ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING POST GRADUATE STUDIES

PREVALENCE OF THROMBOCYTOPENIA AND ITS ASSOCIATED FACTORS AMONG NEONATES ADMITTED IN NEONATAL INTENSIVE CARE UNIT OF ADDIS ABABA PUBLIC HOSPITALS, ETHIOPIA 2020/21.

PRINCIPAL INVESTIGATOR: MARKOS WODAJE

A RESEARCH THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY FOR PARTIAL FULFILLMENT OF THE MASTER'S OF SCIENCE IN NEONATAL NURSING.

MAY, 20 21

ADDIS ABABA, ETHIOPIA

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING POST GRADUATE STUDIES

PREVALENCE OF THROMBOCYTOPENIA AND ITS ASSOCIATED FACTORS AMONG NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT AT PUBLIC HOSPITALS IN ADDIS ABABA 2020.

PRINCIPAL INVESTIGATOR: MARKOS WODAJE

ADVISORS:

1. MR. NIGUSE TADELE (MSC, ASSISTANT PROFESSOR)

2. HANA LIJAEMIRO (MSC)

A RESEARCH THESIS SUBMITTED TO ADISS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY FOR PARTIAL FULFILLMENT OF THE MASTER'S OF SCIENCE IN NEONATAL NURSING.

MAY, 20 21

ADDIS ABABA, ETHIOPIA

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

MASTER OF SCIENCE RESEARCH PROJECT SUBMISSION FORM

Name principal investigator	Markos Wodaje (BSc)
Name of advisors	Mr.Niguse Tadele,(MSc,AssistantProfessor) Hana Lijaemiro (MSc)
The full title of the research project	Prevalence of thrombocytopenia and its associated factors among Neonates Admitted to Neonatal Intensive Care Unit at public Hospitals of Addis Ababa in 2020/21G.c.
Duration of the study	October –June 2020/21
Study area	Addis Ababa
Total cost of the project	A total cost of 26,295Ethiopian Birr.
Address of investigator	Phone: +251-922-89-90-8 Email: markoswodaje8@gmail.com

APPROVAL SHEET

I, the undersigned MSc student, declare that I have submitted my original work in the title of prevalence of thrombocytopenia and its associated factors among neonates admitted in neonatal intensive care units of public hospitals of Addis Ababa, Ethiopia, 2020/21.

Submitted by: -

Markos Wodaje _____ _____

Signature Date

This thesis work has been submitted for examination with my approval as:

Advisors:

1. **Name of Major Advisor**: Mr. Niguse Tadele(MSC, Assistant Professor)

   Signature_____

   Date_____

2. **Name of Co-Advisor**: Hana Lijaemiro (MSC)

   Signature_____

   Date_____

DECLARATION

I, the undersigned, declare that this thesis is my original work and has not been presented for a degree in this or another university and that all sources of materials used for this thesis have been fully acknowledged.

Name: Markos Wodaje (BSc)

Signature: _____

Date_____

Place: Addis Ababa University, College of Health Sciences, School of Nursing and Midwifery, Department of Nursing.

Date of submission: _____

This thesis is submitted for examination with my approval as university advisors.

Approved by:

Name of Major Advisor: Mr. Niguse Tadele (MSC.Assistant Professor)

Signature_____

Date_____

Name of Co-Advisor: Hana lijaemiro (MSC)

Signature_____

Date_____

STATEMENT OF THE AUTHOR

By my signature below, I declare and confirm that this thesis is my own work. I have followed all ethical and technical principles of scholarship in the preparation, data collection, data analysis and compilation of this thesis. Any scholarly matter that is included in the thesis has been given recognition through citation.

This thesis is submitted in partial fulfillment of the requirements for a master's degree in neonatal nursing at the Addis Ababa University. It will be submitted to Addis Ababa University Library and is made available to readers under the rules of the library. I declare that this thesis has not been submitted to any other institution anywhere for the award of any academic degree, diploma of certificate.

Name: Markos Wodaje

Signature_____

Date_____

School/Department: Nursing and Midwifery/Nursing

ACKNOWLEDGMENT

I would like to express my deepest appreciation and heartfelt thanks to my advisors Mr. Niguse Tadele, (MSc, Ass't Professor) and Hana Lijaemiro (MSc) for their valuable encouragement and unreserved support to develop this thesis. And also I would like to thanks Dr.Asrat Demste for her support and huge encourage throughout my work.

Next, I want to thank St. Peter specialized hospital for giving me the opportunity to study MSc in neonatal nursing as well as Addis Ababa University, college of health science, School of Nursing and Midwifery.

I also express my thanks to Vermont Oxford Network, especially thanks to Danielle Ehret for her fruitful comments and suggestion, who is voluntarily assigned by Vermont Oxford Network which supports Neonatal MSc program at Addis Ababa University.

ABBREVIATIONS AND ACRONYMS

ANC	Antenatal care
AOR	Adjusted Odds Ratio
APA	American Academy of Pediatrics
CI	Confidence interval
COR	Crude Odds Ratio
EDHS	Ethiopian demographic health survey
EOT	Early onset thrombocytopenia
GA	Gestational age
GMH	Gandhi Memorial Hospital
ICH	Intracranial hemorrhage
IUGR	Intrauterine Growth Retardation
LBW	LOW birth weight
LOT	Late Onset Thrombocytopenia
NICU	Neonatal Intensive Care unit
NT	Neonatal Thrombocytopenia
PNA	Perinatal Asphyxia
PROM	Prolonged Rupture Of Membrane
SPE	Sever Pre-Eclampsia
SPMMC	Saint Paul millennium medical college
SPSS	Statistical Package for Social Science
TASH	TikurAnbessa Specialized Hospital
Y-12HMC	Yekatit-12 Hospital Medical College
μ L	micro litter

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

SUMMARY

Background

Thrombocytopenia is one of the most frequent hematologic disorders encountered in the sick neonate. This is evidenced by a fairly high prevalence among neonates admitted to the neonatal intensive care unit 22%-35%, especially in very-low-birth-weight and preterm neonates its prevalence is up to 70%-80%. In Africa, the prevalence of neonatal thrombocytopenia in Nigeria is 53%, 12.4% in Tunisia, and 16.2% in Libya. However, in Ethiopia, no study assessed both its prevalence and associated factors. This study assessed the prevalence of thrombocytopenia and its associated factors among neonates admitted to neonatal intensive care unit at public hospitals in Addis Ababa in 2020/21.

Methodology: Institution based cross sectional study was conducted at NICU of selected Addis Ababa public hospitals from February 15thto March 15th, 2021. Single population proportion formula is used to determine sample size. The final sample size is 423. Data collected by using pretested, data extraction checklist for chart review by data collector. The collected data entered using Epi data and exported to SPSS version 25 for analysis. Variables that have P-value <0.05 in bivarite entered in to multivariable logistic regression model to control for confounder. Statistical significance declared at p-value <0.05.

Results: The prevalence of neonatal thrombocytopenia in the study area is 66%.In this study variables such as eclampsia(AOR=4.8, 95%CI: 1.66-13.94), Prolonged rupture of membrane(AOR=0.26, 95%CI:0.101-0.669), Intra uterine growth retardation(AOR=0.26, 95%CI: 0.1-0.68), neonatal sepsis (AOR=11.98, 95%CI: 4.023-35.7), Perinatal asphyxia(AOR=6.68, 95%CI: 1.616-27.6), Necrotizing enterocolitis (AOR=14.6, 95%CI: 2.84-75.61) and prolonged nothing per oath(AOR=0.243,95%CI: 0.084-0.705) were factors associated with neonatal thrombocytopenia.

Conclusion and recommendation: Prevalence of neonatal thrombocytopenia in Addis Ababa public hospitals neonatal intensive care unit is high. Therefore, identifying factors associated with it used as an input in reducing the problem.

Keyword: neonate, thrombocytopenia, platelet, neonatal intensive care unit

1. INTRODUCTION

1.1 Background

Neonatal period is the most vulnerable period of human life as it accounts for very high morbidities and mortalities and most of these are preventable(1). Platelets are tiny blood cells that help body form clots to stop bleeding. If bone marrow makes too few platelets or platelets are destroyed due to different conditions results low platelet count (thrombocytopenia) which predisposes for bleeding(2). Bleeding problems or a tendency to bruise or bleed are common problems in neonates(3).

Thrombocytopenia is defined as platelet count less than 150,000 platelet per micro liter of blood regardless of the gestational age(1), and multiple disease processes can cause neonatal thrombocytopenia and is classified based on platelet count as mild thrombocytopenia platelet count between 100 to 149 $\times 10^3$ /μL, moderate thrombocytopenia platelet count between 50 to 99 $\times 10^3$/μL, and severe thrombocytopenia platelet count less than 50 x 10^3/ μL(4,5). It is also categorized based on onset of duration to early onset thrombocytopenia which occurs before 72 hours after birth and late onset thrombocytopenia which occurs after 72 hours of birth(6). The age of onset of thrombocytopenia is an important predictor of the likely cause. The most common causes of early onset thrombocytopenia are almost all related to complications of pregnancy or deliveries. By contrast, the vast majority of neonates (greater than 80%) develop late onset thrombocytopenia mostly as a result of neonatal factors like infection/sepsis, necrotizing enterocolitis, prenatal asphyxia, prolonged NPO, and neonatal jaundice(7). The symptoms of thrombocytopenia in neonate include bruising of skin (petechiae), bleeding in other body systems, intravenous site bleeding and yellow skin and eye color (jaundice) because of bruising(8).

Among hematological disorder in neonate thrombocytopenia is the most common disorder which occurs in the neonatal intensive care unit(9,10). This group of disorders results when platelets are either decreased in number due to placental insufficiency, increased destruction (consumption) of platelets, or a combination of both mechanisms(11).

