

**PERINATAL OUTCOMES OF WOMEN WITH HYPERTENSIVE
DISORDERS OF PREGNANCY IN JIMMA MEDICAL CENTER,
SOUTHWEST ETHIOPIA: RETROSPECTIVE COHORT STUDY**

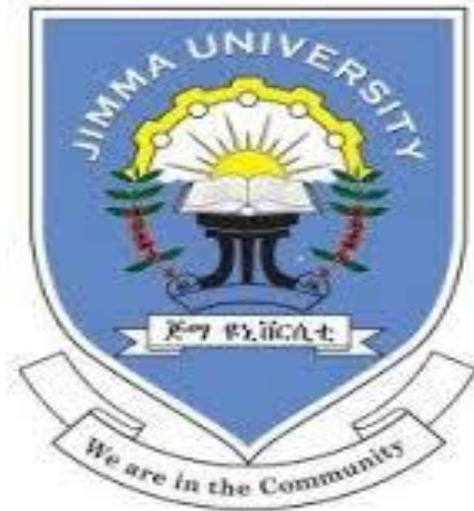
BY:

DEBELA DEREJE (BSc)

**THESIS SUBMITTED TO JIMMA UNIVERSITY INSTITUTE OF
HEALTH SCIENCE FACULTY OF PUBLIC HEALTH DEPARTMENT
OF EPIDEMIOLOGY IN PARTIAL FULFILLMENT FOR THE
REQUIREMENT OF MASTERS OF PUBLIC HEALTH IN
EPIDIMOMOLOGY.**

AUGUST, 2020

JIMMA, ETHIOPIA



**PERINATAL OUTCOMES OF WOMEN WITH HYPERTENSIVE
DISORDERS OF PREGNANCY IN JIMMA MEDICAL CENTER,
SOUTHWEST ETHIOPIA: RETROSPECTIVE COHORT STUDY**

BY:

DEBELA DEREJE (BSc)

ADVISERS: MULUSEW GERBABA (PhD)

AND

TADESSE GEBREMEDHIN (MPH)

AUGUST, 2020

JIMMA, ETHIOPIA

Abstract

Background: Hypertensive disorders of pregnancy (HDP) increased adverse perinatal outcomes in women with the disorder. About 16% of all still birth and 10% of early neonatal deaths were accounted by pregnancies complicated by HDP. In Ethiopia, HDP complicate about 6% of all pregnancies but, the risk of perinatal outcome is more daunting. Hence, this study aims to determine the risk of adverse perinatal outcomes among women with HDP in Jimma medical center, southwest Ethiopia

Methods: A retrospective cohort study was conducted on a total of 777 women gave birth between June 2017 to March 2020 at Jimma Medical Center, southwest Ethiopia. Women who gave birth at 28 weeks of gestation and above with HDP were enrolled as exposed and normotensive women as unexposed group. Simple random sampling technique without replacement method was used after preparing sampling frame independently for both groups. Data were reviewed using structured data collection format that prepared after reviewing relevant literatures. Data were entered to Epi-Data manager version 3.1 and exported to STATA version 13 for analysis. The adverse perinatal outcomes risk were examined using log binomial and modified Poisson regression model with robust standard errors.

Results: In this study, the overall incidence of adverse perinatal outcome was higher among women with hypertensive disorders of pregnancy (HDP) than normotensive women (64.1% versus 32.8%). After adjusted for confounders women with HDP were at higher risk of babies with low birth weight (adjusted RR= 2.88 at 95% CI:(2.2, 3.75)), preterm birth(aRR= 2.31(1.7, 3.14)), fifth minute low Apgar score (aRR = 2.6(1.53, 4.42)), admission to neonatal intensive care unit (aRR=1.77(1.32, 2.37), stillbirth (aRR=2.02(1.11, 3.01)), and perinatal mortality (aRR=3.88(1.97, 7.66)) than normotensive women.

Conclusion: women with hypertensive disorder of pregnancy were at higher risk of adverse perinatal outcomes than normotensive women gave birth at Jimma Medical Center, southwest Ethiopia. Hence, programmers and health care providers; design intervention for better perinatal outcomes and strengthen the primary prevention, secondary prevention and treatment strategy to improve better perinatal outcomes.

Key words: Hypertension Disorders of Pregnancy, Perinatal outcomes, Adverse perinatal outcomes

Acknowledgement

First of all, I would like to present my profound thanks to Almighty God for all the blessings in my life to arrive at this point. Secondly, I would like to present my special thanks for my advisories **Dr. Mulusew Gerbaba** and co-advisor **Mr. Tadesse G/Medhin** for their unreserved advice, suggestions they provided me through my entire step and for their patience with all of my inconvenience. I am also grateful to Jimma Medical Center maternity ward, neonatal intensive care unit, statistics office, and labor staffs for their cooperation during data collection.

Finally, I would also like to extend my thanks to data collectors and Jimma University, Institute of Health Sciences, and Faculty of Public Health that provide me this opportunity.

Table of Contents

Abstract	I
Acknowledgement	II
List of Tables	V
List of Figures	VI
Abbreviations and Acronyms	VII
1. Introduction.....	1
1.2 Statement of the problem	2
1.3 Significance of the study.....	5
2. Literature Review.....	6
2.1 Conceptual Framework.....	11
3. Objectives	12
3.1 General objective	12
3.2 Specific Objectives	12
4. Methods and materials	13
4.1 Study area.....	13
4.2 Study design and period.....	13
4.3 Source population	13
4.3.1 Study population	13
4.4 Inclusion and exclusion criteria.....	13
4.4.1 Inclusion criteria	13
4.4.2 Exclusion criteria	14
4.5 Sample size determination	14
4.6 Sampling techniques	16
4.7 Variables	16
4.8 Data collection tools	16
4.9 Data collection procedure	16
4.10 Data quality control.....	17
4.11 Data processing and analysis	17
4.12 Ethical consideration.....	18
4.13 Definition of terms.....	18
4.14 Plan for Dissemination of the Result	19

5. Results.....	20
6. Discussion.....	24
7. Conclusion and recommendation.....	30
Conclusion	30
Recommendation	30
References.....	31
Appendix.....	31
Declaration.....	38

List of Tables

Table 1: <i>Sample size determination with parameters for the second objective</i>	14
Table 2: <i>Sample size determination with parameters for the first objective</i>	15
Table 3: <i>Socio-demographic and Obstetric characteristics of pregnant women who gave birth at JMC in Jimma Town, Southwest Ethiopia between June, 2017- March, 2020</i>	20
Table 4: <i>Incidence of adverse perinatal outcomes with confidence interval among women with HDP and Normotensive women who gave birth at JMC, June, 2017 to March 2020</i>	23
Table 5: <i>Bivariate and multivariate analysis on the association between HDP and adverse perinatal outcomes among women gave birth at JMC, southwest Ethiopia, June, 2017 to March, 2020</i>	24

List of Figures

<i>Figure 1:</i> Conceptual frame work after reviewing different Literatures (36, 41, 43, 47).	11
--	----

Abbreviations and Acronyms

ANC- Antenatal Care

APGAR-A-Appearance, P-Pulse, G-Grimace, A-Activity and R-Respiratory

aRR- Adjusted Relative Risk

BP- Blood Pressure

CI- Confidence Interval

ENND- Early Neonatal Death

HDP- Hypertensive Disorder of Pregnancy

IQR- Inter-quartile Range

JMC- Jimma Medical Center

LBW- Low Birth Weight

NICU- Neonatal Intensive Care Unit

OR- Odd Ratio

PMR- Perinatal Mortality Rate

PNM- Perinatal Mortality

RR- Relative Risk

SDG- Sustainable Development Goal

SSA-Sub-Saharan Africa

WHO-World Health Organization

1. Introduction

Hypertensive disorders of pregnancy (HDP) are multisystem diseases, which include chronic hypertension (preexisting), gestational hypertension, preeclampsia, eclampsia, and superimposed preeclampsia on chronic hypertension(1). Hypertension is defined as a sustained systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg based on the average of at least two measurements, using the same arm for measurement(2).

Hypertensive disorders affect 10% of pregnancies around the globe and it is an important cause of maternal and perinatal morbidity (1, 3, 4). However, it is disproportionately distributed across the world, of that estimated magnitude of HPD in developing countries reaches up to 16.7%(5).

In addition to that, studies conducted in Ethiopia revealed a high burden of HDP which ranges from 2.23 to 18.25% (6-8). Similarly, according to a study conducted in Jimma University specialized hospital; the prevalence of hypertensive disorders of pregnancy was 8.5%, which is higher than the national pooled prevalence of HDP (6.29%)(7, 9).

HDP is associated with disturbed vascular manifestations, oxidative stress and endothelial damage. This affects placental function resulting in poorer perfusion and nutrient supplementation to the fetus(10) and that enhance adverse perinatal outcomes. Different studies conducted in developed and developing countries on adverse perinatal outcomes of HDP revealed, it is associated with higher rates of morbidity and mortality including intrauterine growth restriction, intrauterine fetal death, preterm birth (delivery at less than 37 completed weeks of gestation), birth asphyxia, low birth weight and perinatal mortality(11-14).

Hence, this study aims to determine adverse perinatal outcomes (preterm birth, 1st and 5th-minute Apgar score less than 7, still birth, small for gestational age, low birth weight, admission to NICU, early neonatal death and perinatal mortality) effect of hypertensive disorders of pregnancy among women with the disorders to normotensive women who gave birth at Jimma Medical Center between June 26, 2017- March 16, 2020.

