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Perinatal outcomes of Pregnancies Complicated by Hypertensive disorders of pregnancy In Late Preterm in Three Teaching Hospitals in Addis Ababa, Ethiopia

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ABBREVIATIONS AND ACRONYMS

AAU-Addis Ababa University

ANC-Antenatal care

AOR-Adjusted odd ratio

BMI- Body mass index

C/S - Cesarean section

CIC - Confidence Interval

DC- Data Collector

EDHS -Ethiopian Demographic Health Survey

FMOH-Federal Ministry of Health

GA- Gestational Age

GMH- Gandhi memorial hospital

HDP- Hypertensive Disorders of Pregnancy

IRB- Institutional Review Board

IUGR- Intra-Uterine Growth Restriction

LMIC- low and middle income countries

LNMP- Last Normal Menstrual Period

NGO-Nongovernmental Organization

NICU-Neonatal Intensive Care Unit

PI- principal investigator

SPSS - Statistical Package for Social Science

SSA-Sub-Saharan Africa

TASH-Tikur Anbesa Specialized Hospital

WHO - World Health Organization

ZMH- Zewditu memorial hospital

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Abstract

Background: Hypertensive disorders of pregnancy (HDP) are multisystem diseases known to increase the risk of perinatal mortality worldwide, with a significant proportion of these deaths occurring in low income countries. However, little is known about the obstetric and treatment predictors of perinatal mortality in women with HDP. Until now, only few studies focused on the management of women with hypertensive disorders between 34 0/7 and 36 6/7 weeks of gestational age in Ethiopia.

General objective: To investigate the perinatal outcomes of late preterm pregnancies complicated by hypertensive disorders in low resource settings

Methods: Hospital based cross sectional descriptive study was conducted on 274 newborns delivered from December 15, 2020 to June 15, 2021 at the three teaching hospitals. Structured and pretested questionnaire were used to collect socio-demographic data and medical records were reviewed. Neonatal status was checked every other day through phone call till 7 days after delivery date. Descriptive statistics were used to describe parameters collected from the files. Bivariate and multiple logistic regressions were done to determine factors associated with unfavorable perinatal outcome. A P-value of less than 0.05 was considered statistically significant.

Result*:* Among 10,129 deliveries during the study period, 952 (9.4%) were preterm. Of these preterm deliveries 680 were late preterm and 274 neonates fulfill the inclusion criteria and analyzed. About 83(30.3%) neonates were delivered 34+0-34+6 weeks, 45 (16.4%) at 35+0-35+6 weeks and the majority 146 (53.3%) at 36+0-36+6 weeks. Cesarean section was the most common mode of delivery 191 (69.7%) followed by SVD, 74 (27%) and 6 (2.2%) by AVD. About 173 (63.1%) newborns were LBW (1500-2499 grams), 76 (27.8%) were NBW and the remaining 25(9.1%) were VLBW. Fifty eight (21.5%) of neonates need resuscitations at delivery. Hundred forty eight (55.2%) of these neonates were referred to NICU and 102 (68.9%) of them required NICU admission. On day seven neonatal assessment the cumulative survival was 93.7%. The survival rate of late preterm neonates is 87.7%, 90.9% and 97.9% at 34, 35, and 36 weeks respectively. The perinatal mortality rate in late preterm pregnancy in hypertensive disorders of pregnancy in this study was 76.6/1000 live births. Over half, 9/17 (52.9%) of neonatal deaths occurs within the first 48 hours while majority (76.5%) of neonatal deaths occurs

with in the first 3 days. In this study one fourth (25.9%) of women had at list one maternal complication. Fetal weight at birth, gestational age during delivery and Apgar score at delivery found to be independent predictors of perinatal survival.

Conclusion and Recommendation: During the study period the rate of late preterm birth was 71.4%. This study shows preeclampsia as the most common cause for late preterm birth (84.7%) from hypertensive disorders of pregnancy. Late preterm neonates are at higher risk for neonatal morbidities and mortality contrary to the belief that they are nearly mature. Neonatal birth weight and Apgar score during delivery were the important predictors for the neonatal survival. Critical attention should be paid on the first 72 hours of newborn life to reduce factors contributing to high neonatal loss at this particular time.