Neonates develop thrombocytopenia in 22–35% of all babies admitted to NICU and in up to 50% of those admitted to NICU who require intensive care. A considerable proportion (20%) of these episodes of thrombocytopenia is severe. About 8% of preterm and 6% of all neonates admitted to NICU have severe thrombocytopenia and are at increased risk of hemorrhage, presenting a common management problem(10).

The prevalence of neonatal thrombocytopenia varies throughout the world, in India ranges from19% to 45%(12,13), in Iran17.9%-24.1%(14,15), in Nepal 18%(16), in Nigeria 53%(17), and 16% in Libya(18).

Neonatal thrombocytopenia had a major impact on haemostatic integrity. It can cause gastrointestinal, pulmonary bleeding, and intracranial hemorrhage. Preterm neonates have one of the highest rates of intracranial hemorrhage (ICH), which affects up to a quarter of those with low birth weight(19). The most serious complication of severe fetal and neonatal thrombocytopenia is intracranial hemorrhage (ICH), which is detected in 10-20% of affected fetuses/neonates, with most cases occurring after a week of life. Intracranial hemorrhage leads to neurological squeal in 20%, and deaths in 5-10% cases(20). In high-risk neonates in neonatal intensive care unit 2.5–5% develop severe thrombocytopenia, sometimes lasting for several weeks and requiring >20 platelet transfusions(21).

The tendency to bleed is proportional to the number of platelets within the circulation. As such, there is no risk of bleeding with platelet counts greater than 100,000/μL and the risk is moderate with platelet counts below 50,000/μL, and the risk is severe and/or there is spontaneous bleeding with platelets below 20,000/μL(7).

Detection of thrombocytopenia is a useful initial assessment for sick neonates and thrombocytopenia is considered as one of the complications of the disease process, but in some cases, thrombocytopenia is detected accidentally. Though thrombocytopenia is so prevalent it is often ignored. However, if it is not detected and managed properly can result in devastating complications or internal bleeding and death(22).

1.2 Statement of problem

Globally thrombocytopenia occurs in 220–350/1000 newborns admitted to a neonatal intensive care unit and up to 700-800/1000 in very low-birth weight and preterm neonates admitted to neonatal intensive care unit who require intensive care(23).The occurrence of developing thrombocytopenia is higher with the lower gestational age(24). Thrombocytopenia rate in preterm neonates with birth weight less than 1000g and 750g is reported to occur in up to 75% and 90% of neonates, respectively(25). Expert review on hematology report showed that low-birth weight infants were at a 2.5fold increased risk for thrombocytopenia(19).

Most studies report higher rates of neonatal thrombocytopenia ranging between 53-70% in developing countries when compared to developed countries it ranges 18-35%, (26). Neonatal morbidity and mortality are concerning health problems among low and middle-income countries, among sick neonates thrombocytopenia is prevalent from hematologic disorders(27). In developing country neonatal death secondary to bleeding is high due to sepsis is prevalent in neonatal intensive care unit and also Preterm birth is high in low income countries which is the leading cause of morbidity and mortality in neonates worldwide (26).

In Africa studies on neonatal thrombocytopenia are scarce however studies were done in some African countries the prevalence of neonatal thrombocytopenia ranges from 12.4%-53% (17,18,28). So this shows there is a variation along with countries. In sub- Sahara African countries, about 90% of cases of severe thrombocytopenia presenting after the first few days of life are due to late-onset bacterial sepsis, necrotizing enterocolitis, or both(29). In a study done in Ethiopia the prevalence of thrombocytopenia among preterm neonates is 48.9% (30) but does not include term neonates.

Even though the federal ministry of health and other partners take actions to reduce neonatal mortality, the rate was decreased from 39 to 29 between 2005 and 2016 but it slightly rises back to 30 according to the 2019 Ethiopian demographic health survey (EDHS) report(31,32). This may be due to preventable and treatable causes of the hematologic disorder, such as thrombocytopenia.

Various studies attempt to identify associated factors of thrombocytopenia in neonates. According to the studies eclampsia, prolonged rupture of membrane, intrauterine growth retardation, prematurity, prenatal asphyxia, sepsis, and necrotizing enterocolitis all are risk factors (33–35). But it is not well investigated whether these factors parallel in our country or not. Similarly, among those factors prematurity, perinatal asphyxia, and sepsis are the leading cause of neonatal morbidity and mortality in Ethiopia(36).

Most of the time thrombocytopenia diagnosed as a complication of other medical problems but after occurring it exacerbates the morbidity and it prolongs the hospitalization of sick neonates. And also it has several complications, such as pulmonary, gastrointestinal, and intracranial hemorrhage which had permanent neurological impairment in neonates and may end up with death (26), the occurrence of hemorrhages in thrombocytopenic neonates is approximately 20-30%(37).

Even if thrombocytopenia has a high prevalence, complications, and economic burden, the emphasis given to the problem is insignificant in our setup as well as in our country. While prevention and early management of this condition by identifying factors associated with thrombocytopenia may enhance the prognosis of neonates. Therefore this study will show the prevalence of neonatal thrombocytopenia and its associated factors in neonates admitted to neonatal intensive care units in Addis Ababa public hospitals.

1.3 Justification

The motivation to conduct this study was made after local observation of neonatal intensive care unit setup with which most admitted neonates, especially those with critical case, become thrombocytopenic and prone to bleeding lastly develop chronic complication or they will die. After extensive web search about studies done on neonatal thrombocytopenia able to get only one study done in Ethiopia among preterm neonates which determines only prevalence. The previous study does not identify associated factors and does not include term neonates in the study. So I'm motivated to conduct my thesis on prevalence and associated factors of neonatal thrombocytopenia in Addis Ababa public hospitals neonatal intensive care unit.

1.4 Significance of the study

The aim of this study is to determine the prevalence of neonatal thrombocytopenia and its associated factors among neonates admitted to NICU at Addis Ababa public hospitals. This study aims to enhance the knowledge of health care providers on how it prevalent and what factors are associated with it. And also it helps them to diagnose and treat neonatal thrombocytopenia early. Moreover, the study contributes to the achievement of the goal of the 2030 sustainable development agenda which is reducing neonatal mortality to at least 12 deaths per 1000 live births by ending preventable neonatal death.

Also, the identification of possible factors for the occurrence of neonatal thrombocytopenia in neonatal intensive care unit will have a greater input to program managers and policymakers for designing, proper implementation, and evaluation of programs on reduction of neonatal morbidity and mortality. The study will also serve as baseline information for future studies.

2. LITERATURE REVIEW

2.1Prevalence of neonatal thrombocytopenia

Globally thrombocytopenia is prevalent in neonates admitted to neonatal intensive care unit it ranges 22%-35%, especially in very low-birth weight and preterm neonates its prevalence is up to 70%-80%(38).

In a study conducted in India the prevalence of neonatal thrombocytopenia was found to be 45%, from this mild thrombocytopenia was observed in 73% neonates, moderate thrombocytopenia in 19% and severe thrombocytopenia in 8%(13). Another study in India the prevalence of mild, moderate, and severe thrombocytopenia was 19%, 37.5%and43.5% respectively(12). Similarly the prevalence of thrombocytopenia in Indonesia is estimated to be 12.2%(39).

According to a study conducted in Iran, the prevalence of thrombocytopenia was 17.9%, the prevalence of mild, moderate, and severe thrombocytopenia was recorded to be 43.5%, 29.8%, and 24.1% respectively(14).In another study conducted in the same country the prevalence was 24.1%. Prevalence of mild, moderate, and severe thrombocytopenia was 49.4%, 47.1%, and 3.5% respectively(40).

A study conducted in Austria found that 84.1% of thrombocytopenic neonates had early onset thrombocytopenia while the rest 15.9% acquire late onset thrombocytopenia. The majority had mild (n = 122, 33%), followed by moderate and sever NT with the prevalence of 38% and 29.6% respectively(33).

In Nepal the prevalence of neonatal thrombocytopenia is 18%. From the thrombocytopenic neonates, mild thrombocytopenia was seen in 58.1% neonates while 29.7% were with moderate thrombocytopenia and 12.2% neonates had severe thrombocytopenia. And based on the onset early onset thrombocytopenia comprised 91.8% while late onset thrombocytopenia comprised 8.2% of the total thrombocytopenia(16).

In Nigeria, the prevalence of neonatal thrombocytopenia was 53.0%. Mild thrombocytopenia was found in 39.4% of the neonates, 12.1% had moderate thrombocytopenia, while severe

thrombocytopenia was detected in 1.5% of the neonates. From thrombocytopenic neonates, 84% of the cases were early onset thrombocytopenia(17).

In a study conducted in Libya the prevalence of neonatal thrombocytopenia was 16.2%, out of this 43.2% have mild thrombocytopenia, 25.8% have moderate thrombocytopenia and 24.6% have severe thrombocytopenia(18). In Tunisia the prevalence is 12.4%(28).

2.2 Associated Factors of Neonatal Thrombocytopenia

Neonatal thrombocytopenia is related to several factors, which are categorized into two main groups. These are maternal and neonatal factors.

2.2.1 Maternal obstetric associated factors

According to UK Saint Thomas hospital department of hematology maternal/placental disorders during pregnancy that result in chronic fetal hypoxia e.g. sever pre-eclampsia(SPE), eclampsia, prolonged rupture of membrane and gestational diabetes usually cause thrombocytopenia during early neonatal age(34,41).

Different studies across the world found different results on SPE associated with neonatal thrombocytopenia. A study conducted in India in 2020 among maternal factors showed that 48.7% of babies had SPE as the maternal risk factor(13). Different studies conducted in India, Austria, Iran, Nepal, and Tunisia also showed SPE as a maternal risk factor in 81.81%(12), 2.7%(33), 46.4%(15), 9.5%(16)and12%(28) of cases respectively. Similar study in India also exhibited 19% of neonates born from a mother with SPE could develop the condition (42).

According to a study conducted in India 7.5% of neonates born from a mother with prolonged rupture of membrane (PROM)develop neonatal thrombocytopenia(12). Another study conducted in India showed 30% of the neonates with similar maternal condition develop NT (42).