1.2 Statement of the problem

Hypertensive disorders of pregnancy are a common (6 to 10%) pregnancy complication affecting millions of expectant mothers and perinatal outcomes worldwide (15-17).

Studies have shown that HDP accounts for 15% of perinatal deaths globally(18, 19). Among the estimated 2.6 million stillbirths annually, approximately 16% occur in pregnancies complicated by hypertension disorder of pregnancy(20). It has been estimated that the HDPs precede 10% of early neonatal deaths (8/1000 live births) (15). Despite, perinatal mortality rate (PMR) has been widely used as a key indicator of maternal and neonatal quality of care reflection that available during pregnancy, delivery and post-delivery(21). There is disproportionately high perinatal mortality in Sub-Sahara Africa that mostly attributed to HDP especially in low resource settings(21).

Different Studies described hypertensive disorders of pregnancy increased adverse perinatal outcomes in women with HDP (22, 23). For instances, perinatal mortality is three to five folds higher in women with preeclampsia/eclampsia syndrome as compared to those without the disorders(24, 25). In addition, the rate of perinatal mortality among women with HDP was found to be 317/1000 births in Ethiopia(9); 230/1000 births in Pakistan (26); and 144/1000 births in Turkey(27) which is quite high compared with the overall perinatal mortality rate of respective country.

According to data from multi-country study conducted by World Health Organization; eclampsia/pre-eclampsia was the primary obstetrical cause for 1 out of 4 perinatal deaths, with similar proportions affected by stillbirths and early neonatal deaths(28). A larger institutional based study conducted in 29 low and middle-income countries, explored the most important obstetric causes for perinatal deaths was hypertensive disorders, with life-threatening eclampsia and pre-eclampsia underlying 7.5% of macerated late fetal deaths, 9% of fresh late fetal deaths and 10% of early neonatal deaths(29).

Hypertensive disorders of pregnancy account about 7% of perinatal mortality causes in Ethiopia which play great contribution to label Ethiopia among the countries with highest perinatal mortality rate in Sub Saharan Africa(10).

In 2018, systematic review reported that, hypertensive disorders of pregnancy complicated around 6% of all pregnancies in Ethiopia(7). Additionally, Prevalence of perinatal and maternal mortality among pregnant women with one of the hypertensive disorders were found to be higher than rates reported from high income as well as most of the middle and low income countries(7).

In Ethiopia, One in four pregnancies complicated by hypertensive disorder end up in perinatal death and newborn with low birth weight was found to be 37%(8). The 5-minute APGAR score of <7 in women with HDP was highest (52.8%) in Addis Ababa (30) and the lowest rate being 13.4% in Southern Ethiopia(31).

Preterm birth complicates as high as 65.3% of women with HDP in Somalia regional state Ethiopia (32) to as low as 31% in Oromia regional state(33).

Even though, hypertensive disorders of pregnancy has adverse outcomes on both maternal and newborns; the risk of maternal death is less than 1% in severe preeclampsia, where as perinatal death was about 13%. The situation is worse in eclampsia; where the risks of maternal and perinatal deaths occur in about 5% and 28% respectively(34). Study from India reported the rate of maternal mortality was 5.55% and perinatal deaths occurred in 37.5% of the deliveries(35).

Despite of the fact that, most obstetricians worry more about the risk of maternal death in women whose pregnancies are complicated by hypertensive disorders, but the risk of perinatal outcome is more daunting(34).

Adverse perinatal outcomes of HDP may place surviving newborns at risk of neuro-developmental deficits such as hypoxic-ischemic encephalopathy, post-traumatic stress disorders, neurologic disability, low cognitive functions, and neurological sequel(36-38).

In Ethiopia, despite of the inconsistent findings on the incidence of adverse perinatal outcomes across the studies, the available limited studies revealed a higher incidence of low birth weight, stillbirth, early neonatal death, 5-minute APGAR score less than 7 and preterm birth among women with HDP(6, 33, 39).

Existing studies revealed that age of the mother, socioeconomic status, maternal education, ANC utilization, complications during pregnancy and childbirth, multiple births, sex, and position at birth are potential risk factors for perinatal outcomes(40).

However, this study is going to use secondary data to assess adverse perinatal outcomes in women with HDP by controlling for variables such as maternal age, residence, parity, gravidity, fetal mal-presentation at birth, type of pregnancy (single or multiple births), mode of delivery, anemia status, number of ANC visit, maternal malaria infection during current pregnancy and maternal HIV status that have potential adverse effect on perinatal outcomes. Additionally, many available studies conducted in Ethiopia were descriptive; they did not address the relative risk of HDP on adverse perinatal outcomes to compare with normotensive pregnant women who gave birth.

This study aimed to show, adverse effect of hypertensive disorders of pregnancy on a number of important perinatal outcomes in women with HDP compared to normotensive pregnant women gave birth at JMC. The study provides evidence based information about effect of HDP on adverse perinatal outcome in order to improve maternal and child health care.

1.3 Significance of the study

Many mothers and newborns are affected by the adverse outcomes of hypertensive disorders of pregnancy (HDP). There are many causes for this problem such as poor access to health service and quality of maternal and newborn care. Therefore, this study will help public health policymakers and programmers to have a clear picture about the effect of HDP on adverse perinatal outcomes to make an evidence-based decision and resources mobilization for prevention (primary and secondary), management and its associated perinatal complications. Additionally, unless effort would be made to reduce contribution of HDP for perinatal mortality causes, the ambitious SDG-3.2 cannot be attained to reduce neonatal mortality to the target plan.

For the reason, exploring the risk of adverse perinatal outcomes in women with HDP compared with normotensive pregnant women will help programmers to design; interventions for better perinatal outcomes and also guide health care providers working in clinical areas to make evidence-based decisions for the prevention and management of adverse perinatal outcomes of hypertensive disorders of pregnancy. It will also be used by other researchers for further investigation.

2. Literature Review

According to a cohort study in Tigray regional state showed, the mean maternal age of women with HDP and normotensive women were almost similar 27.27 versus 27.34 years respectively (41) and Women with HDP were of similar age to those without the disease (42). Women with HDP were more likely residing in rural areas than normotensive women 31.5% versus 16.7% (41).

A cohort study from the Tigray region showed, the proportion of primigravidas was more likely higher among women with HDP than normotensive women that were 41.2% versus 31.8%(41) and proportion of anemia higher among women with HDP than normotensive women were 27.3% and 10% respectively. The majority, 66.4% of women with HDP and 22.2% of normotensive women developed adverse perinatal outcomes in their newborns (41).

Preterm birth

According to a retrospective cohort study in the US found, the proportion of preterm birth less than 37 weeks among women with HDP versus normotensive was 17.4%, 7.8% respectively with relative risks of 2.23 at 95% CI: (2.20–2.25)(43). According to studies in Ghana, India, and São Paulo city, preterm birth in women with HDP was 21.7%, 24.6%, and 10.6% respectively (44-46).

A cross-sectional study from Nigeria reported that HDP was associated with an elevated risk of preterm birth with the adjusted OR of 3.3 at 95% CI: (2.42–4.40)(47). Additionally, higher preterm births occurred among pregnant women with HDP than normotensive pregnant women 40.8% and 5.6% respectively. Women with HDP were more likely to have a lower gestational age at delivery than normotensive women (37.3 ± 2.5 weeks vs. 39.0 ± 1.6 weeks, $p = 0.001$) with adjusted relative risks of 5.19 at 95% CI: (3.37, 7.99)(41).

Small for gestational age

A cross-sectional study from Nigeria showed a high risk of fetal growth restriction with an adjusted OR of 2.94 at 95% CI : (1.84, 4.71) among women with hypertension when compared to normotensive women(36). Studies reported that small for gestational age among women with HDP was 6.3% in Ghana, 25.7% in Madagascar, 15.3% in Nigeria, and 17% in South Africa (36, 44, 48, 49).

According to a cohort study in the Tigray region, the incidence of small for gestational age among women with hypertensive disorders and normotensive women was 36.7% and 10.7% respectively with adjusted relative risk of 3.29 at 95% CI of (2.33, 4.65)(41).

Low Apgar score

The retrospective cohort study revealed that gestational hypertension did not significantly increase the risk of gestational age-specific risk of the 5th-minute low Apgar score in twin pregnancies. In contrast, the risk of 5th-minute low Apgar score was increased by over 50% for singleton hypertensive pregnancies at term or post-term (43). The same study found the proportion of 5th-minute low Apgar score among women with HDP versus normotensive were 2.6% and 2% respectively with relative risks of 1.33 at 95% CI: (1.21–1.45)(43). According to a prospective case-control study from New Delhi revealed; 24.49% of babies from women with hypertensive disorder of pregnancy had Apgar score <7 at 5 minutes as compared to only 14% of babies from normotensive women(41) . A cross-sectional study reported, high-risk low Apgar scores at 1 minute with adjusted OR of 2.99 at 95% CI :(1.37–6.51) and 5 minutes Apgar score with adjusted OR of 2.08 at 95% CI:(1.54–2.81) among women with hypertensive disorders of pregnancy compared to normotensive women(36). The same study from Zimbabwe reported the proportion of low Apgar score among women with hypertensive disorders of pregnancy versus normotensive women 10% and 2% respectively with four times more likely to have a baby with a low Apgar score at 5 minutes ($p = 0.0155$) compared to normotensive women(47).

