjects from sampling frame. Finally the selected study subject medical records number was used to take out card from the record unit.

4.9. Instrument and Measurement

The questionnaire was adapted from Onyango O and Sang jin kim studies (27, 46) with a careful modification and was validated by an ophthalmologist and researcher. It was prepared as a check list which was used to gather information from infant's medical record. It was composed of six parts which were infant characteristics factors (2 items), major risk factors (3 items) and alternative risk factors(4 items), ROP description (3 items) and infant co morbidities (4) and others (3items) which made16 multiple choice and 3 open ended questions.

4.10. Data Collection Procedure

One Bachelor of Science nurse was engaged as supervisor and two diploma nurses were also engaged as a data collector. The data collectors were responsible to review medical records of the infants and record in a consistent manner in the questionnaires, finally the result was submitted to the investigator as scheduled.

4.11. Data Quality Assurance

Supervisor and data collectors were oriented and trained on how to review the medical records and record the information. Afterward, they were assigned to the hospital in order to assess appropriateness of wording and clarity of the questions, it was pre-tested on 5% of the calculated sample size of the infants medical records those who were not be the actual study participants and adjustment was made based on the results of the pre-test. If medical records were not found during data collection period, repeated trial would attempt to get it. During the data collection period monitoring and supervision was conducted by supervisor and the investigator to ensure the data quality. Finally, the collected data was checked by the supervisor and investigator for its completeness.

4.12. Data management and Analysis

The collected data was checked for completeness and consistencies, and then it was coded and entered in to EPI data 6.4.2.0 and exported to SPSS version 25 for analysis. Moreover, descriptive analysis like frequency was used to present the result. The binary logistic regression and multivariate analysis was used to recognize the associated factors. Strength of association was measured using odds ratio, and 95% confidence intervals. Statistical significance was declared at P value <0.05.

4.13. Ethical Consideration

After getting acceptances from institutional review board of Addis Ababa University, Department of Nursing and Midwifery has written letter of cooperation to Addis Ababa health bureau then Addis Ababa health bureau was written a letter to Minilik II hospital. After receiving permission from the hospital administration, the request letter was written for the concerned bodies of ophthalmology departments. Following this, searching and obtaining of the selected samples' medical record was processed with assigned person. Lastly, confidentiality of the study participant from their medical records which identify them was protected. This was achieved through anonymous and by removing the study subject's identifiable information, which specifically refers to identity of patient like MRN and coding was used instead.

4.14. Dissemination and Utilization of Results

Result of the study was submitted and presented to department of Nursing and Midwifery, College of Health Sciences, Addis Ababa University. Effort will be made to present the result in local or international workshops, conferences and meetings. For the publication purpose, the abstract of this thesis was submitted to national or international peer reviewed publishers.

CHAPTER FIVE

5. RESULT

5.1. Infant characteristics

A total of 960 infants had visited pediatrics outpatient referral clinic of Minilik II hospital for vision problem during the period from January 2018 to January 2020.Of these, 301infants were enrolled in the study based on the inclusion criteria. The medical records of those 301 infants were reviewed. The ratio of male to female was 1:1 with 151(50.2%) female and 150(49.8%) male. Majority (42.5%) of the infants were between the age of one month and six months. However, 46(15.3%) of neonates were below the age of less than one month and 127(42.2%) of infants were between six months and12 months. (Table 1)

Table 1: Demographic characteristics of infants who were visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		Frequency	Percent
Age			
	< 1month	46	15.3
	1 to <6 months	128	42.5
	6 to 12months	127	42.2
Total		301	100
Gender			
	Male	150	49.8
	Female	151	50.2
Total		301	100

5.2. Major risk factors

Most (83.1%) of infants were ≥32weeks of gestational age that is reaching the nasal retina and develop temporal retina. The rest, 51(16.9%) were < 32weeks of gestation. With regard to birth weight, 243 (80.7%) infants had a birth weight of above 1500gm which is a low birth weight, 49 (16.3%) infants were with a birth weight between 1001 and 1500gm which is very low birth weight, and nine (3%) infants had a birth weight of ≤1000gm that is extremely a very low birth weight. In the case of oxygen therapy, majority (65.1%) of the infants had no oxygen therapy whereas, 105 (34.9%) infants had oxygen therapy. Of those who had oxygen therapy, 50(47.6%) infants had the therapy for less than seven days and the remaining 55(52.4%) had the treatment for seven and more days. (Table 2)

Table 2: Major risk factors of infants who visited Minilik II hospital from January 2018-December 2019, Addis Ababa, Ethiopia, 2020

		Frequency	Percents
Gestational age			
	≥32WK	250	83.1
	<32 WK	51	16.9
Birth weight		301	100.0
	<1000gm	9	3.0
	1001-1500gm	49	16.3
	>1500gm	243	80.7
Oxygen therapy	Yes	105	34.9
	No	196	65.1
Duration of oxygen therapy			
	<7 days	50	47.6
	≥ 7days	55	52.4

5.3. Maternal related risk factors

Majority (59.5%) of mothers were between29 and39 years of age. In the case of maternal diabetes, most (99.3%) of them had no diabetes. The same scenario occurred in the case of preeclampsia. Two hundred eighty-five (94.7%) mothers had no preeclampsia. With regard to mode of delivery, majority (78.1%) of mothers gave birth by spontaneous vaginal delivery. (Table 3)