In different studies eclampsia has an association with neonatal thrombocytopenia 81%(13), 9.4%(33), 33.3%(P-value=0.002; PR 3.97 (95% CI 1.70-9.25) (39), and 4.3%(15) of neonates born from a mother with eclampsia in India, Austria, Indonesia and Iran respectively

developed NT. Another study in India showed 20% of neonates with similar maternal condition develop NT (42).

Thrombocytopenia in neonates occurred among mothers with maternal diabetes in different studies like in Nepal among thrombocytopenic neonates 31.2% had history of maternal diabetes(16), in Iran 66.7%(15) and 50% in India(13).

According to a study done in India Ante partum hemorrhage(APH) has an association with neonatal thrombocytopenia 8%(13).

2.2.2 Neonatal related factors

Several studies showed that neonatal conditions like prematurity, low birth weight, and IUGR are causes of neonatal thrombocytopenia (41).

Among different studies on neonatal thrombocytopenia prematurity was found as an associated factorin56%(33), 56.2%(43), 63%(28), 58.2%(44), and 63.33% (p-value(0.0001)) (13) of the cases in Austria, Pakistan, Tunisia, Sri Lanka, and India respectively.

According to a study done in Pakistan among neonates who developed thrombocytopenia 18.1%(43),in Tunisia 24%(28) ,and in Sri Lanka 57.6% (44)was low birth weight .

Results of different Study showed among neonates with IUGR11.8% in Iran(15),9.5% in Nepal (16),80% in India with p-value(0.00)(13), 70.7%in Sri Lanka (44)and 26% in Tunisia (28) developed neonatal thrombocytopenia.

According to the American Academy of Pediatrics (APA), prolonged NPO is a cause of thrombocytopenia. Breast milk and formula milk contain linoleic acid among essential fatty acids which is the precursor of platelet production (thrombopoiesis). Neonates who are NPO for a prolonged time develop thrombocytopenia due to a lack of getting the precursor for platelet production. Maintenance fluid does not have any component for platelet production(45,46).

2.2.3 Neonatal clinical co-morbidities

Different co-morbidities like sepsis, birth asphyxia, neonatal jaundice, necrotizing-enterocolitis and neonatal surgical disorders can cause thrombocytopenia in newborns.

Newborns who had clinical co-morbidity of Sepsis found associated with neonatal thrombocytopenia in different studies across the world in Austria, Netherland, India, Iran, Nepal, Tunisia, Indonesia and in Nigeria neonatal sepsis was found 47.1%(33),49%(47), 48.5% with p-value(0.0001) (12), 50%(15), 29%(16), 29%(28), 43% with (p-value=0.000) ;PR5.33 (95% CI,2.33-12.19)(39), and 16.7%(17) respectively. Another study in India sepsis was found 53% of thrombocytopenic neonates it was statistically significant (P value= 0.0001)(42).

Neonates who develop thrombocytopenia PNA has association and found in different studies 25%(33), 20%(12), 28.8%(43), 17.3% (15),42.1% with P=0.000; PR 5.66 (95% CI 2.49-12.86(39) , 35.1%(16), 33.3%(17) and 3.2% (17)found in Austria, India, Pakistan, Iran, Indonesia, Nepal, Nigeria, and Tunisia respectively.

In different studies necrotizing enterocolitis found has an association with NT in Austria, Iran, India, Indonesia, and Tunisia showed 4.1%(33),10% (15),100% with p-value(0.001)(13), 36% [P=0.014; PR 9.2 (95% CI 5.17-14.84)](39)and 1.9% in (28) respectively.

Neonates with neonatal jaundice in India 19.5%(12),in another study in India is also 6%, in Nigeria 19.7%(17)neonates admitted in NICU developed neonatal thrombocytopenia.

Hematologic profiles of Ethiopian preterm infants with clinical diagnoses of early-onset sepsis, prenatal asphyxia, and respiratory distress syndrome the study shows, lower platelet counts less than 150000/micro litter were found in 48.5% of preterm infants with Early Onset Neonatal Sepsis (EONS), of which 16.8% had platelet counts less than 50000 and 49.7% of preterm babies with prenatal asphyxia developed thrombocytopenia(30).

A study done in Egypt 2020 among thrombocytopenic neonates, 9.09% neonates had surgical disorders like TEF, gastroshesis, omphalocele and aneorectal malformations develop thrombocytopenia in postoperative state(48).

2.3 Conceptual framework

The conceptual framework of this study adapted after reviewing different related literatures and modified according to our context. Based on this framework, this study conceptualized neonatal thrombocytopenia as a result of interaction between various factors such as maternal obstetric related complications, neonatal factors and neonatal clinical co-morbidities.

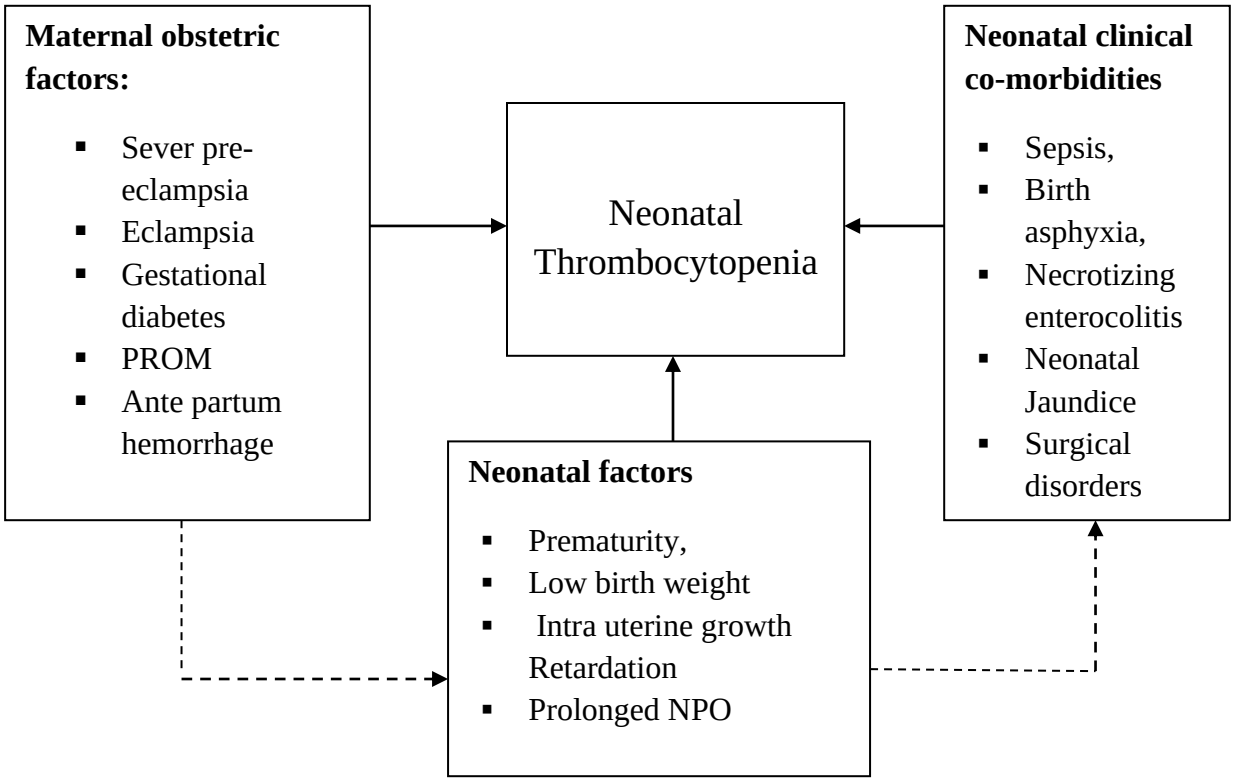

Figure 1: conceptual framework on neonatal thrombocytopenia adapted from different literatures (19, 20, 39, 45, and 46).

3 OBJECTIVES

3.1 General Objective

- To assess the prevalence of thrombocytopenia and its associated factors among neonates admitted to neonatal intensive care unit in public hospitals of Addis Ababa, Ethiopia in 2020/21.

3.2 Specific Objectives

- To determine the prevalence of neonatal thrombocytopenia among neonates admitted to neonatal intensive care unit in public hospitals of Addis Ababa, Ethiopia in 2020/21.

- To identify factors associated with neonatal thrombocytopenia among neonates admitted to neonatal intensive care unit in public hospitals of Addis Ababa, Ethiopia in 2020.

4 METHODOLOGY

4.1 Study Area and Period

4.1.1 Study Area

The study was conducted in Addis Ababa, which is the capital city of Ethiopia and the seat of the African Union and the United Nations World Economic Commission for Africa. It covers an area of 527 square kilometers and has 11 sub-cities. According to population projection value for 2019, the city has an estimated population of 4.592 million(49). The city has 12 public Hospitals; from those 11 hospitals have neonatal intensive care unit. These are Tikur Anbesa, Zweditu Memorial, Yekatit 12, Gandi Memorial, Minellik II, Tirunesh Bejing, Alert, Ras Desta, Eaka Koteba, St.Peter and St. Paul Hospital. Among these hospitals, the study has been conducted in four selected hospitals. These hospitals were selected randomly. The study was conducted in Ghandi Memorial Hospital, Saint Paul Millennium Medical College Hospital, Yekatit 12 Hospital and Tikur Anbessa Specialized Hospital.

Gandhi Memorial Hospital (GMH) is one of the public Hospitals under Addis Ababa City administration Health Bureau. The number of admitted neonates varies from time to time; the average annual admission rate being 2,400 and the average monthly admission 200 neonates.

Yekatit 12 Hospital Medical College(Y-12HMC) is also under Addis Ababa Health Bureau has 150 average monthly admissions of neonates in the neonatal intensive care unit and 1800 annual admission.

Saint Paul Millennium Medical College Hospital (SPMMC) is under the ministry of health, The Hospital has 2880 annual admission of neonates and it has 240 average monthly admissions of neonates.