According to a cohort study in Tigray, the incidence of low 5th-minute Apgar score was higher among newborn babies delivered from women with HDP than normotensive women (20.4% versus 3.4%) with an adjusted relative risk of 2.69, 95% CI (1.91 - 3.80) for women with HDP versus normotensive women(41).

Low Birth Weight

According to an analytic cross-sectional study in Zimbabwe, higher low birth weight occurred among pregnant women with HDP than normotensive pregnant women 16% and 6% respectively. Women with Pregnancy-induced hypertension were three times more likely to deliver a low birth weight baby (OR 3.00, $p = 0.0115$)(47). The study from Nigeria reported, low birth weight adjusted OR of 4.68 at 95% CI:(3.24–6.76)(36).

According to a cohort study in Ethiopia, the incidence of low birth weight babies was higher among women with HDP than normotensive women. Which was 37.7% and 6.1% respectively with relative risks of 5.13 at 95% CI: (3.36, 7.84)(41). The mean birth weight of babies born from women with HDP was 2647.2g and 3176g among normotensive pregnant women (p -value < 0.001)(41).

Stillbirth

A cross-sectional study from Zimbabwe revealed that the proportion of stillbirth among women with hypertensive disorders versus normotensive was 6% and 1% respectively with the odds ratio of 4.3 times more likely to have stillbirth(47).

A cohort study in Tigray found Stillbirths occurred in 10.0% of women with HDP and 1.7% normotensive pregnant women respectively with relative risks of 3.46 at 95% CI:(1.40,8.54)(41). The stillbirth rate among women with HDP was 100/1000 live births. The stillbirth rate for women with HDP cohort was 49.3 stillbirths per 1000 live births as found by retrospective surveillance Haiti(11) and the stillbirth rate was 21.9 per 1000 births in women with a hypertensive disorder in pregnancy from China(51).

Admission to NICU

The proportions of admission to neonatal intensive care units were higher among babies delivered from mothers with HDP's than normotensive women, which was 28.8%, 5.4% respectively. A similar study reported, the risk of admission to NICU for newborns from women with HDP was 3.29 at 95% CI: (2.33, 4.65) as compared to newborns of the normotensive mother (41). According to the study from Lagos Nigeria, newborn admission to NICU whose born from mothers with HDP as compared to newborns of normotensive women were 3.22 times higher at 95% CI: (2.35, 4.43) with the proportion of admission 14.7% from with HDP's(36). Studies reported that newborns delivered from women with HDP admitted to the neonatal intensive care unit (NICU) in Iran (13%) and in Egypt (18.8%)(23, 52). According to a study from New Delhi, 25.5% of newborns of women with HDP, and 11.2% of newborns of normotensive women were admitted to NICU that has a statistical significance difference with $p= 0.014$ (41).

Perinatal Mortality

According to a retrospective cross-sectional study conducted in Turkey revealed, Perinatal mortality rate was found to be 144 per 1,000 births(53), a study from Ghana found that perinatal mortality rate of 106 per 1000 births whereas stillbirth and early neonatal death proportion were 64.1%, 35.9 % respectively(44). According to a retrospective cohort study in Hawassa shows, there was a perinatal mortality rate of 290 per 1000 total births, and proportion of stillbirths was more than 4-fold higher than early neonatal deaths, which mean that 81% were stillbirths and early neonatal deaths account 18.9% (54).

According to a cohort study in Ethiopia, early neonatal death occurred in 5.0% of mothers with HDP and 1.0% for normotensive mothers with relative risks of 3.22 at 95% CI: (1.06,9.74) (41).

Overall perinatal death occurred in 15.0% women with HDP and 2.5% normotensive pregnant women with relative risks of 3.67 at 95% CI:(1.83,7.38) were significantly higher in women with pregnancy-induced hypertension compared to normotensive women(41). Similarly, the perinatal mortality rate among women with HDP was 150 per 1000 live births, and 25 per 1000 live births among normotensive pregnant women (41).

The following variables were found as potential confounders: characteristics of the women and newborns such as maternal age, wealth status, educational status, residence, gravidity, type of pregnancy (single or multiple births) and mode of delivery, anemia status, maternal HIV status, fetal mal-presentation at delivery, sex of the newborn, maternal undernutrition, antepartum hemorrhage and malaria infection in current pregnancy (36, 41, 55-57).

women and newborns such as maternal age, wealth status, educational status, residence, gravidity, type of pregnancy (single or multiple births) and mode of delivery, anemia status, maternal HIV status, fetal mal-presentation at delivery, sex of the newborn, maternal undernutrition, antepartum hemorrhage and malaria infection in current pregnancy(36, 41, 55-57).

Generally, HDP has adverse perinatal outcomes, but the majority of the study could not adjust for some other penitential variables that may have adverse effect on perinatal outcome. Additional this study compared the effect of HDP on adverse perinatal outcome as compared to child born for normotensive women. Therefore, the study provides evidence based information about effect of HDP on adverse perinatal outcome in order to improve maternal and child health care.

2.1 Conceptual Framework

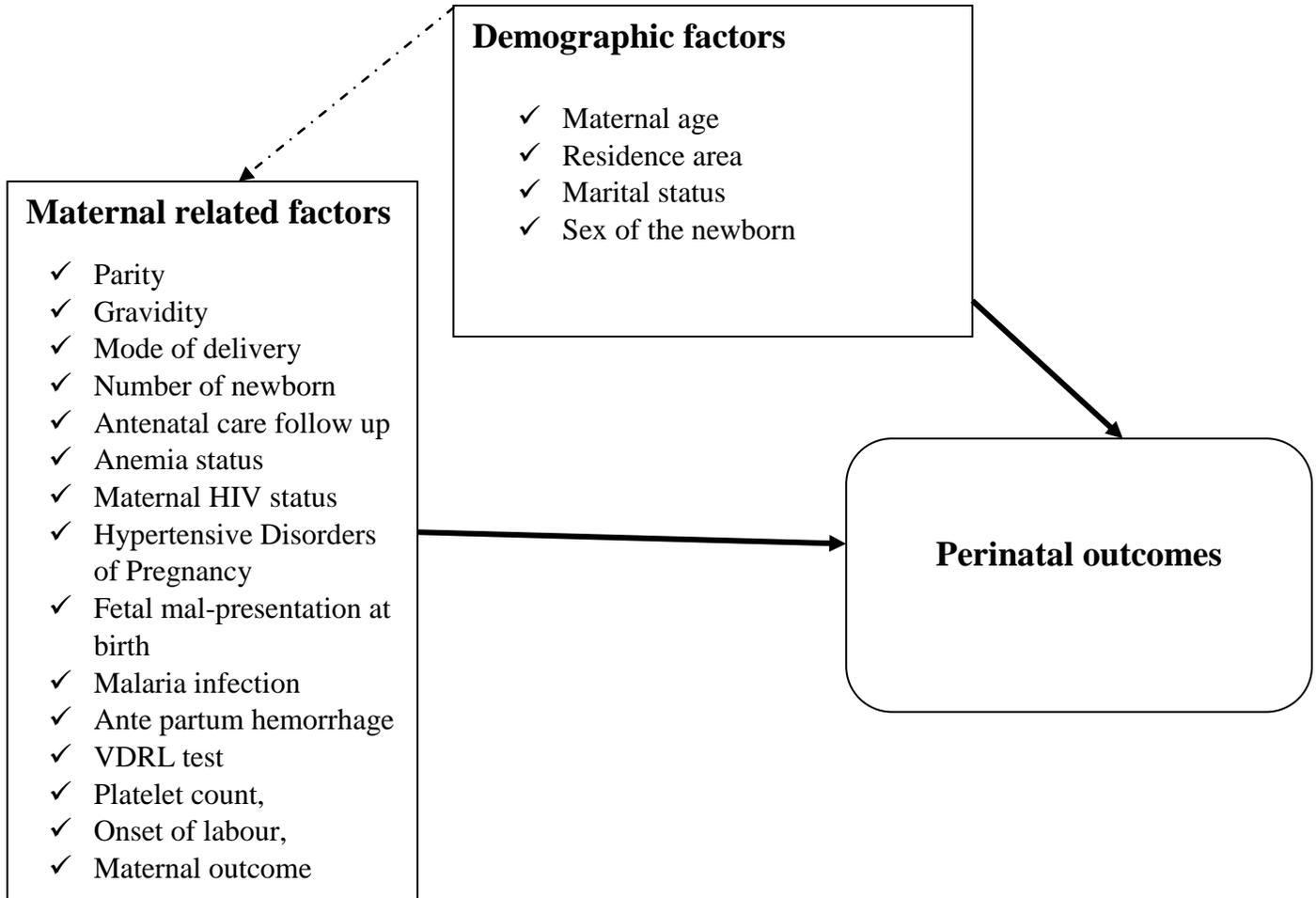


Figure 1: Conceptual frame work after reviewing different Literatures (36, 42-44).

3. Objectives

3.1 General objective

To determine effect of hypertensive disorders of pregnancy on adverse perinatal outcomes among women who gave birth at Jimma Medical Center, southwest Ethiopia, 2017-2020

3.2 Specific Objectives

1. To determine incidence of adverse perinatal outcomes among women with hypertensive disorders of pregnancy at Jimma Medical Center, southwest Ethiopia, 2017-2020
2. To determine the risk of adverse perinatal outcomes among women with hypertensive disorders of pregnancy at Jimma Medical Center, southwest Ethiopia, 2017-2020

4. Methods and materials

4.1 Study area

This study was conducted in Jimma Medical Center (JMC) which is located in Jimma town, Oromia region, southwest Ethiopia, 343km away from Addis Ababa, Capital city of Ethiopia. Approximately, greater than 15 million people are served and during study time period 9,590 deliveries were conducted in Jimma Medical Center. The total numbers of children served in the JMC catchment area are 2,250,000 and it provides service with 1600 staff members, 32 intensive care units, and 800 beds. According to cross sectional study in this hospital in 2011, prevalence of hypertensive disorders of pregnancy was 8.5% (9) and in average there is 153 women with hypertensive disorders of pregnancy in a year.