Introduction

1.1 Background

Hypertensive disorder of pregnancy is one of the major causes of maternal morbidity and mortality leading to 10–15% of maternal deaths especially in the developing areas of the world [**1**]. It occurs in around 12–22% of pregnancies depending on the population and the definitions used [**2**]. Five classes of hypertensive disorders were identified according to the latest classification system described by the National High Blood Pressure Education Working Group (2000) including preeclampsia, eclampsia, transient hypertension of pregnancy, chronic hypertension and preeclampsia superimposed on chronic hypertension [**3**]. Differentiating between these groups is mandatory regarding the determination of best management strategies.

Approximately 30% of hypertensive disorders of pregnancy were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension/ preeclampsia [**4**].

The majority of hypertensive disorders of pregnancy (gestational hypertension [GH], preeclampsia [PE]) present at term or late preterm, only 10% occur before 32 weeks and late preterm accounts about 22.5% of HDP. Hypertension in pregnancy is associated with severe complications such as eclampsia, placental abruption, HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome, preterm delivery, or even fetal or maternal death. The probability of adverse perinatal outcome increases with lower gestational age.[**5**]

The prevalence of hypertensive disorders of pregnancy is 5.3% in Addis Ababa Tikur Anbesa specialized hospital. 85.2% of cases are pregnancy induced hypertension (PIH), the majority (78.2%) are severe preeclampsia and eclampsia; the remaining 14.8% had pregnancy aggravated hypertension (PAH) or chronic hypertension. The preterm delivery rate is 48.6% for cases of HDP, intervention rate is high with 44.3% induction of labor and 44.3% caesarean section, Perinatal mortality rate(PNMR), case fatality rate (CFR), and intrauterine growth restriction rate(IUGR) are 300/1000 deliveries, 27/1000 deliveries and 41.6% respectively in mothers with hypertensive disorders of pregnancy. [**6**]

The only causal treatment for hypertensive disorders of pregnancy is to deliver the baby.[**7**] There is a general consensus that in pregnancies complicated by early preeclampsia (eg, 32 weeks' gestational age), temporizing management with close monitoring of the mother and fetus is justified, and prolongation of pregnancy can be achieved without irreversible maternal morbidity and with improved neonatal outcome.[**8**] Unlike preterm pregnancies with hypertensive disorders of pregnancy, in women with mild GH or PE at term, delivery of the baby resulted in a decrease of progression to severe disease or complications as well as a decreased number of cesarean sections compared with temporizing management.[**9**]

Until now, only a few studies have focused on the management of women with hypertensive disorders between 34 and 37 weeks of gestational age. The National Institute for Health and Clinical Excellence (NICE) guideline for hypertensive disorders during pregnancy refers in the 2010 consensus statement to the issue of mild or moderate preeclampsia between 34 and 36 weeks of gestation in terms of a gray zone at which the optimal timing of birth is not clear.[**10**] Babies born late preterm (eg, 34 to 36 weeks + 6 days' gestational age) account for more than 70% of the preterm deliveries (37 weeks). There are reports that these late preterm children have significantly more morbidity than babies born at term.[**11-17**] However, it is not known whether this finding also applies to infants born from mothers with a hypertensive disorder because in most studies these women were excluded from analysis. This also makes it difficult to determine the optimal obstetric management for these patients.

1.2. Statement of the problem

Preterm birth rates continue to rise due to demographic changes, infertility treatments, increases in maternal age, multiple gestations, increasing obesity rates, and maternal comorbid conditions. Practicing in a setting where survival of preterm delivery is difficult to predict is usually challenging particularly in counseling patients about the outcome of the preterm neonate.

Several studies have reported an increased incidence of late preterm birth among women with GH or preeclampsia and hypertensive disorders of pregnancy is recognized as a significant contributor to iatrogenic preterm birth and associated neonatal morbidity [**18, 19**]. Numerous studies have shown increased rates of morbidity and mortality in late preterm infants of women with GH or preeclampsia, including more neonatal intensive care unit (NICU) admissions, hypoglycemia, need for respiratory support, and rehospitalization.[**20**] Optimising the timing of delivery involves striking a balance between the benefits and risks of pregnancy prolongation. Birth of the baby is always in the best interest of the woman. For her pregnancy prolongation has no direct benefit, but for the baby, the benefits may be large at gestational ages remote from term. This can be a heart-wrenching decision for families and their care providers.

The overall aim of the current study is to know the perinatal outcomes from pregnancies complicated by hypertensive disorders of pregnancy in late preterm and determinants for neonatal survival in our set up so as to generate local data to direct management protocol modifications and policy decisions.