Tikur Anbessa Specialized Hospital (TASH) is one of the tertiary referral hospitals in the country and is affiliated under Addis Ababa University. It has 260 neonates on average monthly admission. The Hospital has 3120 annual admission of neonates.

4.1.2 Study period

The study was conducted from February 15th –March 15th, 2021

4.2 Study Design

An institution-based Cross-sectional study design was conducted in selected Addis Ababa public hospitals.

4.3 Population

4.3.1 Source Population

All neonates medical chart who were admitted in selected Addis Ababa public hospital NICU from January 2020- December 2020 G.C.

4.3.2 Study Population

All randomly selected neonates medical chart who were admitted in neonatal intensive care unit of selected Addis Ababa public hospitals from January 2020- December 2020 G.C.

4.4 Inclusion and Exclusion criteria

4.4.1 Inclusion Criteria

All eligible medical charts (records) of neonates admitted to neonatal intensive care units from January 1st 2020 to December 30th 2020GC in the selected Addis Ababa public hospitals.

4.4.2 Exclusion Criteria

- Medical charts /CBC results/ which are unable to read
- Incomplete information of neonates and their mother in the chart
- Newborn who is diagnosed with syndromic baby like: Down syndrome, Edward syndrome and Patau syndrome were excluded.

4.5 Sample size determination and sampling procedure

4.5.1 Sample size determination

The sample size is determined by using a single population proportion formula using the prevalence of Neonatal thrombocytopenia (48.9%) from the previous study conducted in Ethiopia(30).

By using Single proportion formula

$$n = \frac{Z^{\alpha}/_{2}{}^{2} \times p(1-p)}{d^2}$$

$$= \frac{1.96^2 \times p(1-p)}{d^2}$$

$$= \frac{1.96^2 \times 0.489(1-0.489)}{0.05^2} = 384$$

By adding 10% non response rate 39

Then the final sample size n=423

Where:

n=the required sample size

d=margin of error between the sample and population=5%=0.05

Z=standard normal distribution value at 95% confidence level Z α/2=1.96 for 95% confidence interval

p = prevalence of neonatal thrombocytopenia previously done.

4.5.2 Sampling technique and procedure

The study was conducted in Addis Ababa public hospitals. The city has 12 public Hospitals, form those 11 hospitals have neonatal intensive care unit. Among the hospitals, 30% (four hospitals) were selected by using a simple random sampling technique. Then allocation of the sample size to each hospital is made based on their average number of neonate admission per year which is from the annual neonatal admission report of each hospital. The overall sample will be taken proportionally from all selected public hospitals. The first participants (medical chart of the neonate) was selected randomly during the beginning of the data collection time, and then each neonatal medical records selected using a systematic sampling technique in

which every k^{th} (24) interval included until the required sample size obtained. The Proportionate allocation is shown in the schematic presentation below:

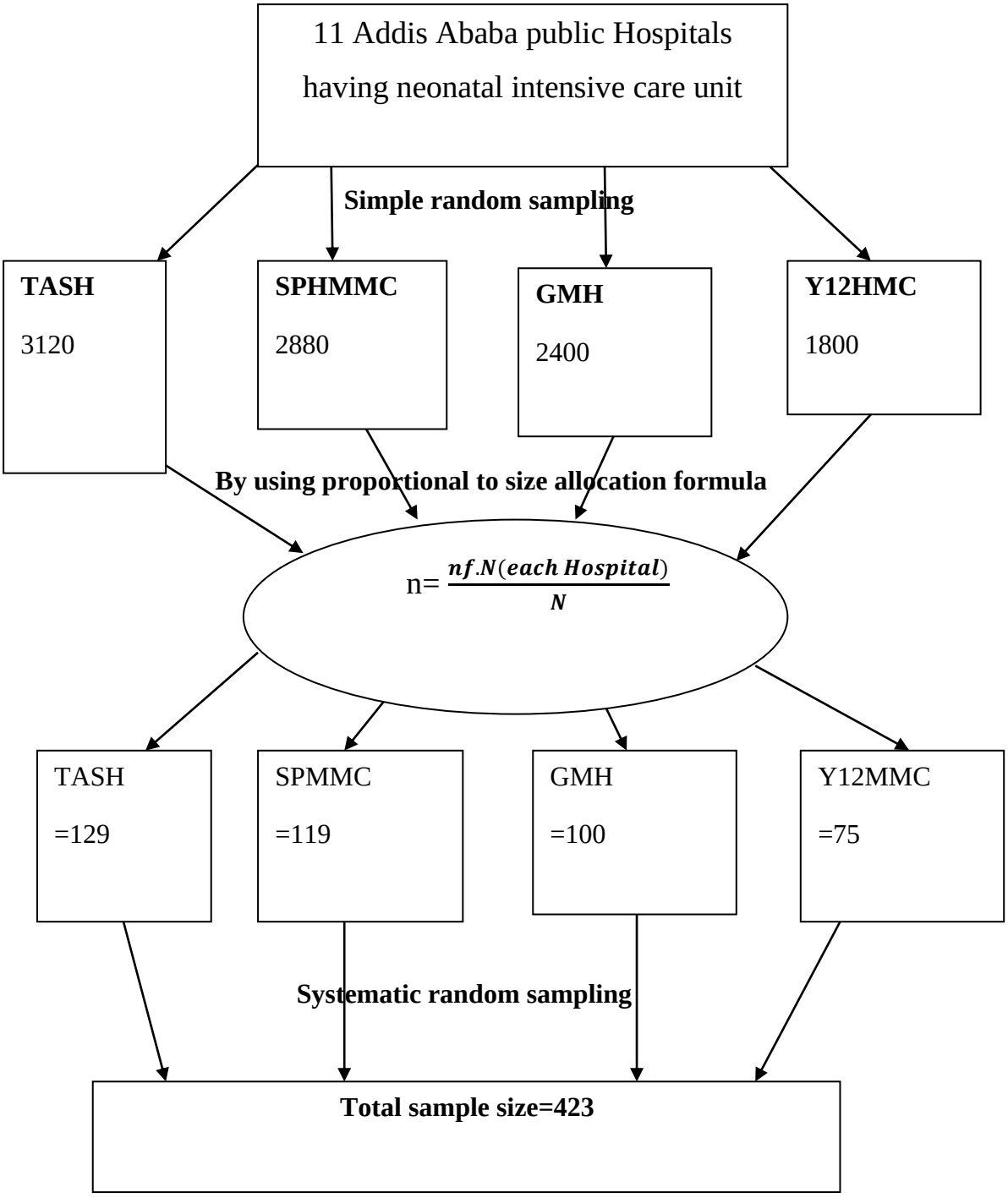

Figure 2: Schematic presentation of sampling procedure

4.6 Operational Definition

Co-morbidity: newborns with thrombocytopenia and have other illness.

Prolonged NPO: a neonate who is NPO for greater than 24 hours(50)

Thrombocytopenia: defined as a platelet count of less than 150,000 platelets per micro liter of blood regardless of the gestational age(4,5)

Mild thrombocytopenia: platelet count between 100 to 149 × 10^3 / micro litter(4,5)

Moderate thrombocytopenia: platelet count between 50 to 99 × 10^3 / μ L(4,5)

Severe thrombocytopenia: platelet count less than 50 x 10^3 / μ L(4,5)

Prolonged rupture of membrane: Rupture of membrane more than 18 hours(51).

4.7 Study Variables

4.7.1 Dependent variable

- Neonatal thrombocytopenia

4.7.2 Independent variables

- ✓ Socio-demographic variables of the mother and the neonate
  - Maternal age
  - Residence
  - Sex of the baby
  - Age at admission of the baby
- ✓ Maternal obstetric variables
  - Gravidity
  - Parity
  - Antenatal Care (ANC) follow up
  - Mode of delivery
  - Type of pregnancy
- ✓ Maternal obstetric complication variables
  - Sever Pre-eclampsia
  - Eclampsia
  - Diabetes during pregnancy
  - Prolonged rupture of membrane

- ✓ Neonatal related factor variables
    - Gestational age
    - Birth weight
    - APGAR score, Prolonged NPO
- ✓ Neonatal clinical co-morbidity variables
    - Sepsis
    - Necrotizing enterocolitis
    - Perinatal Asphyxia
    - Neonatal jaundice
    - Neonatal surgical disorders

4.8 Method of data collection and Data collection tool

Data extraction cheeklist was adapted by reviewing related literatures (12,13,17,18,43)and modified according to our context. The medical charts of neonates admitted to selected Addis Ababa public hospitals over one year (January 2020-december 2020 GC), was collected by using sampling frame from registration book. Then using the checklist, socio-demographic characteristics of the mother, maternal obstetric history during pregnancy, maternal obstetric complications for the index pregnancy, neonatal related factors and clinical co-morbidities of the neonate was included in the data extraction checklist. During the process, the principal investigator was supervising the trained data collectors.

4.9 Data Quality control and management

Before starting data collection, the tool was pretested on five percent of the sample size (n=22) at Ras Desta hospital for its applicability, appropriateness, clarity, length, skip patterns and correctness of filled checklist. After the pretest result, based on the response the checklist was modified. And also the tool was given to experts and modified based on their comments. Two days training and clear orientation was given for all data collectors (8 Bsc neonatal nurses) and supervisors (4 Msc neonatal nurses) on how and what information they should collect from neonate's medical chart.

In addition, the close supervision of data collectors by the supervisors was continued during the process of data collection.