Table 3: Maternal related risk factors of infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		Frequency	Percent (%)
Maternal age			
	18-28yrs.	112	37.2
	29-39yrs.	179	59.5
	≥40 yrs.	10	3.3
Maternal Diabetes mellitus			
	Yes	2	0.7
	No	299	99.3
Maternal preeclampsia			
	Yes	16	5.3
	No	285	94.7
Mode of delivery			
	SVD	235	78.1
	CS	62	20.6
	Vacuum	1	0.3
	Forcipes	3	1.0

5.4. Description of Retinopathy of prematurity

Out of 301 infants who visited pediatrics referral outpatient clinic for vision problem during the period from January 2018 to January 2020, 39(13%) infants developed retinopathy of prematurity (Figure 2). Among the 39 infants, more than half of them who had ROP on Zone II + Stage 1 were 22(56.4%); followed by Zone II + stage 2 accounts (12.8%) and Stage-5 accounts 4(10.2%). (Table 4)

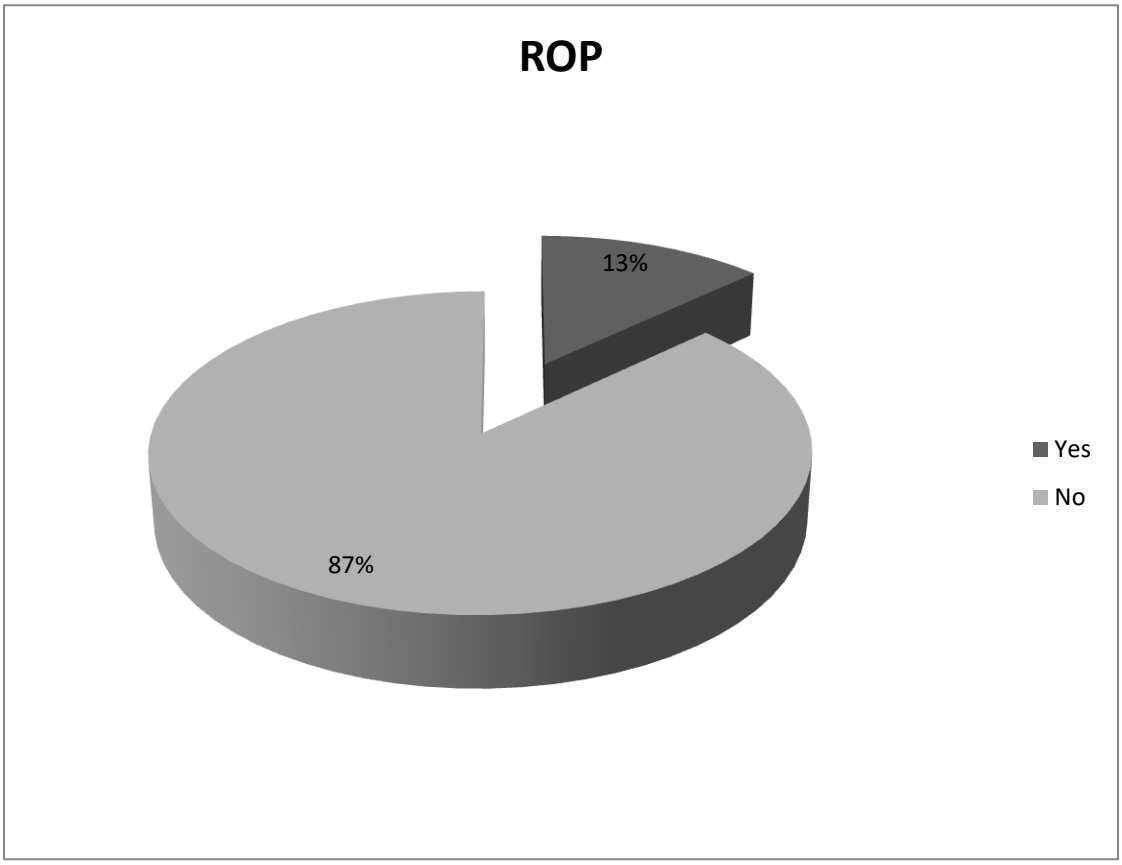

Figure 2: Prevalence of ROP for infants who visited Minilik II hospital from January 2018-December 2019, Addis Ababa, Ethiopia, 2020

Table 4: Prethreshold related with ROP for infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		Zones with ROP	
		Frequency	Percent (n/39)
Prethreshold	Zone II + stage 1	22	56.4
	Zone II + stage 2	5	12.8
	Stage 5	4	10.2
	Stage 4	2	5.1
	Zone III + stage 2	2	5.1
	Zone I + stage 2	1	2.6
	Zone III + stage 4	1	2.6
	Zone II + stage 3	1	2.6
	Zone III + stage 1	1	2.6

Out of 301 infants, 64(21.3%) were checked for fully vascularization. Fully vascularized infants were 37(57.8%) whereas 27 (42.2%) were not vascularized. From those infants who had ROP, 16(41%) infants were regressed spontaneously with follow up and 23(59%) infants were not fully vascularized. Furthermore, infants who had no ROP and fully vascularized were 21(84%). From infants that had no ROP but follow for vascularization, 4(16%) infants were not fully vascularized. (Table 5)

Table 5: Fully vascularized related to ROP for infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		ROP		Total (n/64)
		Yes(n/39)	No(n/25)	
Fully vascularized	Yes	16(41%)	21(84%)	37(58%)
	No	23(59%)	4(16%)	27(4%)