1.3 Literature review

Hypertensive disorder of pregnancy is the commonest medical complication of pregnancy. [**21**] The incidence varies in different populations and is also affected by the definition used. Generally the problem is more common in the developing countries than it is in the developed countries. The complications are also more common and worse in the underdeveloped countries; poor pregnancy outcomes are also associated with lack of ANC follow up which is associated with delayed recognition and intervention in the affected mothers [**21-23**].

Hypertensive disorders in pregnancy were risk factors for preterm birth in almost a quarter of the patients in the reports of study from authors in Nigeria [**24**] Nepal [**25**] and Thailand [**26**]. Onyiriuka and Okolo [**27**] carried out a study on neonatal morbidity pattern in infants born in Benin City to Nigerian mothers with hypertensive disorders in pregnancy. They reported that the rate of preterm delivery was significantly higher in the hypertensive mothers compared to their normotensive counterparts. Hypertension in pregnancy is believed to predispose to acute or chronic utero-placental insufficiency resulting in antepartum and intrapartum fetal hypoxia with associated adverse outcomes of which preterm delivery is one [**28**]

An estimated 5.9 million children under 5 years of age died in 2015, with a global under-five mortality rate of 42.5 per 1000 live births. Of those deaths, 45% were newborns, with a neonatal mortality rate of 19 per 1000 live births. Levels of child mortality are highest in subSaharan Africa, where 1 child out of 12 dies before their fifth birthday, followed by South Asia where 1 in 19 dies before age five.[**29**]

Late-preterm infants, defined by birth at 340⁄7 through 366⁄7 weeks' gestation, are less physiologically and metabolically mature than term infants. Studies show that late-preterm infants were 7 times more likely to have morbidity at birth than term infants (22.2% vs. 3.0%). Morbidity rates approximately doubled for each gestational week earlier than 38 weeks. Compared with infants born at 40 weeks' gestation, those born at 34 weeks' gestation had a 20-fold increase in risk, and infants born at 35 and 36 weeks' gestation had, respectively, 10 times and 5 times the morbidity risk. These infants are at higher risk than are term infants of developing medical complications that result in higher rates of mortality and morbidity during

the birth hospitalization. In addition, late-preterm infants have higher rates of hospital readmission during the neonatal period than do term infants. Both late-preterm birth and maternal medical disorders are independent risk factors for newborn morbidity and, when combined, greatly increase the risk of newborn morbidity compared with infants escaping exposure to either of these risks.[**30**]

Factors that influence the success in the management of prematurity include level of prenatal care, gestational age at birth, sex, availability of resources and adequate and well trained personnel [**31**]. The evolution of neonatal intensive care is one of the recent advances that ensure survival of the preterm neonate but sadly this is not readily available in most developing countries [**32**]. This is not surprising as neonatal intensive care is expensive because of the cost of sophisticated equipment, need for constant power supply, constant use of laboratory facilities and high staff to patient ratio [**33**].

The clinical course of severe preeclampsia results in progressive deterioration of both maternal and fetal conditions. Traditional management of severe preeclampsia has focused on maternal safety, with expedited delivery. Because these pregnancies are associated with high rates of maternal morbidity and mortality and with potential risks for the fetus, it is generally agreed that such patients should be delivered if the disease develops at >34 weeks of gestation [**34**].

Gestational age is the most important predictor of neonatal survival in preterm neonates Every one week increment of GA, neonatal survival increases by 2.5 folds (COR-2.45, 95% CI 2.04-2.9, P<0.01 [**35**]

Among the women who developed preeclampsia between 34 and 37 weeks, the results of the observational studies had a wide range of findings: the progression to severe forms of the disease was as high as 51% and 35% [**5**, **36**] in 2 of the considered studies, and as low as 5% in the other. [**37**] The association with the risk of complications, even though significantly lower when compared with the women with early-onset preeclampsia, was only observed in one of the studies evaluated. [**38**] Among the clinical trials, one of them, with 703 women, showed that the option of expectant management added 5 to 10 days to the gestation, with no significant increase in maternal complications, such as HELLP syndrome, thromboembolic events, placental abruption, eclampsia and maternal death. [**39**] Another study involving 169 women found a significant difference in the progression to other severe forms of the disease among women under expectant management (41% versus 3%). [**40**]

Considering the perinatal outcomes, one of the observational studies identified significant weight gain at birth in the comparison between expectant management and immediate delivery, as well as a lower need for ICU admission and decreased risk of perinatal death.[**5**] One of the clinical trials indicated similar perinatal outcomes in the two groups, [**40**] while another showed an increased risk of significant neonatal complications for newborns who were delivered immediately compared with cases in which expectant management was adopted. [**39**]