4.2 Study design and period

A retrospective cohort study was conducted using document review of women with hypertensive disorder of pregnancy and normotensive women who gave birth at Jimma Medical Center. Data of three consecutive years from June 26, 2017- March 16, 2020 were retrieved by 15days.

4.3 Source population

All pregnant mothers with hypertensive disorder of pregnancy for exposed and all normotensive mothers for non-exposed group, who gave birth at JMC during study period, were a source population.

4.3.1 Study population

Study population were randomly selected mothers with hypertensive disorder of pregnancy and normotensive mothers who gave birth in 28weeks of gestation or more at JMC during study period for exposed and non-exposed group respectively.

4.4 Inclusion and exclusion criteria

4.4.1 Inclusion criteria

Women with hypertensive disorders of pregnancy and normotensive women gave birth at 28 weeks of gestation and above in JMC during study time period for exposed and unexposed groups were included respectively.

Hypertension in pregnancy is defined as: Systolic blood pressure greater than or equal to 140 mmHg and/or diastolic blood pressure greater than or equal to 90 mmHg which usually confirmed within four hours apart measurement.

HDP encompasses chronic hypertension, gestational hypertension, preeclampsia/eclampsia, and superimposed hypertension.

Normotensive women: Systolic blood pressure \leq 140 mmHg and diastolic blood pressure \leq 90mmHg.

4.4.2 Exclusion criteria

The following exclusion criteria were applied: Record with no registered of gestational age at birth, age of newborn at death, birth weight, and multiple birth more than twin, birth with congenital anomalies, mothers with(DM, heart disease, incompetent cervix, Rh sensitization).

4.5 Sample size determination

Sample size was calculated by using STATCALC command of Epi-info version 7 with the following assumption of 95% confidence level, 80% power, ratio of unexposed to exposed of 2, by taking 1.7% of still birth among healthy mothers (normotensive) to detect the minimum relative risk of 3.46(44). Accordingly the sample size becomes **777** of which 259 from exposed and 518 from non-exposed for the second objective.

Table 1: Sample size determination with parameters for the second objective

Variables	% of outcome in unexposed	Ratio	CI	Power	aRR	Among exposed	Among unexposed	Estimated sample size
Low birth weight	6.1%	2	95%	80	5.13	31	62	93
Preterm delivery	5.6%	2	95%	80	5.2	34	67	101
Still birth	1.7%	2	95%	80	3.46	259	518	777
1 st minute APGAR score<7	10.2%	2	95%	80	2.93	53	105	<u>158</u>
5-minute APGAR score<7	3.4%	2	95%	80	3.46	125	250	375
SGA	10.7%	2	95%	80	3.29	38	76	114
Admission to NICU	5.4%	2	95%	80	5.11	36	72	108
Perinatal mortality	2.5%	2	95%	80	3.67	154	308	462

Source(44).

Sample size for first objective, calculated using clincalc by considering the following parameters: incidence of adverse perinatal outcome among women with hypertensive disorders of pregnancy and normotensive women, 5% alpha and 80% of power.

(<https://clincalc.com/stats/samplesize.aspx>).

Table2: *Sample size determination with parameters for the first objective*

Variables	Incidence	Alpha	Power	Among exposed	Among unexposed	Total sample size
Perinatal mortality	Normotensive = 2.5%	0.05	80%	63	126	189
	Among HDP=15%					
Still birth	Normotensive = 1.7%	0.05	80%	100	200	300
	Among HDP=10%					
Low Apgar score	Normotensive = 3.4%	0.05	80%	45	90	135
	Among HDP=20.4%					
Low birth weight	Normotensive = 6.1%	0.05	80%	20	40	60
	Among women with HDP =37.1%					
Early neonatal death	Normotensive = 1%	0.05	80%	229	458	687
	Among women with HDP = 5%					
Small for GA	Normotensive = 10.7%	0.05	80%	32	64	96
	Among HDP=36.7%					
Preterm birth	Normotensive = 5.6%	0.05	80%	17	34	51
	Among HDP=40.8%					

Source(44).

4.6 Sampling techniques

All eligible Women with hypertensive disorders of pregnancy and normotensive pregnant women who gave birth in 28 weeks and above at study time period were obtained using maternity HIMS log book as an entry point to identify women with their exposure status using their medical record number. Sampling frames were prepared and simple random sampling technique without replacement method was employed to select individual medical record separately for both exposed and non-exposed women using computer random number generator. Then, total required sample size of 777 was recruited using 259 from exposed (women with hypertensive disorders of pregnancy) and 518 from non-exposed groups (normotensive women).

4.7 Variables

Dependent: Perinatal outcomes (preterm birth, low birth weight, small for gestational age, first and fifth minute APGAR score of <7, still birth, admission to NICU, early neonatal death, perinatal mortality)

Exposure: Blood pressure of sustained systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg based on the average of at least two measurements, using the same arm for measurement.

Exposed: Women with hypertensive disorders of pregnancy gave birth at JMC

Non-exposed: Normotensive women who gave birth at JMC

Covariates: Maternal age, residence place, marital status, sex of the newborn, gravidity, mode of delivery, history of anemia, fetal mal-presentation at birth, ANC follow up, malaria infection in current pregnancy, ante-partum hemorrhage, VDRL test, platelet count, onset of labour, maternal outcome and maternal HIV status.

4.8 Data collection tools

Data were collected from the medical record by using structured data collection format that have been prepared after reviewing different literatures (36, 44-47)[see [Appendix](#)].

4.9 Data collection procedure

Structured data collection format was used to retrieve relevant data from individual medical chart. For data collection, six health professionals were recruited to collect data from JMC maternal and neonatal records after two day training given on the objective of the study and one MPH student was supervised and facilitate the data collection process. The principal investigator

coordinates the overall activity of the study. At a time of data collection supervisor and principal investigator were checked the way data collectors done their task and solved the problems on spot.

4.10 Data quality control

Prior to data collection, training was given for data collectors for two days on how to fill the recording format by taking 39 samples of cards from archive of JMC that simultaneously used for pre-test. To ensure the completeness of information during data collection, newborn information such as sepsis diagnosis, early neonatal status were extracted from neonatal intensive care unit logbook by admission date, sex, mother's name and age at death, and the principal investigator was made a thorough check before receiving the filled format from each data collector and in the meantime the cards were selected and cross checked for completeness and errors on spot. Data need transformations were re-coded to meaningful information and assumptions were checked for the models.

4.11 Data processing and analysis

Data were entered into Epi data manager version 3.1 and exported to STATA version 13 software package for analysis. Descriptive statistics (frequency and percentage for categorical variables and summary statistics for continuous variables were used to characterize the study population and the median difference between groups for continuous variables such as; age of the mother, gestational age and birth weight were tested using Mann-Whitney test because of failed normality assumption. Bivariate regression was done to select independent variables for all outcome variables using p-value cut of point ≤ 0.25 to be considered as candidate variables for multivariable regression analysis. The relative risk of adverse perinatal outcomes (small for gestational age and early neonatal death) were calculated using log-binomial model. As a first approach to the multivariable analysis, log-binomial models were used for all outcome variables. But, owing to the sparseness of data, failed for convergence assumption encountered for still birth, low birth weight, first and fifth minute low APGAR scores, preterm birth, Admission to NICU and perinatal mortality. Therefore, modified Poisson regression were opted with lowest Akaike's information criteria (AIC) and Bayesian information criteria (BIC) to select the final model using backward methods. For early neonatal death and small for gestational age, log-binomial models were used. Maternal age, residence place, marital status, sex of the newborn,

gravidity, mode of delivery, history of anemia, fetal mal-presentation at birth, ANC follow up, malaria infection, ante-partum hemorrhage, VDRL test, platelet count, onset of labour, maternal outcome and maternal HIV status were controlled in the statistical models. After adjusted for confounders relative risk with 95% confidence interval and p-value < 0.05 was considered to declare statistical significance.

4.12 Ethical consideration

This study was carried out after obtaining ethical clearance from Jimma University; Faculty of Public Health research ethical review committee. Letter of cooperation was written to JMC and permission was obtained from the hospital before conducting the study. No personal identifiers were used for analysis, to maintain confidentiality of the information and privacy.

4.13 Definition of terms

Hypertension disorder of pregnancy: encompasses chronic hypertension, gestational hypertension, preeclampsia/eclampsia, and superimposed hypertension.

Chronic hypertension: - is hypertension (i.e. a systolic blood pressure of 140 mmHg or higher or a diastolic pressure of 90 mmHg or higher) before pregnancy or before 20 weeks' gestation.

Gestational hypertension: -is a syndrome of hypertension appearing after 20 weeks of gestation without proteinuria.

Preeclampsia: -is hypertension and proteinuria after 20 weeks' gestation or hypertension plus the involvement of at least one organ or system.

Eclampsia: -is diagnosed when preeclampsia progressed to the convulsive phase.