5.5. Retinopathy of prematurity related to infant characteristics

Majorities (58.9%) of the infants with ROP were presented between the age one and six months; seven (18%) infants with ROP were presented before month. Regarding to gender, twenty two (56.4%) infants with ROP were female. (Table 6)

Table 6: Retinopathy of prematurity related to demographic characteristics of infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		ROP		Total n/301
		Yes(n/39)	No(n/262)	
Age	<1month	7(18%)	39(15%)	46(15.3%)
	1 to <6months	23(58.9%)	105(40%)	128(42.5%)
	6 to 12months	9(23.1%)	118(45%)	127(42.2%)
Gender	Male	17(43.6%)	133(50.8%)	150(49.8%)
	Female	22(56.4%)	129(49.2%)	151(50.2%)

5.6. Retinopathy of prematurity related to major risk factors

Twenty-three (59%) infants who had ROP were with the gestational age of less than 32 weeks. Regarding their birth weight, majority (51.3%) of the infants who had ROP were with birth weight of 1001gm to1500 gm. Infants with a birth weight of ≥ 1500gm (28.2%) and less than 1000 gm (20.5%) had also developed ROP. With regard to oxygen therapy, 24 (61.5%) of infants who were on oxygen therapy for seven and more days had developed ROP. Infants who were on oxygen therapy for less than seven days and were not on oxygen therapy at all also developed ROP, 12(30.8%) and 3(7.7%) respectively. (Table 7)

Table 7: Major risk factors related to ROP for infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		Did infant has ROP		Total (n/301)
		Yes(n/39)	No(n/262)	
Gestational age	≥ 32wks	16(41%)	234(89.3%)	250(83.1%)
	<32wks	23(59%))	28(10.7%)	51(16.9%)
Birth weight	<1000gm	8(20.5%)	1(0.4%)	9(3%)
	1001-1500gm	20(51.3%)	29(11.1%)	49(16.3%)
	≥1500gm	11(28.2%)	232(88.5%)	243(80.7%)
Duration of oxygen Therapy	<7 days	12(30.8%)	38(14.5%)	50(16.6%)
	≥7days	24(61.5%)	31(11.8%)	55(18.3%)
	had no oxygen	3 (7.7%)	193(73.7%)	196(65.1%)

5.7. Maternal related risk factors related to retinopathy of prematurity

Majority (54%) of the infants with ROP were born from mothers aged between 29 and 39 years. None of the infants with ROP were born from diabetic mothers and six (15.4%) of them were born from mothers who had preeclampsia. Regarding to the mode of delivery, more than half (56.4%) of the infants who had ROP were delivered by SVD. (Table 8)

Table 8: Maternal related risk factors related to retinopathy of prematurity for infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		ROP		Total (n/301)
		Yes(n/39)	No(n/262)	
Maternal Age	18-28yrs	15(38.4%)	97(37%)	112(37.2%)
	29-39yrs	21(54%)	158(60.3%)	179(59.5%)
	≥ 40yrs	3(7.6%)	7(2.7%)	10(3.3%)
Maternal DM				
	Yes	0	2(0.8%)	2(0.7%)
	No	39(100%)	260(99.2%)	299(99.3%)
Preeclampsia				
	Yes	6(15.4%)	10(3%)	16(5.3%)
	No	33(84.6)	252(96.2%)	285(94.7%)
Mode of delivery				
	SVD	22(56.4%)	213(81.3%)	235(78.7%)
	CS	17(43.6%)	45(17.2%)	62(21%)
	Vacuum	0	1(0.38%)	1(0.3%)
	Forcipes	0	3(1.12%)	3(1%)

5.8. Retinopathy of prematurity related to co morbidities and other factors

Out of 39 infants who had ROP, 37(94.9%) had sepsis, 32 (82%) had RDS, 14(36%) had apnea and 12 (30.8%) had anemia. Moreover, 36(92.3%) infants who had ROP were having a length of hospital stays for greater than seven days. Other factors that presents in infants with ROP were phototherapy (12.8%), twin birth (10.3%), triple birth (5.1%), hydrocephalus (5.1%) and PDA (2.6%). (Table 9)

Table 9: Retinopathy of prematurity related to co morbidities and other factors for infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020

		Did infant has ROP		Total n/301
		Yes(n/39)	No(n/262)	
Apnea	Yes	14(36%)	21(8%)	35(11.6%)
	No	25(64%)	241(92%)	266(88.3%)
Anemia	Yes	12(30.8%)	18(6%)	30(10%)
	No	27(69.2%)	244(81%)	271(90%)
RDS	Yes	32(82%)	56(21.4%)	88(29.2%)
	No	7(18%)	206(78.6%)	213(71.5%)
Sepsis	Yes	37(94.9%)	63(24%)	100(33%)
	No	2(5.1%)	199(76%)	201(67%)
Length of hospital stay	<7 days	3(7.7%)	55(21%)	58(19.3%)
	≥7 days	36(92.3%)	64(24.4%)	100(33.2%)
	Had no hospital stay	0	143(54.6%)	143(47.5%)
Other factors	Phototherapy	5(12.8%).	11(4.2%)	15(5%)
	Hydrocephalus	2(5.1%)	0	2(0.7%)
	Twin	4(10.3%)	7(2.7%)	11(3.7%)
	Triple	2(5.1%)	1(0.38%)	3(1%)
	PDA	1(2.6%)	0	1(0.3%)
	Had no other factor	25(64.1%)	234(89.3%)	259(86%)
	VSD	0	1(0.38%)	1(0.33%)
	Asphyxia	0	8(3.1 %)	8(2.66 %)