Studies in Ethiopia show that the incidence of hypertensive disorders of pregnancy is around 5% of which majority were due to severe preeclampsia; according to one study eclampsia complicates 0.7% of the pregnancies. These disorders are major causes of maternal and perinatal morbidities and mortalities [**3, 4, 22**]. Even though there are few studies exploring HDP in Ethiopia, there has not been a single study in the study area. Based on the limited data available, HDP has been found to be common and has been associated with poor perinatal outcomes. Therefore, this study will be conducted to explore the pattern and perinatal outcomes of pregnancies complicated by hypertensive disorders and survival status of these neonates in our set up.

1.4 Significance of the Study

The result of this study has information on the perinatal outcomes from pregnancies complicated by hypertensive disorders of pregnancy in late preterm which will be a vital input for improving maternal and neonatal care. The finding of this study provides important insight for stakeholders. This in turn will play a role to improve the overall obstetrics care especially developing hypertension treatment guidelines, local protocol and timing of delivery. In addition, as there is scarcity of published data on this topic the information generated from the study will be an eye opener for further study and as a source of information for other researchers to conduct similar study in different areas of Ethiopia.

3. Objective

3.1 General objective

To assess the perinatal outcome of late preterm pregnancy complicated by hypertensive disorders

3.2 Specific objectives

1. Identity classes of HDP resulting in late preterm delivery
2. To describe the rates of late preterm birth as a proportion of preterm births in the study sites.
3. Describe the perinatal outcome of late preterm pregnancies with hypertensive disorder
4. Describe the survival trends of late preterm babies born to hypertensive women

4. Methods and materials

4.1. Study area

The study was conducted in Addis Ababa, the capital city of Ethiopia. Specifically, it was carried out in three teaching hospitals. Namely, Tikur Anbesa specialized hospital, Zewditu memorial hospital and Gandhi memorial hospital. Zewditu memorial hospital and Gandhi memorial hospitals are teaching hospitals affiliated with Addis Ababa University however managed by Addis Ababa city Health administration bureau. The hospitals offer antenatal, delivery and post natal services to pregnant women coming from all over Ethiopia following the referral system set out by Federal Ministry of Health.

4.2. Study design

Hospital based cross sectional descriptive study

4.3. Source Population

Women with late preterm pregnancy at TASH, ZMH and GMH

4.4. Study population

Women with hypertensive disorders of pregnancy that give birth between 34 – 36weeks + 6days of gestation in study hospitals during the study period

4.5. Inclusion and Exclusion Criteria

4.5.1 Inclusion criteria

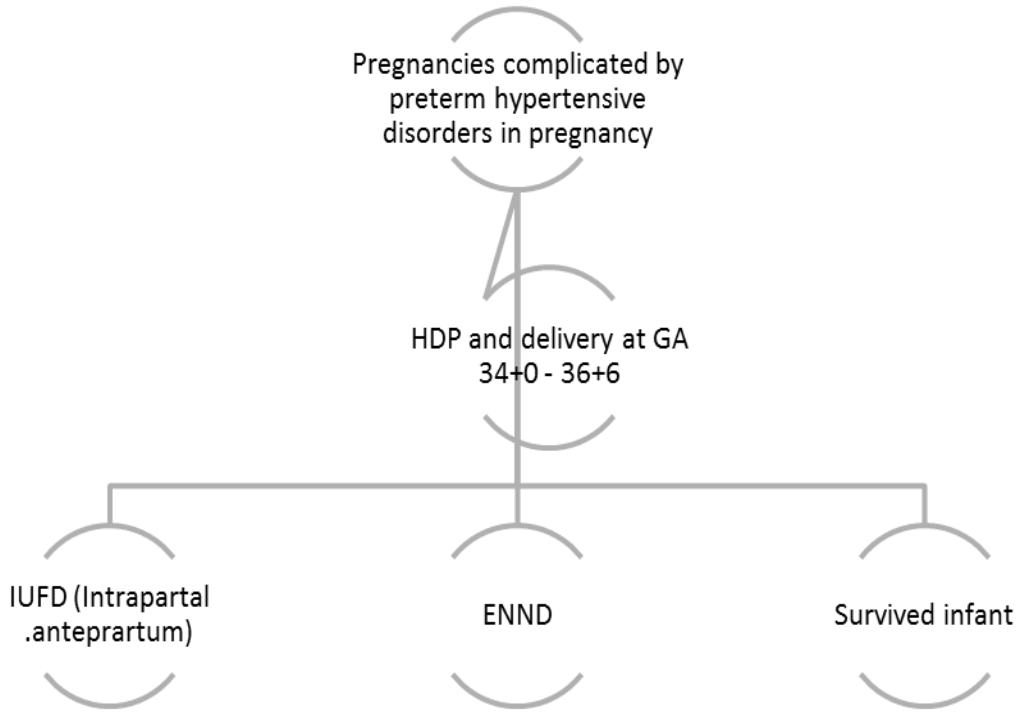
All singleton deliveries at GA of 34 weeks to 36 weeks+ 6 days diagnosed with hypertensive disorder of pregnancy.