Adverse perinatal outcome: - is defined as a newborn with the occurrence of any of the following outcomes: low birth weight, low Apgar score, small for gestational age, preterm delivery, admission to neonatal intensive care unit and perinatal death.

Low birth weight: -is defined as a birth weight of alive born infant of less than 2,500 g

Preterm delivery: -is a birth of infants occurring after 28 completed weeks but before 37 completed weeks of gestation.

Small for gestational age: -is defined as a birth weight of newborn below the tenth percentile of weight distribution at the specified gestational age of a pregnancy.

A low Apgar score: -when 1st minute and 5th minute Apgar score is less than 7.

Stillbirth: -is death prior to the complete expulsion or extraction from its mother of a product of conception after 28 weeks of pregnancy; the death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscles.

Early neonatal deaths: -is a death that occurred in the first week of neonatal life before discharge from the study hospital after 28 weeks of gestation

Perinatal mortality: -are stillbirths and newborn deaths within the first seven days of delivery.

Perinatal mortality rate: - is the sum of stillbirths and early neonatal deaths divided by the summation of live births and stillbirth, expressed per 1,000.

Sources (36, 44-47)

4.14 Plan for Dissemination of the Result

The findings of the study will be submitted to Jimma University; Department of Epidemiology and Jimma Medical Center. It will be presented to Jimma University Department of Epidemiology and on different research conference and finally, efforts will be made to publish on local or international journals to communicate with scientific society.

5. Results

5.1 Socio-demographic and Obstetric characteristics of study participants

Overall, a total of 259 women with hypertensive disorders of pregnancy and 518 normotensive pregnant women documents were reviewed in the study. Among a total of 259 women with HDP's participated in the study: 3.9%, 10.4%, 65.6% and 20.1% had chronic hypertension, gestational hypertension, pre-eclampsia and eclampsia respectively.

The median age of the mothers with HDP and normotensive women's were 26(inter-quartile range (IQR) = 8) and 27(IQR= 6) years respectively and there was no significant age difference between both group using Mann-Whitney U test of $p= 0.104$. Moreover, 136 (52.5%) of mothers with HDP and 211 (40.7%) of the controls were rural dwellers. The proportion of primigravidas was higher among women with HDP than normotensive women (41.7% versus 33%).The proportion of having anemia was roughly similar among women with HDP and normotensive women (21.6% versus 19.1%). The number of ANC visit among mothers with HDP and normotensive women were statistically different with $X^2 = 9.35$, $p=0.009$.From the total deliveries attended, 61.8% of women with HDP and 42.1% of normotensive women gave birth vaginally from each groups.

Table 3: *Socio-demographic and Obstetric characteristics of pregnant women who gave birth at JMC in Jimma Town, Southwest Ethiopia from June 2017- March 2020*

Variable		Women with HDP Frequency (%)	Normotensive women Frequency (%)
Residence	Urban	123 (47.5)	307 (59.3)
	Rural	136 (52.5)	211 (40.7)
Marital status	Single	3(1.2)	3 (0.6)
	Married	256 (98.8)	515 (99.4)
Gravidity	Primigravida	108 (41.7)	171 (33)
	Multipara (II–IV)	110 (42.5)	272 (52.5)
	Grand multipara (V+)	41 (15.8)	75 (14.5)
History of anemia	Yes	56 (21.6)	99 (19.1)

	No	203 (78.4)	419 (80.9)
Malaria diagnosed current pregnancy	Yes	21 (8.1)	20 (3.9)
	No	238 (91.9)	498 (96.1)
Maternal HIV status	Reactive	11 (4.25)	12 (2.3)
	Non reactive	248 (95.8)	506 (97.7)
VDRL test positive	Yes	4 (1.5)	5 (1.0)
	No	255 (98.5)	513 (99)
Number of ANC visit in current pregnancy	Zero	11 (4.3)	12 (2.3)
	1 to 4	208 (80.3)	381 (73.6)
	5+	40 (15.4)	125 (24.1)
On set of labour	Induced	101(39)	48 (9.3)
	Spontaneous	122 (47.1)	385 (74.3)
	Direct cesarean Section	36 (13.9)	85 (16.4)
Fetal mal-presentation at birth	Yes	31 (12)	129 (24.9)
	No	228 (88)	389 (75.1)
Platelet count	100,000+	225 (86.9)	511 (98.6)
	<100,000	34 (13.1)	7 (1.4)
Mode of delivery	Vaginal	160 (61.8)	218 (42.1)
	Cesarean Section	99 (38.2)	300 (57.9)
Type of pregnancy	Single	249 (96.1)	498 (96.1)
	Twin	10 (3.9)	20 (3.9)
Maternal outcome	Alive on discharge	253 (97.7)	517 (99.8)
	Died	6 (2.3)	1 (0.2)
Maternal Age (year)		Median (IQR)	Median (IQR)
		26 (IQR=8)	27(IQR=6)

5.2 Incidence of adverse perinatal outcomes among study participants

About 64.1% of women with HDP and 32.8% of normotensive women developed adverse perinatal outcomes in their newborns.

The incidence of still birth was higher among newborn babies delivered from women with HDP than normotensive women (11.2% versus 4.1%). The stillbirth rate among women with HDP was 112/1000 live births. Similarly, first and fifth minute low APGAR scores of the babies were higher among women with HDP than normotensive women (37.8% versus 19.5%), (12.6% versus 4.4%) respectively. Prematurity among mothers with HDP and normotensive mothers was about 39.4% and 10.6% respectively [**Table 4**]. Women with HDP were more likely to have a lower gestational age at delivery than normotensive women with median gestational age of (37 with IQR= 3 weeks versus 39 with IQR= 3) weeks, $p < 0.001$. Low birth weight babies of mothers with HDP and normotensive were 39.8% and 12.7% respectively. Women with HDP were more likely to have a low birth weight babies than normotensive women at $p < 0.001$. Median birth weight and IQR of babies born to women with HDP and normotensive were 2600g (IQR=1000g) and 3200g (IQR=740g) respectively.

Overall perinatal death in women with HDP was 21.2% and 6.2% among normotensive women. Similarly, the perinatal mortality rate among women with HDP was 212 per 1000 live births and 62 per 1000 live births among normotensive women.

Incidences of all adverse perinatal outcomes were higher among women with HDP. Incidence of all adverse perinatal outcomes between women with HDP and normotensive women has statistical significance difference between both groups [**Table 4**].

Table 4: Incidence of adverse perinatal outcomes with confidence interval among women with HDP and Normotensive women who gave birth at JMC, June, 2017 to March 2020

Perinatal outcomes	Incidence of adverse perinatal outcome with (CI) among Women with HDP(n=259)	Incidence of adverse perinatal outcome with (CI) among Normotensive women (n=518)
Still birth	11.2 (7.63 – 15.68)%	4.1 (2.53 – 6.13)%
First low minute APGAR score*	37.8 (31.53 – 44.44)%	19.5 (16.12 – 23.28)%
Fifth minute low APGAR score*	12.6 (8.61– 17.6)%	4.4 (2.79 – 6.63)%
Small for gestational age(SGA)	9.3 (6.03 – 13.47)%	2.3 (1.2– 4.01)%
Low birth weight	39.8 (33.76 – 46.01)%	12.7(9.99 – 15.92)%
Preterm birth	39.4 (33.39 – 45.61)%	10.6(8.1 – 13.6)%
NICU admission*	33.9 (27.82 – 40.43)%	15.1(12.06 – 18.54)%
Early neonatal death (ENND)*	11.3 (7.52 – 16.12)%	2.2 (1.11 – 3.93)%
Perinatal mortality(PNM)	21.2 (16.42 – 26.73)%	6.2 (4.26 – 8.61)%
Overall adverse perinatal outcome	64.1 (57.9 – 69.9)%	32.8 (28.78 – 37.05)%

*For all with the * (n= 230 for women with HDP and n=497 for normotensive women)*

5.3 Risk of adverse perinatal outcomes associated with hypertensive disorders of pregnancy

Risk estimates for adverse perinatal outcomes among women with HDP compared with normotensive women are shown in [Table 5]. In the final multivariable analysis, women with HDP were significantly at higher risk of: preterm birth with adjusted RR: 2.31 at 95% CI of (1.7, 3.14), still birth; adjusted RR: 2.02 at 95% CI of (1.21, 3.40), first minute low APGAR score; adjusted RR: 1.93 at 95% CI of (1.52, 2.46), fifth minute low APGAR score adjusted RR: 2.6 at 95% CI of (1.53, 4.42), small for gestational age; adjusted RR: 3.21 at 95% CI of (1.56, 6.58), admission to NICU adjusted RR: 1.77 at 95% CI of (1.32, 2.37), low birth weight; adjusted RR: 2.88 at 95% CI of (2.2, 3.75), and perinatal mortality; adjusted RR: 3.88 (1.97, 7.66) were significantly higher in women with hypertensive disorders of pregnancy compared to normotensive women after adjusted for maternal age, residence place, marital status, sex of the newborn, gravidity, mode of delivery, history of anemia, fetal mal-presentation at birth, ANC follow up, malaria infection, ante-partum hemorrhage, VDRL test, platelet count, onset of labour, maternal outcome and maternal HIV status.