4.10 Data Analysis Procedure

The collected data cleaned and sorted using Epi-Data software version 4.6. Entered data was exported and analyzed using SPSS Software version 25. Descriptive statistics like frequency, measure of central tendency and standard deviation was computed to describe the study variable in relation to the population. In order to check the correlation between two independent variables, multi-colinearity (colinearity diagnostic taste) was done by using the value of correlation coefficient, variance inflation factors and tolerance. Hosmer and Lemeshow goodness of fit test and omnibus tests of model coefficients were done to test the fitness of the logistic regression in the final model, then it was found good (statistically insignificant value, P value >0.05). Bivariate and multivariable logistic regression carried out to see associations between dependent and independent variables. Those variables that have p value < 0.05 in bivariate logistic regression were taken to the multivariable logistic regression model to adjust for possible confounders. The strength of the association will be declared at p-values <0.05 with 95% CI.

4.11 Ethical Consideration

Ethical clearance was obtained from Addis Ababa University, department of nursing and midwifery research committee institution review board (IRB), Addis Ababa Public Health Research and Emergency Management Directorate, and St.paul Hospital Millinium Medical College. The ethical clearance was submitted to Tikur Anbessa Specialized Hospital, St. Paul hospital Millennium Medical College, Gandhi Memorial Hospital, and Yekatit12 Hospital to get permission for conducting the Study.

After getting permission from the hospital administration cooperation letter written for the concerned bodies of respective departments. Following this, searching and obtaining the selected samples' medical records processed with the assigned person. Finally, strict care for the patients' medical records and the confidentiality of records that could identify study participants was protected.

4.12 Dissemination and Utilization of the Result

The thesis will be presented to Addis Ababa University, School of Nursing and Midwifery as partial fulfillment of Master's Degree in Neonatal Nursing. The thesis will also be disseminated to the Federal Minister of Health, Addis Ababa Health Bureau, and Addis Ababa Town Public Hospitals. The hard and soft copy will be available in the library of Addis Ababa University for graduate students as well as for other concerned readers. The findings will be presented in different seminars and meetings. Moreover, an attempt will be made to publish the finding in peer-reviewed and reputable journals.

5 RESULTS

5.1 Socio-demographic characteristics

In this study, the medical records of 423 neonates were reviewed. The mean maternal age for the index pregnancy was 28.11(±4.903) and 155(36.6%) of mothers were in the age group of 25-29 year. Ninety-one percent of mothers were urban residents the rest nine percent is from rural. Out of 423 neonates 229(54.1%) were male and 194(45.9%) were female. More than half of neonates 260(61.5%) were admitted before 24 hours of postnatal age.

Table 1 : Socio-demographic characteristics of mothers and neonates at NICU of selected public hospitals of Addis Ababa, Ethiopia, 2021 (n=423).

Variables	**Frequency**	**Percentage (%)**
Age_ group of the mother (Year)		
≤24	111	26.2
25-29	155	36.6
30-34	115	27.2
≥35	42	9.9
Residency		
Urban	385	91
Rural	38	9
Age at admission of the newborn		
<24hours	260	61.5
≥24hours	163	38.5
Sex of the newborn		
Male	229	54.1
Female	194	45.9

5.2 Pre-existing maternal chronic disease

Among 423 reviewed charts regarding to pre-existing maternal chronic disease the proportion of chronic hypertension 17(4%), diabetes millets 12(2.8%) and HIV/AIDS 10(2.4%).

Table 2: Pre-existing maternal chronic disease among mothers whose neonates were admitted in NICU of selected Addis Ababa public hospitals, Ethiopia, 2021 (n=423).

Variables	Frequency	Percentage (%)
Hypertension		
Yes	17	4
No	406	96
Diabetes millets		
Yes	12	2.8
No	411	97.2
Chronic heart disease		
Yes	5	1.2
No	418	98.8
Renal disease		
Yes	3	0.7
No	420	99.3
HIV/AIDS		
Yes	10	2.4
No	413	97.8
Others	4	0.9

Others include; leukemia, hypothyroidism, systemic lupus erythematos and chronic liver disease.

5.3 Obstetrical history of mother's

Majority of the mothers, 410 (96.9%) had ANC follow up for the index pregnancy. Among those mothers who had ANC follow up, 353(86.1%) of them having four and above visit. Majority of mothers 403 (95.3%) delivered their baby's at health institution.

Table 3: Obstetric history of mothers whose neonates were admitted in NICU of selected Addis Ababa public hospitals, Ethiopia, 2021 (n=423).

Variables	Frequency	Percentage (%)
ANC visit		
Yes	410	96.9
No	13	3.1
Number of ANC visit(n=407)		
1-3	57	13.9
≥4	353	86.1
Place of delivery		
Health institution	403	95.3
Home	20	4.7
Parity		
Primi para	119	28.1
Multi-para	304	71.9
Mode of delivery		
SVD	211	49.9
Assisted vaginal delivery	69	16.3
C/S	143	33.8
Type of pregnancy		
Single	378	89.4
Multiple	45	10.6
VDRL Test		
Reactive	30	7.1
Non-reactive	384	90.8
Unknown	9	2.1

5.4 Obstetric Complications of the Mother

Regarding to maternal obstetric complications more than half 273(64.5%) mothers had obstetric complication during the index pregnancy. Among maternal obstetric complications for the current pregnancy proportion of PROM, eclampsia and APH is 123 (45.1%), 118(43.2%), and 64(23.4%) respectively.

Table 4: Obstetric complication of mothers whose baby were admitted in NICU of selected Addis Ababa public hospitals, Ethiopia, 2021 (n=273).

Variables	Frequency	Percentage (%)
Sever pre-eclampsia(SPE)		
Yes	98	35.9
No	175	64.1
Eclampsia(n=273)		
Yes	118	43.2
No	155	56.8
APH		
Yes	64	23.4
No	209	76.6
GDM		
Yes	48	17.6
No	225	82.4
IUGR		
Yes	109	39.9
No	164	60.1
PROM		
Yes	123	45.1
No	150	54.9

5.5 Neonatal related factors

Among 423 reviewed neonatal records more than half of the neonates 243(57.4%) birth weight was greater than 2500 gram. The mean birth weight is 2491(±728) gram. Regarding gestational age almost half of the baby 223(52.7%) was born after 37 completed weeks of gestation.

Table 5: Characteristics of neonates who were admitted in NICU of selected Addis Ababa public hospitals, Ethiopia, 2021 (n=423).

Variables	Frequency	Percentage (%)
Birth weight		
<2500 g	180	42.6
≥2500 g	243	57.4
Gestational Age		
<37 wks	200	47.3
≥37 wks	223	52.7
Weight for gestational age		
Appropriate for gestational age**(AGA)**	355	83.9
Small for gestational age **(SGA)**	66	15.6
Large **(LGA)**	2	0.5
Did the newborn NPO		
Yes	187	44.2
No	236	55.8
How long NPO		
<24 hours	5	2.7
≥24 hours	182	97.3
APGAR score 1st min		
0-3	24	5.7
4-6	196	46.3
7-10	203	48

APGAR score 5th min		
0-3	1	0.2
4-6	50	11.8
7-10	372	87.9
Source of admission		
Inborn	353	83.5
Out born	70	16.5

5.6 Neonatal clinical co-morbidities

Out of 423 reviewed charts neonates admitted in NICU regarding co-morbidities more than half of neonates 285(66%) had neonatal sepsis, 101 (22.5%) had necrotizing enterocolities and 95(22.5%) had perinatal asphyxia.

Table 6: clinical co-morbidities of the neonates in selected Addis Ababa public hospitals 2021G.c (n=423).

Variables	Frequency	Percentage (%)
Sepsis(n=423)		
Yes	279	66
No	144	34
PNA		
Yes	95	22.5
No	328	77.5
NHB		
Yes	77	18.2
No	346	81.8
NEC		
Yes	95	22.5
No	328	77.5
Surgical Disorders		
Yes	70	16.5
No	353	83.5

5.7 Prevalence of neonatal thrombocytopenia

Out of 423 neonates who were admitted in NICU of Addis Ababa public hospitals between January 1st 2020 and 30th December, 2020 G.c,279(66%) neonates developed thrombocytopenia with mean (SD) of platelet count of the newborn were 65,515**(**±41,402) platelet/micro liter. From thrombocytopenic neonates 73(26.2%) had mild thrombocytopenia, 107(38.3%) had moderate thrombocytopenia and 99(35.5%) neonates had sever thrombocytopenia. Based on onset of thrombocytopenia 78(28%) had early onset thrombocytopenia and 201(72%) had late onset thrombocytopenia.

5.8 Factors associated with neonatal thrombocytopenia

To identify factors associated with neonatal thrombocytopenia logistic regression model was used. Variables that were used in bi-variable regression with the crude odds ratios (COR) and P value <0.05 associated with neonatal thrombocytopenia includes age at admission of the baby, PROM, eclampsia, IUGR, neonatal sepsis, PNA, neonatal hyperbilirubinemia, NEC, neonatal surgical disorders, birth weight, gestational age, and prolonged NPO.

Then multivariable logistic regression analysis was used to adjust possible confounders. In multivariable logistic regression analysis factors that were significantly associated which showed p-value of below 0.05 with the outcome variable (neonatal thrombocytopenia) were PROM, eclampsia, IUGR, Sepsis, PNA, NEC and prolonged NPO.

Eclampsia had statistically significant association with neonatal thrombocytopenia. The odds of babies born from mother who had obstetric complication of eclampsia were 4.8 times more likely develop thrombocytopenia than those delivered from mother who had no eclampsia during pregnancy [AOR: 4.82, 95%CI:(1.668-13.949)].

Sepsis had significantly associated with neonatal thrombocytopenia. Those neonates who had clinical co-morbidity of sepsis were 12 times more likely develop thrombocytopenia than those who had no co-morbidity of sepsis [AOR: 11.987; 95%CI (4.023-35.72)].

The odds of neonates who had clinical co-morbidity of perinatal asphyxia were 6.68 [AOR=6.68, 95% CI :(1.616-27.653)] times more likely develop thrombocytopenia when compared to those neonates who had no clinical co-morbidities of perinatal asphyxia.

The odds of neonates who had co-morbidity of necrotizing enterocolities were 14.65 [AOR=14.653, 95% CI: 14.653(2.84-75.618)] times more likely develop thrombocytopenia compared to those neonates who had no NEC.