5.9. Factors associated with retinopathy of prematurity

To identify factors associated with retinopathy of prematurity, logistic regression model was used. The variables that were used first correlated with bivariate logistic regression and that had a P<0.05 were used for the multiple regression analysis as independent variables. On bivariate analysis, gestational age, birth weight, duration of oxygen therapy, preeclampsia, apnea, RDS, anemia, sepsis and blood transfusion were associated with the occurrence of ROP. (Table 10)

After obtaining statistically significant variables at p<0.05 in binary logistic regression analysis, multiple logistic regression analysis was carried out to see the independent predictors of retinopathy of prematurity. The multi variable logistic regression was carried out by taking retinopathy of prematurity as a covariate in addition to those variables where significant association was obtained in binary logistic regression. After adjusting potential confounders, having an extremely low birth weight [AOR: 12.51; 95%CI (1.218-128.532)], very low birth weight [AOR: 39.28; 95%CI (3.204-481.658)], duration of oxygen therapy for more than seven days [AOR: 5.317; 95%CI (1.009-28.28.019)] having sepsis [AOR: 9.805; 95%CI (1.592-60.388)] were independent predictors of retinopathy of prematurity. However, gestational age, preeclampsia, apnea, RDS, anemia and blood transfusion were lost their significance.

Birth weight had statistically significant association with ROP. Those infants with extremely low birth weight (<1000gm) were 12.51 times more exposed to ROP than those with birth weight above 1500gm [AOR: 12.51; 95%CI (1.218-128.532)]. Those Infants with very low birth weight (1001-1500gm) were 39.2 times more vulnerable to develop ROP than those with birth weight of above 1500 gm [AOR:39.28; 95%CI (3.204-481.658)].

Duration of oxygen therapy had significant association with ROP. Those infants with oxygen therapy for more than seven days were 5.31 times more vulnerable to develop ROP than those without oxygen therapy [AOR: 5.317; 95%CI (1.009-28.28.019)].

Sepsis had significantly associated with retinopathy of prematurity. Those Infants with sepsis were 9.8 times more vulnerable to develop ROP than those without sepsis [AOR: 9.805; 95%CI (1.592-60.388)]. (Table 10)

Table 10: Factors associated with ROP of infants who visited Minilik II hospital from January 2018- December 2019, Addis Ababa, Ethiopia, 2020.

Variables	ROP		P-value	95% Confidence interval	
	Yes	No		COR	AOR
Gestational age					
<32wk	23(59)	234(89.3)	0.707	12.013(5.681-25.40)	0.811(0.271-2.422)
≥32 or equal	16(41)	28(10.7)		1	1
Birth weight					
≤1000gm	8(20.5)	1(0.4)	0.034	11.600(1.344-100.3)	12.51(1.218-128.532) *
1001-1500gm	20(51.3)	29(11.)	0.004	168.7(19.36-1470.45)	39.28(3.204-481.658)**
>1500gm	11(28.2)	232(88.5)		1	1
Duration of oxygen therapy					
<7 days	12(30.8)	38(14.5)	0.883	0.408(0.176-0.945)	0.927(0.335-2.563)
≥7days	24(61.5)	31(11.8)	0.049	20.31(5.47-75.452)	5.317(1.009-28.019)*
Had no oxygen	3 (7.7)	193(73.7)		1	1
Preeclampsia					
Yes	6(15.4)	10(3)	0.763	4.582(1.563-13.427)	0.800(0.188-3.406)
No	33(84.6)	252(96.2)		1	1
Apnea					
Yes	14(36)	21(8)	0.601	6.427(2.912-14.186)	0.750(0.256-2.198)
No	25(64)	241(92)		1	1

RDS					
Yes	32(82)	56(21.4)	0.838	16.816(7.049-40.12)	1.147(0.309-4.258)
No	7(18)	206(78.6)		1	1
Anemia					
Yes	12(30.8)	18(6)	0.995	6.025(2.623-13.839)	0.993(0.117-8.413)
No	27(69.2)	244(81)		1	1
Sepsis					
Yes	37(94.9)	63(24)	0.014	58.43(13.6-249.32)	9.805(1.592-60.388) *
No	2(5.1)	199(76)		1	1
Blood transfusion					
Yes	12(30.8)	19(7.3)	0.775	5.684(2.491-12.969)	0.734(0.088-6.147)
No	27(69.2)	243(92.7)		1	1

COR=Crude odds ratio, AOR=Adjusted Odds ratio, *=p. Value <0.05, **=p. Value <0.01,

6. DISCUSSION

The results of this study have shown that the prevalence of retinopathy of prematurity in Minilik II referral hospital from January 2018-Jaunary 2020 was 13%. This was less than that reported in many other studies, in Kenya 41.7% (27), in Nigeria 47.2% (22), in India 19.2% (31), in Egypt 19.2% (54) and in China 31.6% (33). This can be explained by the fact that this study included all infants with gestational age of less than 37wks who had eye examination in outpatient since there was no separated screening only for ROP in NICU. However, it was higher than the study conducted in Indonesia 11.9%(59), in Beijing 10.8%(60), in Pakistan 10.5% (43) and in Switzerland 9.3% (34).