Table 5: Bivariate and multivariate analysis on the association between HDP and adverse perinatal outcomes among women gave birth at JMC, southwest Ethiopia, June, 2017 to March, 2020

Outcomes Variable		Women with HDP(n=259) Frequency (%)	Normotensive women(n=518) Frequency (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	P-value
Still birth**	Yes	29 (11.2)	21 (4.1)	2.76(1.61, 4.75)	2.02 (1.11, 3.01)	0.008
	No	230 (88.8)	497 (95.9)	1	1	
First minute low APGAR score **	Yes	87 (37.8)	97 (19.5)	1.94(1.51, 2.47)	1.93 (1.52, 2.46)	< 0.001
	No	143 (62.2)	400 (80.5)	1	1	
Fifth minute low APGAR score**	Yes	29 (12.6)	22 (4.4)	2.85(1.67, 4.85)	2.6 (1.53, 4.42)	0.003
	No	201 (87.4)	475 (95.6)	1	1	

Small for gestational age(SGA)*	Yes	24 (9.3)	12 (2.3)	4(2.03, 7.87)	3.21(1.56, 6.58)	0.001
	No	235 (90.7)	506 (97.7)	1	1	
Low birth weight*	Yes	103 (39.8)	66 (12.7)	3.12(2.38, 4.09)	2.88 (2.2, 3.75)	< 0.001
	No	156 (60.2)	452 (87.3)	1	1	
Preterm birth*	Yes	102 (39.4)	55 (10.6)	3.71(2.77, 4.97)	2.31 (1.7, 3.14)	< 0.001
	No	157 (60.6)	463 (89.4)	1	1	
NICU admission**	Yes	78 (33.9)	75 (15.1)	2.25(1.71, 2.96)	1.77 (1.32, 2.37)	< 0.001
	No	152 (66.1)	422 (84.9)	1	1	
Early neonatal death (ENND)**	Yes	26 (11.3)	11 (2.2)	5.11(2.57,10.16)	3.7(1.89, 7.15)	< 0.001
	No	204 (88.7)	486 (97.8)	1	1	
Perinatal mortality(PNM)**	Yes	55 (21.2)	32 (6.2)	3.61(2.39, 5.46)	3.88 (1.97, 7.66)	< 0.001
	No	204 (78.8)	486 (93.8)	1	1	

**RR- Relative Risk, were adjusted for maternal age, residence place, marital status, sex of the newborn, gravidity, history of anemia, ANC follow up, malaria infection, ante-partum hemorrhage, VDRL test, platelet count, maternal outcome and maternal HIV status.*

***RR- relative risk were adjusted for all variable with * and additional for mode of delivery, fetal mal-presentation at birth, onset of labour and 1 represent control group.*

6. Discussion

This study aims to determine adverse perinatal outcomes (preterm birth, first and fifth minute low Apgar score, stillbirth, small for gestational age, low birth weight, admission to NICU, early neonatal death, and perinatal mortality) effect of hypertensive disorders of pregnancy among women who gave birth at Jimma Medical Center from June 2017 to March 2020. The findings of this study demonstrate that hypertensive disorders of pregnancy independently confer an increased risk for adverse perinatal outcomes compared to normotensive pregnant women.

The finding of this study showed that 39.4% of women with hypertensive disorders of pregnancy gave preterm babies with a confidence interval of (33.39 – 45.61) %. This finding was similar to the study conducted in part of Ethiopia, Tigray region (40.8%), and Nekemt (41.2%)(41, 58). In contrast, it was higher than a study conducted in Ghana (21.7%), India (24.6%), the US (17.4%), and São Paulo city (10.6%)(41, 44-46). The similarity in the incidence of preterm birth across the studies might be due to the similar quality of antenatal care service and the same guideline used for the management of HDP in the areas. The difference might be due to the level of ANC services quality and different management guidelines used across the countries.

Consequentially, there was a higher risk of delivering preterm babies among women with HDP than normotensive women, which was consistent with a study conducted in Nigeria, Tigray region, and US (41, 43, 47). This could be due to interventional delivery being carried out irrespective of gestational weeks. Particularly, in women with severe preeclampsia and eclampsia subtype of HDP early delivering carried out in order to prevent further maternal and perinatal adverse effect. Despite that, prematurity is the leading cause of child deaths, accounting for nearly for 18 deaths per 1000 live birth worldwide(48). Thus, preventing and managing hypertensive disorders of pregnancy should become the priority to accelerate the progress for neonatal survival.

This study revealed that the incidence of low birth weight among women with hypertensive disorders of pregnancy was 39.8% and although, there was a statistically significant difference between the mean birth weight of mothers with HDP and normotensive mothers. This finding was similar with a study conducted in Nekemte (36.2%), Tigray region which reported (37.7%);

Ethiopia (41, 58) and higher than the studies conducted in Ghana (24.7%), Zimbabwe (16%), India (22.2%) and São Paulo city (21%)(41, 44-47).

Incidence of low birth weight difference across the studies might be due to antenatal care service quality and management for HDP difference between the study areas. Similarly, there was a higher risk of delivering low birth weight among women with HDP compared to normotensive women in this study. It is consistent with studies conducted in Nigeria and Tigray region (36, 41). This could be due to the HDP effect on vascular manifestation disturbance that affects placental function, which ends up poorer perfusion and nutrient supplementation to the fetus. Thus, reducing the risk associated with low birth weight demands; increased attention to keeping the newborn warm, including skin to skincare, and assistance with the initiation of breastfeeding.

The incidences of first and fifth minute low Apgar score among babies of women with HDP were 37.8% with 95% confidence interval of (31.5 – 44.4) % and 12.6% with a confidence interval of (8.61– 17.6) % respectively. These findings were similar with a study conducted in Tigray region (40.8% for the first minute), Nigeria (11.9% for the fifth minute) and higher compared to studies conducted in Nigeria for the first minute (6.7%), Zimbabwe (8.9% for the first minute, 10% for the fifth minute) (36, 41, 47). This discrepancy might be due to differences in study design and sample size, and improved early identification of high-risk mothers.

In addition, the risk of both first and fifth minute low Apgar score among newborn babies of women with HDP was higher; these were consistent with studies conducted in Ethiopia, Zimbabwe, and Nigeria (36, 41, 47). This could be related to hypertensive disorders of pregnancy effect on vascular disturbance, oxidative stress, endothelial damage and increased preterm birth that might be vulnerable to the immaturity of muscle tone and reflex irritability. The lungs of preterm birth may be deficient in surfactant that makes the lung more difficult to ventilate. For the reason, all necessary equipment for newborn resuscitation should be ready at every delivery by anticipating the risk of birth with a low Apgar score among women with HDP, since newborn that does not start breathing on their own by 1 min after birth should receive positive pressure ventilation with room air by a self-inflating bag and mask.

Additionally, the incidence of newborn babies with small for gestational age among women with HDP was 9.3% with a 95% confidence interval of (6.03 – 13.47) %. This was slightly similar

with the study conducted in Ghana (6.3%) and lower than the study conducted in Nigeria (15.3%), South Africa (17%), Madagascar (25.7%) and Ethiopia; Tigray region (36.7%)(36, 41, 44, 48, 49). This difference might be due to the frequency of antenatal care services utilization by pregnant women may vary across the areas. For instance, the proportion of antenatal care service visits in this particular study four times and more was 54.2%, which was higher than other study reports (59).

Moreover, the risk of small for gestational age among women with HDP was higher than normotensive women. This finding was consistent with studies conducted in Ethiopia and Nigeria (36, 41). This could be related to intrauterine growth restriction due to insufficient uteroplacental blood flow and the development of ischemia in women with hypertensive disorder of pregnancy.

According to this study, almost one third (33.9%) of the newborns delivered from women with HDP were admitted to the neonatal intensive care unit with a 95% confidence interval of (27.82 – 40.43)%. This finding was roughly similar with others study reported from Ethiopia; Tigray region (28.8%), Nekemte (29.1%), and it was higher than studies reported from Iran (13%), Nigeria (14.7%), Egypt (18.8%) and India (25.5%)(23, 36, 41, 50, 52, 58). The difference across the study might possibly because of the difference in the level of medical care either in management strategies or antenatal care service quality. Additionally, the risk of newborn babies admission to NICU among women with HDP was higher as compared to babies from normotensive women; this was consistent with a study conducted in Nigeria and Tigray region (36, 41). The reason might be related to increased preterm birth, increased numbers of babies with low birth weight, and perinatal asphyxia as an adverse effect of hypertensive disorders of pregnancy.

In this study, the incidence of stillbirth among women with HDP was 11.2% with a 95% confidence interval of (7.63 – 15.68) %. This finding was consistent with the study report in Ethiopia; Mizan Tepi (9.1%), Tigray region (10%), and Mettu (10.2%)(33, 41, 60). Whereas the finding of this study was higher than the study conducted in Zimbabwe (5.4%) and Ghana (6.8%) (44, 47), but lower than the study reported from Nekemte (22.1%) and Hawassa (23.5%) Ethiopia (54, 58). This difference could be due to the difference in the quality of antenatal care service, obstetrics care service among health institutions, and study design used.

Consequentially, finding of this study was consistent with a higher relative risk for stillbirth observed among women with HDP than normotensive women, which was in line with a study conducted in Tigray region and China (41, 51). This might be related with the effect of maternal mal-perfusion and placental ischemia related to HDP.