Table 7: Bi-variable and multivariable logistic regression for neonatal thrombocytopenia among neonates admitted in NICU of selected Addis Ababa public hospitals, Addis Ababa, Ethiopia, 2021. (n=423).

Variables	**Thrombocytopenia**		**COR(95% CI)**	**AOR(95% CI)**
	Yes	**No**		
Age at admission				
<24 hours	182(65.2%)	78(54.2%)	1	1
≥24 hours	97(34.8%)	66(45.8%)	**0.63(0.418-0.949)***	1.944 (0.746-5.068)
ANC follow up				
1-3 times	46(65.7%)	24(34.3%)	1	
≥4 times	233(66%)	120(34%)	1.013(0.59-1.73)	
VDRL test				
Positive	23(76.7%)	7(23.3%)	0.411(0.044-3.87)	
Negative	248(64.6%)	136(35.4%)	0.22(0.028-1.84)	
Unknown	8(88.9%)	1(11.1%)	1	
Parity				
Primi	78(65.5%)	41(43.5%)	1	
Multi	201(66.1%)	103(33.9%)	1.026(0.656-1.603)	
Birth weight				
<2500 g	141(78.3%)	39(21.7%)	1	1
≥2500 g	138(56.8%)	105(43.2%)	**0.364(0.235-0.562)***	0.567(0.161-1.991)
Source of admission				
Inborn	233(66%)	120(34%)	1	
Out born	46(65.7%)	24(34.3%)	0.987(0.57-1.69)	
Eclampsia				
Yes	109(47.2%)	9(21.4%)	1	1
No	122(52.8%)	33(78.6%)	**3.276(1.50-7.154)***	**4.82(1.668-13.949)****

SPE				
Yes	83(84.7%)	15(15.3%)	1	
No	148(84.6%)	27(15.4%)	1.009(0.508-2.005)	
Gestational Age				
<37 wks	163(81.5%)	37(18.5)	1	1
≥37 wks	116(52%)	107(48%)	**4.064(2.609-6.33)***	0.446(0.129-1.542)
PROM				
Yes	96(41.6%)	27(64.3%)	1	1
No	135(58.4%)	15(35.3%)	**0.395(0.199-0.782)***	**0.26(0.101-0.669)****
APH				
Yes	57(89.1%)	7(10.9%)	1	
No	174(83.3%)	35(16.7%)	1.638(0.69-3.89)	
IUGR				
Yes	100(43.3%)	23(54.8%)	1	1
No	131(56.7%)	19(45.2%)	**0.631(0.25-0.951)***	**0.260(0.100-0.680)****
GDM				
Yes	43(89.6%)	5(10.4%)	1	
No	188(83.6%)	37(16.4%)	1.693(0.628-4.55)	
Place of delivery				
Health Institution	266(66%)	137(34%)	0.956(0.373-2.453)	
Home	13(63%)	7(35%)	1	
Sepsis				
Yes	218(78.1%)	61(42.4%)	1	1
No	61(21.9%)	83(57.6%)	**4.863(3.145-7.518)***	**11.98(4.023-35.72)****
PNA				
Yes	84(30.1%)	11(7.6%)	1	1
No	195(69.9%)	133(92.4%)	**5.206(2.67-10.138)***	**6.68(1.616-27.653)****

NHB				
Yes	43(15.4%)	34(23.6%)	1	1
No	236(84.6%)	110(76.4%)	**0.589(0.356-0.975)***	1.978(0.624-6.266)
NEC				
Yes	89(31.9%)	6(4.2%)	1	1
No	190(68.1%)	138(95.8%)	**10.7(4.581-25.3)***	**14.65(2.84-75.618)****
Neonatal surgical disorders				
Yes	62(22.2%)	8(5.6%)	1	1
No	217(77.8%)	136(94.4%)	**4.85(2.256-10.458)***	2.214(0.548-8.943)
NPO				
Yes	175(62.7%)	49(34%)	1	1
No	104(37.3%)	95(66%)	**0.307(0.201-0.467)***	**0.243(0.084-0.705)****

Key

- ✓ 1= Reference
- ✓ *=Statistically significant by COR at p-value <0.05
- ✓ **=Statistically significant by AOR at p-value <0.05
- ✓ Hosmer and Lemeshow test, p-value = 0.765

6. DISCUSSION

Thrombocytopenia is a common clinical problem globally among newborns that are sick and admitted in neonatal intensive care unit which is comparable with other hematologic disorder of newborns like Anemia, hemorrhagic disease of newborns and disseminated intravascular coagulopathy. Despite the significant burden in newborns health across all global regions, thrombocytopenia has been largely ignored until recently, especially in our country NICU setup. So this study assessed the prevalence which is 66% and factors associated with neonatal thrombocytopenias (which are eclampsia, PROM, IUGR, Sepsis, PNA, NEC and prolonged NPO) among neonates admitted in NICU of Addis Ababa public hospitals.

This study revealed that the prevalence of neonatal thrombocytopenia is 66%. This finding is higher than in studies done in India 45%(13), Iran 17.9% (14),Nepal 18%(16) Nigeria 53%(17)**,**Libya 16.2%(18), and in study done in Ethiopia previously 48.9%(30). This may be due to neonatal sepsis and perinatal asphyxia is higher in our country neonatal intensive care unit which is the leading cause of neonatal morbidity and mortality in Ethiopia(32)and also due to poor infection prevention in hospitals. In Ethiopia hospitals the infection prevention practice was 52.2%(52) while in settings in which earlier studies have been conducted was 76.2 % in India(53) and 70% in Iran(54).And also this finding is higher than the average global prevalence of neonatal thrombocytopenia which is 22-35%(38).This may be due to most of the studies are conducted in developed countries so it lowers the prevalence globally.

In this study 78(28%) had early onset thrombocytopenia and 201(72%) had late onset thrombocytopenia. This is similar with a study done in Nigeria, In their results 84% were early onset and 16% late onset(17). It shows higher late onset thrombocytopenia, this may be due to among risk factors of thrombocytopenia neonatal factors are higher (sepsis, PNA, NEC, and prolonged NPO). Since most of the time late onset thrombocytopenia occurs as a result of neonatal factors. In contrast a study done in Austria their result shows among thrombocytopenic neonates 84.1% had early onset thrombocytopenia and 15.9% had lat onset thrombocytopenia(33).the possible reason for this difference may be due to low association of maternal risk factors in our study which is responsible for the occurrence of early onset thrombocytopenia.

This study showed that among thrombocytopenic neonates 26.2% had mild thrombocytopenia, 38.3% had moderate thrombocytopenia and 35.5% neonates had sever thrombocytopenia. This is almost similar with study done in Libya(18),India(12) and Iran(14).the possible justification for this may be due to similarity in risk factors such as sepsis which results the occurrence of higher rate of sever thrombocytopenia and similarity in neonatal intensive care unit setting.

In this study, eclampsia was significantly associated with thrombocytopenia. The odds of babies born from mother who had maternal complication of eclampsia were 4.8 times more likely develop thrombocytopenia than those delivered from mother who had no eclapsia during pregnancy [AOR: 4.824,95%:CI(1.668-13.949)]. This finding is in line with the study conducted in India (13), Indonesia (39) and Austria(33). This may be due to lack of resource and adequate knowledge to manage and follow pregnancy induced hypertension in developing countries. Since eclampsia cause placental insufficiency by which it results decreased platelet production.

Among neonates delivered from mothers who had no prolonged rupture of membrane as obstetric complication were 74% less likely develop thrombocytopenia compared with those born from mother who had PROM. This finding is higher in a study conducted in India 7.5%(12). This may be due to low awareness on birth preparedness and lack of knowledge among pregnant mothers on early rupture of membrane and its complication(55).

In this study neonates with co-morbidity of neonatal sepsis were 12 times more likely to develop thrombocytopenia than those who had no co-morbidity of sepsis. This finding is higher than studies done in Austria 47.1%(33), Indian 48.5% (12), Iran 50%(40) and Indonesia 43% (39). This may be due to sepsis is prevalent in NICU of the study area and low infection prevention in neonatal intensive care unit and also may be due to low pregnant women infection screening. Sepsis increases the risk of thrombocytopenia by destruction and consumption of platelet.

In this study, Perinatal asphyxia had significant association with neonatal thrombocytopenia. The odds of developing thrombocytopenia among neonates who had perinatal asphyxia as clinical co-morbidities is 6.68 times more likely develop thrombocytopenia when compared to those neonates who had no co-morbidity of perinatal asphyxia. This finding was agreed with

studies conducted in Nepal 35.1%(16), Nigeria 33.3%(17), Indonesia 32.1%(39) and Pakistan 28.8%(43).this may be due to inadequate labor and delivery follow up by health professionals and lack of resource to follow intrauterine fetal condition during labor in developing countries. And also most of delivery time is night time in our country during this time there is lower number of staff in duty when compared to day time and they become tired so it results poor labor and delivery follow up.

The odds of neonates who had co-morbidity of necrotizing enterocolities were 14.65 times more likely develop thrombocytopenia compared to those neonates who had no NEC. This finding is higher than studies conducted in Austria 4.1%(33), Iran10%(13) and Tunisia 1.9%(28). The possible reasons for this difference which may be due to preterm delivery is higher in our country since prematurity is the single greatest risk factor for necrotizing enterocolitis. But this finding is lower than when compared to a study conducted in India which is all newborns with NEC develop thrombocytopenia (13) and Indonesia 36%(39).This may be due to preterm delivery is lower in Ethiopia than in India.

The result of this study shown that neonate who is not IUGR was 74% less likely develop thrombocytopenia than those born being IUGR. This finding is lower than in study conducted in India 80% (13), in Sri Lanka 70.7%(44).This may be due to low maternal chronic illness in our country like diabetes Miletus, cardiac disease and renal disease. And it is similar with a study done in Tunisia 26% (28).this may be due to similarity with socio-demographic characteristics of the two countries and also similarity with setup of the healthcare system.