Retinopathy of prematurity is a serious morbidity of prematurity the occurrence and severity rise with low birth weight (55). The findings of this study have also shown that birth weight had significant association with ROP. Those infants with extremely low birth weight (P=0.034) and very low birth weight (P =0.004) had a risk for the development of ROP. This was agreed with many studies.

A study done by Freitas M showed that extremely low birth weight infants were a significant factor for the development of ROP(P=0.001)(23). Another study also showed that extremely low birth infants had 10.8 times risk to develop ROP than that of very low birth weight infants(59). Additionally another study done by Onyango O et al showed that birth weight had significant association with the occurrence of ROP(P=0.027)(27). Besides another study done in India by Dwivedi described that birth weight had independent risk factors for the occurrence of ROP(P=0.02)(61).

Another study done by Arjumand Sohailain a Tertiary Care Hospital in a Lower-Middle Income Country Pakistan showed that birth weight (P=0.037) was an independent risk factor for the occurrence of ROP(43). Furthermore, study done in Palestine by Akkawi mentioned that birth weight had a significant association for the development of ROP with a significant value of P=0.0085(40). Moreover, a study done in India by R,Nikil showed that birth weight was a significant factor for the incidence of ROP (P=0.001)(31).

YunxiaLengin Guangzhou First People's Hospital in China also described that birth weight was a significant factor for the development of ROP (P=0.009)(33).

However, this study was different from some studies, a study done in Egypt by Hakeem et al showed that birth weight was an insignificant factor for the incidence of ROP with a p value of 0.1(54) and a Nigeria study by Adedayo O also showed that birth weight was an in significant factor for development ROP(P=0.94)(22). This is explained as small number of infants with very low birth weight enrolled on their studies although low birth weight infants are more vulnerable to long term oxygen therapy, blood transfusion, sepsis and hospital acquired infection.

The result of this study have shown that oxygen therapy for more than seven days had a significant association for the development of ROP (P=0.049). A study done in Rwanda by F. Mutangana et al have shown that oxygen therapy had a significant association for the development of ROP($p<0.01$)(62). Another study done by Akkawi has shown that oxygen therapy had a significant association for the occurrence of ROP(P=0.038)(40). In addition, a study done by Cut Badriah showed that oxygen therapy for more than seven days was an independent factor for the development of ROP(59).

The finding of this study has also shown that sepsis had a significant association for the development of ROP (P=0.014). Sepsis might be active in the course of cytokines and endotoxins, which directly have an effect on retinal angiogenesis. This process is frequently escorted by hypotension, which can cause tissue perfusion impairment and retinal ischemia (63).

This finding was agreed with other studies, Hakeem et al, described on their studies that sepsis was an independent factor for the development of ROP(P=0.003)(54). Another study done in Turkey said that sepsis was a significant factor for the incidence of ROP (P=0.001) (55). A study conducted in Nigeria also mentioned that sepsis had an independent factor for the development of ROP(P=0.006)(22). Furthermore, a study done in Italy by Cesarina Borroni showed that sepsis was a significant factor for the occurrence of ROP ($p = 0.002$)(56).

However, this study finding was unlike with some studies. An Indonesian study showed that sepsis was an insignificant factor for ROP(0.07) (59). And another study done in Kenya also showed that sepsis was insignificant factor for the development of ROP(27). This is explained as sepsis and hospital acquired infection is depend on the quality of neonatal intensive care unit. Due to the limited financial resource the quality of the care is decreased.

Generally, this study showed that birth weight and oxygen therapy were a major risk factors and sepsis was a co morbidities factor. A systemic review and a meta-analysis study in Iran showed that birth weight, oxygen therapy and sepsis were a significant risk factors for retinopathy of prematurity(42).

7. CONCLUSION AND RECOMMENDATION

7.1. Conclusion

Based on the study result of this study, at Minilik-II referral hospital the prevalence of retinopathy of prematurity (ROP) was found (13%). Birth weight, oxygen therapy and sepsis had shown a significant relation with the development of ROP. Therefore, considering blended oxygen therapy and prevention for underweight at birth and sepsis are very important to reduce the risk of childhood blindness as a complication.

7.2. Recommendation

To Government

Ministry of health needs to establish a strategy with antenatal care unit and neonatal intensive care unit to prevent underweight delivery and sepsis. And it should be support NICU units to use oxygen blender.

Hospital administrators

- Prepare training on infection prevention for neonatal intensive care unit and obstetrics and gynecology unit to reduce before and after delivery infections.
- Prepare materials that used to prevent infection for NICU and Gynecology units.
- Arrange oxygen blender and pulse-ox-meter for NICU.
- Prepare a septic unit in NICU to isolate septic neonate from non-septic.
- Assign ophthalmologist in NICU for periodic screening.
- Give emphasis to antenatal care unit, on educating mothers to avoid the risk of low birth weight.

To researchers:

- Further research in longitudinal study designs such as prospective type is needed to identity prevalence and risk factor of retinopathy of prematurity especially in NICU.

Health professionals' practice:

- Obstetricians and gynecologist works on prevention of intrauterine infection and low birth weight delivery.
- Neonatologist and neonatal units' nurses should work on control sepsis and prevent long term oxygen therapy.
- Neonatal units nurses and physicians should monitor neonatal oxygen saturation
- Health professional in NICU should timely refer to ophthalmologist those underweight, had oxygen therapy and septic infants for further evaluation of ROP.
- Antenatal unit staffs give health education for mothers to prevent ascending infection and underweight birth.