This study also revealed that early neonatal death occurred among women with HDP was 11.3%. Moreover, the risk of early neonatal death was higher among women with HDP than normotensive women. Similarly, the incidence of perinatal mortality among women with HDP was 21.2% with 95% confidence interval of (16.42 – 26.73) %. This finding was higher than the study conducted in Ethiopia (Mettu 12.04%, and Tigray region 15%)(33, 41), Ghana (10.6%), Nigeria (7.6%), and Madagascar (8.7%)(44, 49, 61). The higher perinatal mortality discrepancy might also be attributed to the tertiary status of JMC which serves as the referral centre for the primary and secondary health facilities in the southwestern part of the country and small sample size recruited by others. This finding indicates a higher discrepancy from the sustainable development goal (SDG) target of neonatal mortality reduction to less than 12 per 1000 live births. This show that, it demands to strengthen maternal and newborn health care in order to achieve global and national SDG target plan by focusing prevention and treatment strategy of HDP and other predictors of perinatal mortality.

The present study has advantage that of including large retrospective cohorts of women with HDP, so that data were available to adjust the risk for other confounders. As limitations, variable that may have potential relationship with perinatal outcomes such as maternal nutritional status, smoking, indoor air pollution, maternal educational status, and wealth index were not included and also the data on the subtypes of HDP were not used for calculating the rate and the risk for each subtype.

7. Conclusion and recommendation

Conclusion

Higher incidence of adverse perinatal outcomes occurred among women with hypertensive disorders of pregnancy than normotensive women gave birth at Jimma Medical Center, southwest Ethiopia. HDP was associated with higher risk of preterm birth, low birth weight, low Apgar score, small for gestational age, stillbirth, admission to NICU and perinatal mortality.

Recommendation

Hypertensive disorder of pregnancy was associated with adverse perinatal outcomes. For this reason, evidences should be used by programmers to design intervention for better outcomes.

Healthcare providers should strengthen the primary prevention, secondary prevention and treatment strategy to improve better perinatal outcomes. Intervention focusing on HDP will help in order to achieve global and national sustainable development goal targeted for neonatal mortality in addition to other predictors of perinatal mortality. Hence, health care providers should strengthen prevention, early diagnosis and prompt management strategies of HDP to reduce adverse perinatal outcomes.

Low number of antenatal care visit among women with hypertensive disorder of pregnancy than normotensive women was found in this study. This is associated with an increased risk of adverse perinatal outcomes. Therefore, provision of regular, high quality antenatal care and empowering women with accurate health information help to reduce adverse perinatal outcomes.

Ethiopian Federal Minister of Health needs to set the criteria to identify pregnant women at high risk for hypertensive disorders of pregnancy during antenatal care visit that may be used for secondary prevention.

Other researchers should incorporate those variables did not studied in this study by using prospective method and estimate the risk and rate for each subtypes of HPD.

References

1. National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. "Report of the national high blood pressure education program working group on high blood pressure in pregnancy," *The American Journal of Obstetrics & Gynecology*, . 2000. ;vol. 183, no. 1, pp. S1-S22,.
2. Magee L, Von Dadelszen P, Stones W, Mathai M. *The FIGO Textbook of Pregnancy. Hypertension. An evidence-based guide to monitoring, prevention and management.* 2013. 2017.
3. Duley L. The global impact of pre-eclampsia and eclampsia. *Semin Perinatol.* 2009;33:130-7.
4. Gynecologists AACoOa. Practice bulletin No.33: Diagnosis and management of preeclampsia and eclampsia. . *Obstet Gynecol* 2002;;99:159-67.
5. Osungbade KO, Ige OK. Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. *Journal of pregnancy.* 2011;2011.
6. Asseffa NA DB. Perinatal outcomes of hypertensive disorders in pregnancy at a referral hospital, Southern Ethiopia. . *PLoS ONE* 14(2): e0213240 <https://doi.org/10.1371/journal.pone0213240>. 2019.
7. Berhe AK KG, Fekadu GA, Muche AA. Prevalence of hypertensive disorders of pregnancy in Ethiopia: a systemic review and meta-analysis. *BMC Pregnancy Childbirth.* 2018;18(1):34.
8. Mersha AG, Abegaz TM, Seid MA. Maternal and perinatal outcomes of hypertensive disorders of pregnancy in Ethiopia: systematic review and meta-analysis. *BMC Pregnancy and Childbirth.* 2019;19(1):458.
9. Wolde Z SH, Woldie M. . Hypertensive disorders of pregnancy in Jimma university specialized hospital. . *Ethiop J Health Sci.* 2011;21(3):7.
10. Berhan Y. perinatal mortality trends in Ethiopia *Ethiopian Journal of Health Development.* 2014.
11. Matthew B EH, Michelle H, Reginald J, David F, Carol H, Reynold GP, Hedwige P and Bradley P. . Hypertensive disorders in pregnancy and maternal and neonatal outcomes in Haiti: the importance of surveillance and data collection. *BMC Pregnancy and Childbirth.* 2019;(2019) 19:208.
12. Estimation UNI-aGfCM, Hug L, Sharrow D, Zhong K, You D, Unicef, et al. *Levels & Trends in Child Mortality: Report 2018, Estimates Developed by the: United Nations Children's Fund;* 2018.
13. Duley L. The global impact of pre-eclampsia and eclampsia.*Semin Perinatol.* 2009;2009;33:130-7.
14. Kampruan R, Sukonpan K, Wasinghon P. Pregnancy outcomes amongst normotensive and severe preeclampsia with or without underlying chronic hypertension pregnancy. *Thai Journal of Obstetrics and Gynaecology.* 2016:202-8.
15. Vogel JP SJ, Mori R, et al. . Maternal complications and perinatal mortality: findings of the World Health Organization multicountry survey on maternal and newborn health. *BJOG.* 2014 March;; 121(Suppl. 1):76e88.
16. Solomon CG, Seely EW. Hypertension in pregnancy. *Endocrinology and Metabolism Clinics.* 2006;35(1):157-71.

17. Krotz S, Fajardo J, Ghandi S, Patel A, Keith LG. Hypertensive disease in twin pregnancies: a review. *Twin Research and Human Genetics*. 2002;5(1):8-14.
18. von Dadelszen P, Magee LA. Preventing deaths due to the hypertensive disorders of pregnancy. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2016;36:83-102.
19. Souza JP, Gülmezoglu AM, Carroli G, Lumbiganon P, Qureshi Z, Group WR. The world health organization multicountry survey on maternal and newborn health: study protocol. *BMC health services research*. 2011;11(1):286.
20. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors and potential for progress towards 2030. *Lancet*. 2016;387(10018):587-603.
21. Organization(WHO). WH. Neonatal and perinatal mortality: country, regional and global estimates. . 2006.
22. Yadav S, Saxena U, Yadav R, Gupta S. Hypertensive disorders of pregnancy and maternal and foetal outcome: a case controlled study. *Journal of the Indian Medical Association*. 1997;95(10):548-51.
23. Fatemeh T, Marziyeh G, Nayereh G, Anahita G, Samira T. Maternal and perinatal outcome in nulliparous women complicated with pregnancy hypertension. *JPMMA The Journal of the Pakistan Medical Association*. 2010;60(9):707.
24. Abalos E CC, Carroli G, Qureshi Z, Widmer M, Vogel JP, Souza JP. on behalf of the WHO Multicountry Survey on Maternal and Newborn Health Research Network. Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. *BJOG*. 2014;121(Suppl. 1):14–24.
25. Roberts JM PG, Cutler J, Lindheimer M. Summary of the NHLBI Working Group on research on hypertension during pregnancy. *Hypertension*. 2003;41(3 I):437–45.
26. Nusrat N AM, Munir A. . Hypertensive disorders of pregnancy; frequency, maternal and perinatal out comes. *J Pakistan Army Med Corps*. 2010;26(1):4.
27. Yücesoy G OS, Bodur H, et al. ;: . Maternal and perinatal outcome in pregnancies complicated with hypertensive disorder of pregnancy: a seven year experience of a tertiary care center. *Arch Gynecol Obstet*. 2005;273(1):6.
28. Ngoc N MM, Abdel-Aleem H, Carroli G, Purwar M, Zavaleta N, et al. . Causes of stillbirths and early neonatal deaths: data from 7993 pregnancies in six developing countries. *Bull World Health Organ*. 2006;2006;84(9):699-705.
29. Hodgins S. Pre-eclampsia as underlying cause for perinatal deaths: time for action. *Glob Health Sci Pract* 2015;2015; 3(4):525-527. .
30. Selamawit D, Sisay T. Maternal and Perinatal outcomes of pregnancies complicated by preeclampsia/eclampsia at zewditu memorial hospital. Addis Ababa Aniversity school of graduate studies faculty of Medicine. 2015.
31. Vata PK, Chauhan NM, Nallathambi A, Hussein F. Assessment of prevalence of preeclampsia from Dilla region of Ethiopia. *BMC research notes*. 2015;8(1):816.
32. Gudu W, Bekele D. A prospective review of eclampsia at a regional hospital, Eastern Ethiopia: incidence, clinical correlates, management and pregnancy outcome. *Ethiop Med J*. 2018;56:125-32.