Finally, newborns who were NPO for more than 24 hour had association with neonatal thrombocytopenia .The odds of newborns who were not NPO for longer than 24 hours 76% [AOR=0.243, 95% CI:(0.084-0.705)] less likely develop thrombocytopenia. This is supported by the science of American Academy of Pediatrics (APA)(45,46).

In this study by multivariable logistic regression variables not associated with the adjusted odds ratios (AOR) for neonatal thrombocytopenia includes neonatal surgical disorders, gestational age, birth weight, age at admission and neonatal hyperbilirubinemia.

7 LIMITATION OF THE STUDY

7.1. Strength of the study

The previous study conducted determines only the prevalence of thrombocytopenia in preterm neonates, But this study investigate the overall prevalence of thrombocytopenia and what factors are associated with neonatal thrombocytopenia among neonates admitted in NICU of Addis Ababa public hospitals.

7.2. Limitation of the study

- Lack of adequate literatures on the same topic in Africa, east Africa and Ethiopia
- Being a retrospective study there is variables not included in this study due to unavailability on charts.
- In this study, data were restricted to neonates admitted in public hospital, and hence did not cover those neonates admitted in private hospitals which may under estimate or over estimate the prevalence.

8. CONCLUSION

The overall prevalence of neonatal thrombocytopenia among neonates admitted in neonatal intensive care unit of Addis Ababa public hospitals during the period of from January 1st 2020 to December 30th2020 is 66% which is higher from other studies conducted before. From thrombocytopenic neonates 99(35.5%) had sever thrombocytopenia, 107(38.4%) had moderate thrombocytopenia and 72(26.2%) had mild thrombocytopenia. Out of 279 neonates who developed thrombocytopenia 78(28%) had early onset thrombocytopenia and 201(78%) had late onset thrombocytopenia.

Moreover, the study found that PROM, eclampsia, IUGR, Sepsis, PNA, NEC and prolonged NPO were significantly associated with neonatal thrombocytopenia.

9 RECOMMENDATIONS

Based on the findings of this study the following recommendations forwarded:

For Federal Ministry of health and stakeholders

- Ministry of health should incorporate thrombocytopenia about its prevalence, cause and management in the guideline of national neonatal training manual book and training should be prepared for health professionals who are working on neonatal intensive care unit to highlight about thrombocytopenia prevalence and factors associated with it in our setup.
- The ministry of health should avail parenteral nutrition for those neonates who are NPO due to the clinical condition of the baby.

For Hospitals

- Prepare training to create awareness on the prevalence of neonatal thrombocytopenia and what factors are associated with it.
- Prepare isolation unit in NICU to isolate septic neonate from non-septic to reduce hospital acquired infection and screen pregnant mothers for sepsis, since neonatal sepsis is strongly associated with thrombocytopenia.
- World health organization preterm birth prevention strategies should be applied in hospitals, because among the risk factors of neonatal thrombocytopenia necrotizing enterocolitis is the leading factor; it occurs as major complication of prematurity.
- Proper labor and delivery follow up in delivery ward to prevent PNA which is also significantly associated with thrombocytopenia
- In NICU ward avoid keeping babies NPO more than 24 hours as necessary, start feeding with one hour after delivery which is one component of essential newborn care.

For researchers

- Finally, researchers should conduct longitudinal study designs to get better information including variables not included in this study due unavailability in records.

Reference

1. Eichenwald EC, Hansen AR, Martin C, Stark AR. Cloherty and Stark's manual of neonatal care. Cloherty Stark's Man neonatal care. 2017;8:554–60.

2. American Red Cross. What Are Platelets In Blood. 2021;2021. Available from: https://www.redcrossblood.org/donate-blood/dlp/platelet-information.html

3. Haematological disorders in neonates,bleeding disorder. Am acadamy Pediatr. 2019;10:20–5.

4. Roganović J. Review article NEONATAL THROMBOCYTOPENIA : A COMMON CLINICAL PROBLEM Classification and pathogenesis Immune-mediated neonatal thrombocytopenia. 2015;11(2):115–25.

5. Fernandes C. Clinical manifestations, evaluation, and management of neonatal thrombocytopenia. UpToDate. 2016;1–7.

6. Tiller H, Husebekk A, Ahlen MT, Stuge TB, Skogen B. Current perspectives on fetal and neonatal alloimmune thrombocytopenia - Increasing clinical concerns and new treatment opportunities. Int J Womens Health. 2017;9:223–34.

7. Fernández KS, Alarcón P De. Neonatal Thrombocytopenia. Am acadamy Pediatr. 2020;2020.

8. Thrombocytopenia in the Newborn What is thrombocytopenia in the newborn ? What are the symptoms of thrombocytopenia in the What are the possible complications of thrombocytopenia in. 2020;2020.

9. Thrombocytopenia in the Newborn What Is Thrombocytopenia In The Newborn ? What Causes Thrombocytopenia In The Newborn ? Which Babies Are At Risk For Thrombocytopenia ? What Are The Symptoms Of Thrombocytopenia In The Newborn ? How Is Thrombocytopenia Diag. 2020;2020.

10. Roberts I, Murray NA. Neonatal thrombocytopenia: Causes and management. Arch Dis Child Fetal Neonatal Ed. 2016;88(5):359–64.

11. Martin RJ, Fanaroff AA, Walsh MC. FANAROFF AND MARTIN ' S NEONATAL-PERINATAL MEDICINE 10th edition Diseases of the Fetus and Infant. 2016. 1074–1086 p.

12. Tirupathi K, Swarnkar K, Vagha J. Study of risk factors of neonatal thrombocytopenia. Int J Contemp Pediatr. 2016;4(1):191.

13. Madhavi D, Subuhi S, Zubair M. Outcome of neonatal thrombocytopenia in tertiary care NICU. J Pediatr neonatal care. 2020;10(January 2018):92–6.

14. Khalessi N, Khosravi N, Sanii S, F ZM. The Prevalence and Risk Factors for Neonatal Thrombocytopenia among Newborns Admitted to Intensive Care Unit of Aliasghar Children's Hospital. Iran J Blood Cancer. 2013;5(2):41–5.

15. Eslami Z, Lookzadeh MH, Noorishadkam M, Hashemi A, Ghilian R. Thrombocytopenia and Associated Factors in Neonates Admitted to NICU during Years 2010 _ 2011. 2013;26(6):20894.

16. Bagale BB, Bhandari A. Neonatal Thrombocytopenia: Its associated risk factors and outcome in NICU in a tertiary hospital in Nepal. J Coll Med Sci. 2018;14(2):65–8.

17. Jeremiah Z, OBURU JUSTINA EGWUMA. Pattern and prevalence of neonatal thrombocytopenia in Port Harcourt, Nigeria. Pathol Lab Med Int. 2010;(April 2010):27.

18. Elhassade AS, Belgaid R. Thrombocytopenia in neonate admitted to intensive care unite. 2019;5(5):23–5.

19. Chakravorty S, Roberts I. How I manage neonatal thrombocytopenia. 2011;(September):155–62.

20. Yurdakök M. Immune thrombocytopenia in the newborn. J Pediatr Neonatal Individ Med. 2017;6(1):1–10.

21. Thrombocytopenia N. NEONATAL THROMBOCYTOPENIA AND. 2011;47(3):281–8.

22. Stanworth SJ. Thrombocytopenia, bleeding, and use of platelet transfusions in sick neonates. Hematology Am Soc Hematol Educ Program. 2018;11:512–6.

23. WHO. Recommendations on newborn health: approved by the WHO Guidelines Review Committee. World Heal Organ. 8(May 2019):1–28.

24. Murray NA. Evaluation and treatment of thrombocytopenia in the neonatal intensive care unit. Acta Paediatr Int J Paediatr Suppl. 2017;91(438):74–81.

25. Gunnink SF, Vlug R, Fijnvandraat K, Van Der Bom JG, Stanworth SJ, Lopriore E. Neonatal thrombocytopenia: Etiology, management and outcome. Expert Rev Hematol. 2014;7(3):387–95.

26. Health.vic. Thrombocytopenia in neonates. Victoria State Gov [Internet]. 2015;92857. Available from: https://www2.health.vic.gov.au:443/hospitals?and?health?services/patient?care/perinatal? reproductive/neonatal?ehandbook/conditions/thrombocytopenia

27. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet. 2010;375(9730):1969–87.

28. De S, Charles H, Université N, El T, Faculté M, Tunis D De. Prevalence and outcomes of thrombocytopenia in a neonatal intensive care unit Prévalence et pronostic de la thrombopénie dans une unité de réanimation néonatale . 2016;94(4):305–8.

29. Maternal , Infant , and Child Health :healthy people 2020. african CDC. 2020;5:20201.

30. Demisse AG, Yimer MA, Mekasha A, Worku A, Gebremedhin AD, Mcclure EM, et al. Hematologic Profiles of Ethiopian Preterm Infants With Clinical Diagnoses of Early-Onset Sepsis , Perinatal Asphyxia , and Respiratory Distress Syndrome. 2020;

31. CSA. Ethiopia Mini Demographic and Health Survey. 2019.

32. Kaewkiattikun K. Ethiopian demographic and health survey. Vol. Volume 8, CSA.

2016. 115–123 p.

33. Resch E, Hinkas O, Urlesberger B, Resch B. Neonatal thrombocytopenia—causes and outcomes following platelet transfusions. Eur J Pediatr. 2018;177(7):1045–52.

34. Carr R, Kelly M, Williamson LM. Neonatal Thrombocytopenia and Platelet Transfusion – A UK Perspective. 2015;1–7.

35. Neonatal Thrombocytopenia Aetiology Fetal Thrombocytopenia Early-Onset Neonatal Thrombocytopenia Late-Onset Neonatal Thrombocytopenia Risks of Thrombocytopenia Practice Points Index of Related Documents. 2020;2016(21):2020.