8. STRENGTH AND LIMITATION

8.1. Strength of the study

- The sample size of the study was high consequently representativeness increased.
- As a first study in Ethiopia it will give important information about retinopathy of prematurity.
- Maternal risk factor was studied as a risk factor for ROP.

8.2. Limitation of the study

- Lack of adequate literatures on the same or related topic in sub Saharan countries especially in Ethiopia.
- Being a retrospective study in spite of no missing records.
- The study didn't consider ROP treatment, only focus on prevalence and risk factors of ROP

9. REFERENCE

1. Mutlu FM SS. Treatment of retinopathy of prematurity:a review of conventional and promising new therapeutic options Int J Ophthalmol. 2013;6(2):228-36.
2. Blencowe H, Lawn JE, Vazquez T, Fielder A, Gilbert C, al. e. Preterm associated visual impairment and estimates of retinopathy of prematurity at regional and global levels for 2010. Pediatric. 2013;74:35–49.
3. Beharry KD VG, Lazzaro DR, Aranda JV. Pharmacologic interventions for the prevention and treatment of retinopathy of prematurity. Semin Perinatol. 2016;40:189–202.
4. Rao RC DB. Mechanisms and management of retinopathy of prematurity. N Engl J Med. 2013;368(12):1161.
5. Celebi AR. The incidence and risk factors of severe retinopathy of prematurity in extremely low birth weight infants in Turkey. Med Sci Monit. 2014;20:1647–53.
6. Dave HBea. The societal burden of blindness secondary to retinopathy of prematurity in Lima, . Am J Ophthalmol. 2012;154(4):750-5.
7. Jefferies AL. Retinopathy of prematurity: recommendations for screening. Paediatr Child Health. 2010;15(10).
8. Rastriya_Bal_Swaasthya_Karyakram. Child health screening and early intervention services Health andFamilyWelfare. underNRHMMinistry ofHealth and FamilyWelfare. 2013.
9. Fierson WM. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2013;131(1):189-95.
10. Gilbert C. Retinopathy of prematurity a global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev. 2008;84:77–82.
11. Rahi J GC. Epidemiology of visual impairment in children.Chapter 2. Pediatric Ophthalmology and Strabismus,4th Ed. Scott Lambert and Christopher Lyons. London: Saunders, . Elsevier Ltd. 2016.
12. Sommer A, Taylor HR, Ravilla TD, al. e. Challenges of ophthalmic care in the developing world. Ophthalmol. 2014;132:640-4.

13. Abdel HA. Retinopathy of prematurity:a study of incidence and risk factors in NICU of Al-Minya University Hospital in Egypt. J Clin Neonatol. 2012;2(1):76.
14. Uhumwangho OM, YT. I-A. Awareness and screening for retinopathy of prematurity among paediatricians in Nigeria. J West Afr Coll Surg. 2013;3(3):33.
15. Chaudhry TA, Hashmi FK, Salat MS, al. e. Retinopathy of prematurity: an evaluation of existing screening criteria in Pakistan. Ophthalmol. 2014;98:298–301.
16. Aremsen L, Duran P, Silva J, Brumana LA. cross-sectional observational study of retinopathy of prematurity in Latin America and the Caribbean Revista Panamerica de Salud Publica. 2016;39:322–9.
17. Zin AA, Moreira ME, Bunce C, Darlow BA, CE. G. Retinopathy of prematurity in 7 neonatal units in Rio de Janeiro: Screening criteria and workload implications. Pediatrics. 2010;126(2).
18. Bashinsky AL. Retinopathy of Prematurity. N C Med J 2017;78(2):124-8.
19. Wilson CM EA, Fielder AR. The challenge of screening for retinopathy of prematurity. Clin Perinatol. 2013;40(2):241-59.
20. Courtright P HA, Lewallen S. Visual impairment in children in middle- and lower-income countries. Arch Dis Child. 2011;96(12):1129–34.
21. Srinivas Murki SK. Role of neonatal team including nurses in prevention of ROP. COMMUNITY EYE HEALTH JOURNAL. 2018; 31.
22. Adedayo AO RU, Chidi NG,Augusta EU. Retinopathy of prematurity in Port Harcourt, Nigeria. . . ISRN Ophthalmol. 2014.
23. Freitas AM, Mörschbächer R, Thorell MR, EL. R. Incidence and risk factors for retinopathy of prematurity: a retrospective cohort study. Int J Retina Vitreous. 2018;20(4).
24. Maroufizadeh S, Almasi-Hashiani A, Omani Samani R, Sepidarkish M. Prevalence of retinopathy of prematurity in Iran: a systematic review and meta-analysis. Int J Ophthalmol. 2017;10(8):1273–9.
25. Liegl R, Hellström A, LE. S. Retinopathy of prematurity: the need for prevention. Eye Brain. 2016;91(8):102.
26. Senthil MP SM, Bujang MA, et al. Risk factors and prediction modelsfor retinopathy of prematurity. Malays J Med Sci. 2015;22(5).