33. Seyom E, Abera M, Tesfaye M, Fentahun N. Maternal and fetal outcome of pregnancy related hypertension in Mettu Karl Referral Hospital, Ethiopia. *Journal of ovarian research*. 2015;8(1):10.
34. Zupan J. Perinatal mortality in developing countries. *N Engl J Med*. 2005;352(20):2047-8.
35. F. Gary Cunningham KJL, Steven L. Bloom, John C. Hauth, Larry C. Gilstrap III, Katharine D. Wenstrom (eds), Williams obstetrics, . Hypertensive disorders in pregnancy:. 2005:761-809.
36. Olusanya BO, Solanke OA. Perinatal outcomes associated with maternal hypertensive disorders of pregnancy in a developing country. *Hypertension in pregnancy*. 2012;31(1):120-30.
37. Halloran D, McClure E, Chakraborty H, Chomba E, Wright L, Carlo W. Birth asphyxia survivors in a developing country. *Journal of Perinatology*. 2009;29(3):243-9.
38. Ahearne CE, Boylan GB, Murray DM. Short and long term prognosis in perinatal asphyxia: An update. *World journal of clinical pediatrics*. 2016;5(1):67.
39. Melese MF, Badi MB, Aynalem GL. Perinatal outcomes of severe preeclampsia/eclampsia and associated factors among mothers admitted in Amhara Region referral hospitals, North West Ethiopia, 2018. *BMC research notes*. 2019;12(1):1-6.
40. Fawole AO ea. Determinants of perinatal mortality in Nigeria. . *Int J Gynaecol Obstet*; . 2011 ;114:37-42.
41. Berhe AK, Ilesanmi AO, Aimakhu CO, Mulugeta A. Effect of pregnancy induced hypertension on adverse perinatal outcomes in Tigray regional state, Ethiopia: a prospective cohort study. *BMC Pregnancy and Childbirth*. 2019;20(1):7.
42. Hehir MP, Breathnach FM, McAuliffe FM, Geary MP, Daly S, Higgins J, et al. Gestational hypertensive disease in twin pregnancy: Influence on outcomes in a large national prospective cohort. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2016;56(5):466-70.
43. Luo Z-C, Simonet F, An N, Bao F-Y, Audibert F, Fraser WD. Effect on neonatal outcomes in gestational hypertension in twin compared with singleton pregnancies. *Obstetrics & Gynecology*. 2006;108(5):1138-44.
44. Adu-Bonsaffoh K, Ntumy MY, Obed SA, Seffah JD. Perinatal outcomes of hypertensive disorders in pregnancy at a tertiary hospital in Ghana. *BMC pregnancy and childbirth*. 2017;17(1):388.
45. Badal S, Singh LR. Maternal and perinatal outcome in severe pre-eclampsia and eclampsia. *World J Pharm Med Res*. 2017;3(3):193-5.
46. Chaim SRP, Oliveira SMJVd, Kimura AF. Pregnancy-induced hypertension and the neonatal outcome. *Acta Paulista de Enfermagem*. 2008;21(1):53-8.
47. Muti M, Tshimanga M, Notion GT, Bangure D, Chonzi P. Prevalence of pregnancy induced hypertension and pregnancy outcomes among women seeking maternity services in Harare, Zimbabwe. *BMC cardiovascular disorders*. 2015;15(1):111.
48. Poonyane T. Impact of severe preeclampsia on maternal and fetal outcomes in preterm deliveries 2015.
49. Randriamahavonjy R, Tsifiregna RL, Andrianirina ZZ, Andrianampanalinarivo HR. Materno-fetal outcomes in pre eclampsia in a rural hospital of Antananarivo Madagascar. *Int J Res Med Sci*. 2018;6(4):1064-7.
50. Thakur A, Dangal G. Fetomaternal Outcome in Women with Pregnancy Induced Hypertension versus Normotensive Pregnancy. *Journal of Nepal Health Research Council*. 2019;17(4):495-500.

51. Xiong T, Mu Y, Liang J, Zhu J, Li X, Li J, et al. Hypertensive disorders in pregnancy and stillbirth rates: a facility-based study in China. *Bulletin of the World Health Organization*. 2018;96(8):531.
52. Mahran A, Fares H, Elkhateeb R, Ibrahim M, Bahaa H, Sanad A, et al. Risk factors and outcome of patients with eclampsia at a tertiary hospital in Egypt. *BMC pregnancy and childbirth*. 2017;17(1):435.
53. Yucesoy G OS, Bodur H, Tan T, Caliřkan E, Vural B, Corakçi A. Maternal and perinatal outcome in pregnancies complicated with hypertensive disorder of pregnancy: a seven year experience of a tertiary care center. . *Arch Gynecol Obstet* 2005;;273(1):43-9.
54. Endeshaw G YB. Perinatal outcome in women with hypertensive disorders of pregnancy: a retrospective cohort study. . *International Scholarly Research Notices*. 2015;;2015:1-8.
55. Liyew EF, Yalew AW, Afework MF, Essén B. Distant and proximate factors associated with maternal near-miss: a nested case-control study in selected public hospitals of Addis Ababa, Ethiopia. *BMC women's health*. 2018;18(1):28.
56. Omer SA, Idress HE, Adam I, Abdelrahim M, Noureldein AN, Abdelrazig AM, et al. Placental malaria and its effect on pregnancy outcomes in Sudanese women from Blue Nile State. *Malaria journal*. 2017;16(1):374.
57. Ticconi C, Mapfumo M, Dorrucchi M, Naha N, Tarira E, Pietropolli A, et al. Effect of maternal HIV and malaria infection on pregnancy and perinatal outcome in Zimbabwe. *Journal of acquired immune deficiency syndromes (1999)*. 2003;34(3):289-94.
58. Hinkosa L, Tamene A, Gebeyehu N. Risk factors associated with hypertensive disorders in pregnancy in Nekemte referral hospital, from July 2015 to June 2017, Ethiopia: case-control study. *BMC Pregnancy and Childbirth*. 2020;20(1):16.
59. Muchie KF. Quality of antenatal care services and completion of four or more antenatal care visits in Ethiopia: a finding based on a demographic and health survey. *BMC pregnancy and childbirth*. 2017;17(1):300.
60. GTA R. Prevalence of Pregnancy Induced Hypertension and Its Bad Birth Outcome among Women Attending Delivery Service. *J Preg Child Health*. 2017;4(335):1-4.
61. George IO, Jeremiah I. Perinatal outcome of babies delivered to eclamptic mothers: a prospective study from a Nigerian tertiary hospital. *International journal of biomedical science: IJBS*. 2009;5(4):390.

Appendix

Formant to extract data to assess effect of hypertensive disorders of pregnancy on adverse perinatal outcomes among women gave birth at JMC, southwest Ethiopia, 2016-2019

Code _____ Card number _____

Date of delivery _____

No	Question	Response	Skip
1.	Place of residence	1. Urban 2. Rural	
2.	Age of mother	_____ (in years)	
3.	Marital status	1. Married 2. Single	
4.	Gravidity	1. Primigravida 2. Multipara (I–IV) 3. Grand multipara (V+)	
5.	How many children does the mother have including this birth (Parity)	_____ in number	
6.	Did the mother had hypertensive disorders of pregnancy	1. No 2. Yes	If No skip to Q8
7.	What a subtype of hypertensive disorders she had?	1. chronic hypertension 2. superimposed Preeclampsia 3. gestational hypertension 4. preeclampsia 5. eclampsia	
8.	Maternal HIV status	1. Reactive 2. Non-reactive	
9.	VDRL test	1. Negative	

		2. Positive	
10.	Malaria diagnosis in current pregnancy	1. No 2. Yes	
11.	She had antepartum hemorrhage in current pregnancy?	1. No 2. Yes	
12.	Hemoglobin (gm/dL)	_____ gm/dL	
13.	Platelet count	1. $\geq 100,000/\text{mm}^3$ 2. $< 100,000/\text{mm}^3$	
14.	History of ANC use	1. Yes 2. No	If answer is 2, Skip to Q15
15.	If yes, number of antenatal care visits	_____ (in numbers)	
16.	Maternal nutritional status(first trimester BMI at <16 weeks)	1. weight in kg _____ 2. height in cm _____	
17.	On set of labour	1. Induced 2. Spontaneous 3. Direct CS(cesarean Section)	
18.	Fetal mal-presentation at birth	1. No(if occiput anterior(vertex)) 2. Yes(if any of breech or vertex occiput posterior or transverse lie	
19.	Mode of delivery	1. Vaginal 2. Cesarean Section	
20.	Number of newborn	1. Singleton 2. Multiple	
21.	Sex of the newborn	1. Male 2. Female	If twin more than one is

			possible
22.	Gestational age at delivery in complete weeks	_____ in weeks	
23.	Birth outcome of stillbirth	1. No 2. Yes	If yes skip to Q-30
24.	1 st minute APGAR score < 7 (only for live birth)	1. No 2. Yes	
25.	5 th minute APGAR score < 7 (only for live birth)	1. No 2. Yes	
26.	Birth weight in grams	_____ g	
27.	Newborn is small for gestational age at birth(<10 percentile)	1. No 2. Yes	
28.	Admission to NICU	1. No 2. Yes	
29.	Had neonatal sepsis?	1. No 2. Yes	
30.	Birth outcome of early neonatal death	1. No 2. Yes	
31.	Perinatal mortality(newborn status still 7day after birth)	1. No 2. Yes	
32.	Maternal outcome	1. Alive on discharge 2. Died	

If admitted to NICU, date of neonate admission _____
and Diagnosis of the neonate _____

Name of data collector and signature: _____

Declaration

I, the undersigned, Master of Public Health in Epidemiology student declare that this research is my original work in partial fulfillment of the requirement for the degree of Master of Public Health in Epidemiology.

Name: **Debela Dereje Jaleta**

Signature: _____

Place of submission: Department of Epidemiology, Faculty of Public Health, Institute of Health, Jimma University.

Date of Submission: _____

This proposal work has been submitted for examination with our approval as university advisor(s).

Approval of advisors

Advisors name	Signature
1. Mulusew Gerbaba (PhD, Assistant professor)	_____
2. Tadesse Gebremedhin (BSc, MPH/E)	_____