36. Kotwal J. Approach to neonatal thrombocytopenia: Immature platelet fraction has a major role. Med J Armed Forces India. 2011;67(3):212–4.

37. Arvind R, Arvind R. Neonatal Hematology. Appl Neonatol. 2018;273–273.

38. Saxonhouse MA, Sola-Visner MC. Thrombocytopenia in the neonatal intensive care unit. Neoreviews. 2014;10(9).

39. Kusumasari N, Rohsiswatmo R, Gatot D, Darwis D. Paediatrica Indonesiana. 2010;50(1):31–7.

40. Eslami Z, Lookzadeh MH, Noorishadkam M, Hashemi A, Ghilian R, Pirdehghan A. Thrombocytopenia and Associated Factors in Neonates Admitted to NICU during Years 2010_2011. Vol. 3, Iranian journal of pediatric hematology and oncology. 2013. p. 205–20515.

41. Mak TW, Saunders ME, Response I. Neonatal Thrombocytopenia Thrombocytopenia and thrombocyto- sis. 2016;

42. Meena SL, Singh K, Jain S, Jain A, Karnawat BS. Clinical profile and outcome of neonatal thrombocytopenia in a tertiary care hospital. Int J Contemp Pediatr. 2019;6(3):1344.

43. Arif H, Ikram N, Riaz S, Nafisa A. Risk Factors and Outcome of Neonatal

Thrombocytopenia. Vol. 24, Journal of Rawalpindi Medical College. 2020. p. 229–34.

44. Sharma A, Thapar K. A prospective observational study of thrombocytopenia in high risk neonates in a tertiary care teaching hospital. Sri Lanka J Pediatr. 2015;44(4):213–9.

45. Chan JK, McDonald BE, Gerrard JM, Bruce VM, Weaver BJ, Holub BJ. Effect of dietary α-linolenic acid and its ratio to linoleic acid on platelet and plasma fatty acids and thrombogenesis. Lipids. 1993;28(9):811–7.

46. Hornstra G. Essential fatty acids in mothers and their neonates. Am J Clin Nutr. 2000;71(5 SUPPL.):1262–9.

47. Ree IMC, Fustolo-Gunnink SF, Bekker V, Fijnvandraat KJ, Steggerda SJ, Lopriore E. Thrombocytopenia in neonatal sepsis: Incidence, severity and risk factors. PLoS One. 2017;12(10):1–10.

48. Saber AM, Aziz SP, Almasry AZE, Mahmoud RA. Risk factors for severity of thrombocytopenia in full term infants: a single center study. Ital J Pediatr. 2021;47(1):2021.

49. Ethiopia People 2020. https://theodora.com/wfbcurrent/ethiopia/ethiopia_people.html. 2020;2020.

50. Warner MA, Caplan RA, Epstein BS, Gibbs CP, Keller CE, Leak JA, et al. Practice guidelines for preoperative fasting A report by the american society of anesthesiologists task force on preoperative fasting. Anesthesiology. 1999;90(3):896–905.

51. Al-lawama M, AlZaatreh A, Elrajabi R, Abdelhamid S, Badran E. Prolonged Rupture of Membranes, Neonatal Outcomes and Management Guidelines. J Clin Med Res. 2019;11(5):360–6.

52. Sahiledengle B, Tekalegn Y, Woldeyohannes D. The critical role of infection prevention overlooked in Ethiopia , only one-half of health-care workers had safe practice : A Systematic Review and Meta-Analysis. 2020;0–2.

53. Houssein N. Knowledge and Practices of Infection Prevention and Control Healthcare Workers in Benghazi Medical Centre, Libya. Khalij-Libya J Dent Med Res. 2021;30–42.

54. Tabatabaei SM, Behmanesh Pour F, Azadeh H. Infection Control Practices and Program Management in Labor and Delivery Units: A Cross-Sectional Study From Iran. Int J Infect. 2016;3(2).

55. Mulugeta AK, Giru BW, Berhanu B, Demelew TM. Knowledge about birth preparedness and complication readiness and associated factors among primigravida women in Addis Ababa governmental health facilities, Addis Ababa, Ethiopia, 2015. Reprod Health. 2020;17(1):1–13.

Annex I: Information Sheet

Title of the Research Project: Prevalence of thrombocytopenia and its associated factors among Neonates Admitted to Neonatal Intensive Care Unit at public hospitals in Addis Ababa in 2020/21G.c.

Name of Investigator: Markos Wodaje

Name of the Organization: Addis Ababa University College of Health Science, School of Nursing and Midwifery, Department of Nursing.

Name of the Sponsor: Addis Ababa University.

Introduction: This information sheet is prepared for TASH, GMH, Y12MH, SPMMC administration and NICU coordinating office. The aim of the form is to make the above-concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: to assess the Prevalence of thrombocytopenia and its associated factors among Neonates Admitted to Neonatal Intensive Care Unit at public hospitals in Addis Ababa in 2020/21G.c.

Procedure: In order to achieve the above objective, information which is necessary for the study will be taken from neonatal medical record chart.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from medical chart, it will not cause any harm on the patients. The name or any other identifying information will not record on the questionnaire and all information is taken from the chart will kept strictly confidential and in a safe place. The information retrieved will be only used for the study purpose.

Benefits: The research have no direct benefit for one whose document/ record are included in this research. But it has indirect benefit for other clients. This is because if program planners are preparing predicted plan there is a benefit for clients in the program of getting appropriate care and treatment services for other newly born ones. In all, the research work has a principal direct benefit for health care planners and managers.

Confidentiality: To reassure confidentiality the data on the chart will be collected without the name of the clients and the information collected from this research project will be kept confidential and stored in a file cabinet. In addition, it will not be shown to anyone except the investigator and it has been kept in a key and locked system with computer password.

Person to contact: This research project will be reviewed and approved by the institutional review board of College of Health Science, School of Nursing and Midwifery, Addis Ababa University. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any the time you want.

1-Markos Wodaje, Addis Ababa University, College of Health Science, Neonatal nursing student: principal investigator

Cell phone: Phone: +251-922-89-90-58

Email: markoswodaje8@gmail.com

2-Niguse Tadele (Assistant Professor,) Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Nursing: Main Advisor

Cell phone: +251-913163130

Email: niguse.tadele@aau.edu.et

3-Hana Lijaemiro (BSC, MSc) Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Nursing: Co- Advisor.

Mobile: +251911827629

Email:hanilij2012@gmail.com

Annex II: Data Extraction Checklist

Abstraction sheet to assess the prevalence of thrombocytopenia and its associated factors among neonates admitted in NICU in selected public Hospitals in Addis Ababa Ethiopia, 2021.

Guide to data collectors: Read the variables and fill the data abstraction sheet carefully by making appropriate circle or writing the response on the space provided accordingly.

Name of the organization_____

Data collection date_____ **code number**_____

Part I: Socio Demographic Variable of the mother			
No	**Question/Variables**	**Response option**	**Remarks**
101	Mother's age in years?	_____Years.	
102	Place of Residence?	1. Urban 2. Rural	

Part II-Maternal medical problem

201	Did the mother has history of known chronic illness	1. Yes 2. No	If no skip 202
202	If yes which chronic disease	1. Hypertension 2. Diabetes mellitus 3. Cardiac disease 4. Renal disease 5. HIV/AIDS 6. Other_____	
203	Did the mother took any medication during Px	Yes No	
204	If yes, specify.		

Part III Maternal Obstetric Related Variables

301	Number of pregnancy(gravid)	_____	
302	Number of live births (Parity)?	_____	
303	Dose the mother had ANC follow up for the indexed pregnancy?	1. Yes 2. No	If No skip Q no 304
304	If the answer for question 202 is yes, how many ANC visits?	_____visit.	
305	VDRL test	1. Reactive 2. Non-reactive 3. Unknown	
306	Where was the Place of delivery?	1. Home 2. Health institution	
307	What was the type of pregnancy?	1. Singleton 2. Twin 3. Triple or more	
308	Does she develop pregnancy related Complication During her last Pregnancy?	1. Yes 2. No	If no skip Q no= 309
309	If the answer for Q 206 is yes, what was the complication?	1. Pre-eclampsia 2. Sever pre-eclampsia 3. Eclampsia 4. Gestational DM 5. APH 6. PROM 7. IUGR 8. Other (specify ----------)	
310	What was the mode of delivery for this pregnancy?	1) Spontaneous Vaginal Delivery 2) Assisted vaginal delivery 3) Cesarean section	

Part IV Neonatal Related Data

401	Sex of the baby?	1. Male 2. Female	
402	Age at admission?	_____min/hrs/days	
403	If the pregnancy is twin, triplet or more is he/she	1. First baby 2. Second baby 3. Third baby 4. Fourth baby	
404	Birth weight of the baby?	_____grams	
405	Gestational age	_____weeks _____days	
406	Weight for gestational age	1. AGA 2. SGA 3. LGA	
407	Admission source	1. Inborn 2. out born	
408	Did he/she resuscitate at birth?	1. Yes 2. No	If no skip 409
409	If yes how long	_____min.	
410	What was the APGAR score at the 1st and 5th minute of life respectively?	1st min_____ and 5th min_____	

Part V Neonatal Clinical co-morbidities

501	Did the neonate developed thrombocytopenia.	1.yes 2.no	
502	What was the platelet count	__,__,__,___,__,__,___	
503	At what age he/she develop thro	_____hrs_____ days	
504	What is the diagnosis of the baby during developing thrombocytopenia at NICU?	1. Sepsis 2. Birth asphyxia 3. Neonatal jaundice 4. NEC 5. Surgical disorder 6. Other …….	Multiple response possible
505	Did s the neonate NPO	1. Yes 2. No	If no skip 507
506	If the answer for 507 is yes. how long	_____hrs_____ days.	
507	If the neonate feed, the amount of the feeding he/she took	1. Trophic feeding 2. Full feeding	
508	Type of milk the neonate feed	1. breast milk 2. Formula milk	