27. Onyango O ea. Retinopathy of prematurity in Kenya: prevalence and risk factors in a hospital with advanced neonatal care. Pan Afr Med J. 2018;29(152).
28. Edy Siswanto J SP. Retinopathy of prematurity in Indonesia: Incidence and risk factors. Neonatal Perinatal Med. 2017;10(1):85-90.
29. Brian W. Fleck. Retinopathy of Prematurity. J NeoReviews. 2019;10(1).
30. Kift EV, al e. Retinopathy of prematurity screening criteria and workload implications at Tygerberg Children's Hospital, South Africa: A cross sectional study. SAMJ. 2016;106(6).
31. R. Nikhil, K. Rajendran, Krishnan. B. Prevalence and outcome of retinopathy of prematurity in preterm infants, with low birth weight at KMCH, Tamil Nadu, India. International Journal of Contemporary Pediatrics. 2019 6(2).
32. Xu Y, al. e. Screening for retinopathy of prematurity in China: a neonatal units-based prospective study. Invest Ophthalmol Vis Sci 2013;54(13).
33. Yunxia L, et al. . The treatment and risk factors of retinopathy of prematurity in neonatal intensive care units BMC Ophthalmology 2018;301(18).
34. Gerull R, al. e. Incidence of retinopathy of prematurity (ROP) and ROP treatment in Switzerland 2006-2015: a population-based analysis. Child Fetal Neonatal 2018;103(4):337–42.
35. Anamika Dwivedi DD, Sujata Lakhtakia, Charudutt Chalisgaonkar, Shashi Jain. Prevalence, risk factors and pattern of severe retinopathy of prematurity in eastern Madhya Pradesh. Indian Journal of Ophthalmology. 2019;67(6).
36. Gopal ea. Prospective study of factors influencing timely versus delayed presentation of preterm babies for retinopathy of prematurity screening at a tertiary eye hospital in India. Indian Journal of Ophthalmology 2019;67(6).
37. Vinekar Aea. Role of tele-medicine in retinopathy of prematurity screening in rural outreach centers in India e a report of 20,214 imaging sessions in the KIDROP program. Fetal & Neonatal Medicine. 2015;20:335e45.
38. Ludwig C, al. e. The epidemiology of retinopathy of prematurity in the United States. . Ophthalmic Surg Lasers Imaging Retina. 2017;48(7):553–62.
39. AAoPSo O. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2013;131(1):189–95.

40. Mohammad T. Akkawi MMS, Amjaad N. Abu Shams3, Doaa M. Al-Hardan3, Lara J. Omar, Omar H. Almahmoud and Jamal A. S. Qaddumi. Incidence and risk factors of retinopathy of prematurity in three neonatal intensive care units in Palestine. BMC Ophthalmology. 2019;189(19).
41. Holmström G, Larsson E. Outcome of retinopathy of prematurity. . Clin Perinatol. 2013;2(40):311–21.
42. Milad Azami, et a. Prevalence and risk factors of retinopathy of prematurity in Iran: a systematic review and meta-analysis BMC Ophthalmology 2018;18(83).
43. Arjumand Sohaila ea. Frequency of Retinopathy of Prematurity in Premature Neonates with a Birth Weight below 1500 Grams and a Gestational Age Less than 32 Weeks: A Study from a Tertiary Care Hospital in a Lower Middle Income Country. plusone. 2014;9(7).
44. Cavallaro Gea. The pathophysiology of retinopathy of prematurity: an update of previous and recent knowledge. Acta Ophthalmol. 2014;92:2–20.
45. The BOOST II United Kingdom A, and New Zealand Collaborative Groups. Oxygen saturation and outcomes in preterm infants. N Engl J Med. 2013;368(22):2094-104.
46. Sang Jin Kim, al. e. Retinopathy of Prematurity: A Review of Risk Factors and their Clinical Significance. Surv Ophthalmol. 2018;63(5):618–37.
47. Engels T PJ, Schoofs K,et al. . Automated measurement of sFlt1, PlGF and sFlt1/PlGF ratio in differential diagnosis of hypertensive pregnancy disorders. Hypertens Pregnancy. 2013;32(4):459–73.
48. Gagliardi L RF, Da Fre M, et al. . Pregnancy disorders leading to very preterm birth influence neonatal outcomes: results of the population-based ACTION cohort study. . Pediatr Res [PubMed: 23493168]. 2013;73(6):794–801.
49. Yang C-Y LR, Yang P-H, et al. . Analysis of incidence and risk factors of retinopathy of prematurity among very-low-birth-weight infants in North Taiwan. 2011; 52(6):.]. Pediatr Neonatol[PubMed: 22192259. 2011;52(6):321–6.
50. Schrufer TL, Antonetti DA, Sonenberg N, al. e. prevents hyperglycemia-mediated induction of VEGF expression in the rodent retina and in Muller cells in culture. Diabetes. 2010;59(9):2107–16.

51. Chattopadhyay MP PA, Singh R, Datta S. Incidence and risk factors for retinopathy of prematurity in neonates. Indian Pediatr[PubMed: 25691191]. 2015;52(2):157–8.
52. Araz-Ersan B, Kir N, Akarcay K, al. e. Epidemiological analysis of retinopathy of prematurity in a referral centre in Turkey. Br J Ophthalmol. 2013;97(1).
53. Akter SH HM, Shirin M, Khalil I, Anwar K. Blood transfusion: a risk factor in retinopathy of prematurity. Bangladesh Journal of Child Health. 2010;34(2).
54. H. A. A. Hakeem GBM, and M. F. Othman,. Retinopathy of prematurity: a study of prevalence and risk factors,Middle East African Journal of Ophthalmology. 2012.; 19(3):289–94.
55. Bas AYea. Incidence, risk factors and severity of retinopathy of prematurity in Turkey (TR-ROP study): a prospective, multicentre study in 69 neonatal intensive care units. Br J Ophthalmol 2018;102:1711–6.
56. Borroni. Survey on retinopathy of prematurity (ROP) in Italy. Italian Journal of Pediatrics. 2013; 43(39).
57. Hutchinson AK, al. e. Clinical Models and Algorithms for the Prediction of Retinopathy of Prematurity. A Report by the American Academy of Ophthalmology. 2016;123(4):804–16.
58. FDRE CSA. Population Projection of Ethiopia for All Regions at Wereda Level from 2014 – 2017. 2013.
59. Cut Badriah ea. Prevalence and risk factors of retinopathy of prematurity. Paediatr Indones. 2012;52(3).
60. Chen Y LX-x, Yin H, Gilbert C, Liang JH, Jiang YR, et al. . Risk factors for retinopathy of prematurity in six neonatal intensive care units in Beijing, China. Br J Ophthalmol. 2008;92:326-30.
61. Dwivedi ea. Prevalence, risk factors and pattern of severe retinopathy of prematurity in eastern Madhya Pradesh. Indian Journal of Ophthalmology. 2019;67(6).
62. Francis Mutangana ea. Retinopathy of prematurity in Rwanda: a prospective multi-centrenstudy following introduction of screening and treatment services. The Royal College of Ophthalmologists. 2019;34:847–56.
63. Lee J DO. Perinatal infection, inflammation, and retinopathy of prematurity. Semin Fetal Neonatal Med. 2012;17:26-9.

10.ANNEXES

10.1. Annex I: Informed Consent

I am Hana Endale Aliyou, post graduate student at Addis Ababa University, College of Health Sciences, Department of Nursing and midwifery in Neonatal nursing track. Now I am conducting a study on Prevalence and risk factors of ROP among infants less than age 1 year in Minilik II hospital. Addis Ababa, Ethiopia, 2020.

The objective of the study is to assess prevalence and risk factors of ROP among infants less than age 1 year in Minilik II hospital Addis Ababa Ethiopia 2020. The study will have no risk but there is no doubt that the study will have the positive impact on reducing ROP. I ensure confidentiality by protecting the medical records that could identify study participants, the individual identifiers will be removed and not to be presented at all, privacy and confidentiality rules in accordance with the applicable regulatory requirements are all respected during the data collection through the presentation of the finding. As purpose of the study has been explained for me in the language I can understand, on behalf of pediatrics outpatient eye department of Minilk II hospital for safeguarding the registration book and patients' data.

I agree to allow the data collection process and ensure with my signature below.

Name ……..

Qualification ……..

Date……...

Signature…….

With regards Hana Endale

Tel no 251-913-24-25-24

aliyouhana@gmail.com

10.2. Annex II: Data Extraction Check List

Data collector name: _____

Card number: _____

Telephone number_____

Signature: _____

Code: _____

Circle the correct answer

Part I: Infant characteristic factors			
		Number	Remark
Characteristics	Variables		
1. Gender	a) Male b) Female		
2. Age of presentation	_____		
Part II: Major risk factors			
Characteristics	Variables	Number	Remark
1. Gestational age	a) ≥32wks b) <32wks		
2. Birth weight	a) ≤1000gm b) 1001-1500gm c) >1500gm		
3. Duration of oxygen therapy	a)< 7 days b) ≥7 days		
Part III :Alternative risk factors			
1. Maternal age	a) <18yrs b) 18-28yrs c) 29-39yrs d) ≥40yrs		
2. Maternal DM	a) Yes b) No		

3. Preeclampsia	a) Yes b) No		
4. Mode of delivery	a) SVD b) Cesarean section c) Vacuum d) Forcipes		

Part III: Description of Retinopathy of prematurity

Number	Characteristics	Variables	Remarks
1	ROP	a) Yes b) No	
2	Which prethreshold?	_____	
3	Did the infant fully vascularize?	a) Yes b) No	

Part IV: Infant co morbidities factor

Characteristics	Variables	Number	Remark
1. Apnea	a) Yes b) No		
2. RDS	a) Yes b) No		
3. Anemia	a) Yes b) No		
4. Sepsis	a) Yes b) No		

Part V:Other factors

1. Length of hospital stay(days)	a) < 7days b) ≥7days		
2. Blood transfusion	a) Yes b) No		
3. Other factor	_____		

APPROVAL BY THE BOARD OF EXAMINATION

THIS THESIS WORK BY HANA ENDALE ALIYOU IS ACCEPTED IN ITS PRESENT FORM BY THE BOARD OF EXAMINERS AS SATISFYING THESIS REQUIREMENT FOR THE DEGREE OF MASTER OF SCIENCE IN NEONATAL NURSING.

FULL NAME: HANA ENDALE (BSC)

SIGNATURE: _____

DATE: _____

EXAMINER

FULL NAME: FEKADU AGA

RANK: PHD, ASSISTANT PROFESSIOR

SIGNATURE: _____

DATE: _____

RESEARCH ADVISORS

ADVISER

FULL NAME: YOSIEF TSIGE

RANK: ASSISTANT PROFESSIOR

SIGNATURE: _____

DATE: _____

CO-ADVISER

FULL NAME: EMEBET BERHANE

RANK: LECTURER

SIGNATURE: _____

DATE: _____