4.5.2 Exclusion criteria

Neonates with lethal congenital anomalies, births for which gestation age could not be determined, and neonates born from mothers with other medical conditions (e.g diabetes, cardiac, renal) were excluded from the study to avoid their potential confounding effect on the unfavorable perinatal outcomes associated with HDP.

4.6. Sample Size Determination

Sampling frame



The study was done on 274 women who were diagnosed with hypertensive disorder of pregnancy and fulfill the inclusion criteria over a period of 6 months, from December 15/2020 G.C to June 15/2021 G.C at three teaching hospitals in Addis Ababa

4.7. Sampling technique

All pregnancies complicated by hypertensive disorders and delivered at 34 to 36 weeks +6 days of GA were taken sequentially over six months and the newborns were followed for 7 days.

4.8. Data Collection methods

4.8.1. Data Collection Instruments

Data on socio-economic and demographic variables of mothers were collected by interview method using structured pretested questionnaires. Both maternal and neonatal medical records were reviewed. Neonatal status was checked every other day through phone call till 7 days from delivery date. Data collection tools were prepared in English.

4.8.2. Data Collection Procedures

Data was collected by four obstetrics and gynecology residents and two pediatrics residents and they were trained by principal investigators for one day and all were conducted interview questionnaires. The training was given in English and was about selection of study participants, interviewing technique and filling questionnaires, and how to approach respondents. Data was collected from post-partum women with hypertensive disorders of pregnancy. Selected mother were informed by the data collectors as she is selected as study participant. After selected study participant agreed, informed verbal consent was taken and data was collected.

4.9. Study Variables

4.9.1. Dependent variables

Perinatal outcome in late preterm deliveries

4.9.2. Independent variables

- ✓ Age
- ✓ Educational level
- ✓ Occupation
- ✓ Parity
- ✓ Marital status
- ✓ ANC
- ✓ Use of drugs i.e Aspirin, antihypertensive
- ✓ Mode of delivery

- ✓ History of HDP
- ✓ History of chronic hypertension
- ✓ BMI
- ✓ Use of antenatal corticosteroids
- ✓ Gestational age
- ✓ Birth Weight
- ✓ 1^{st} and 5^{th} minutes Apgar score
- ✓ Neonatal resuscitation
- ✓ NICU admission
- ✓ Obstetric complications

3.10. Operational Definitions

Admission to ward - A minimum of 24 hours stay at high risk obstetrics ward for conservative managements before delivery.

Placental abruption – antepartum hemorrhage which is caused by separation of normal implanted placenta before delivery and diagnosed by first physician.

4.11. Data quality and management

Data quality was assured through carefully designed of structured questionnaire and data collection procedure. One day training was given for data collectors regarding data collection method, ethical issue and purpose of the study and the training was given by principal investigator (PI). For the clarification of data collection instruments and familiarization of data collectors with instruments as well as to estimate the time required for one study participant, pretest was done on five women with hypertensive disorders of pregnancy at Zewditu memorial hospital. Overall supervision was done by principal investigator and data double entry was used in Epi data to check discrepancies.

4.12. Data Entry and Analysis

After completeness was checked, data were coded and entered into EpiData version 3.1 statistical software and exported to SPSS version 25 statistical software for analysis. We used descriptive statistics to describe parameters collected from the files. The survivals of neonate were assessed with Kaplan Mayer curve. Bivariate and multiple logistic regressions were done to determine factors associated with unfavorable perinatal outcome. Variables which did not show statistical significance in the bivariate analysis were excluded from the multivariate analysis. P-value less than 0.05 was considered statistically significant.

4.13. Ethical Considerations

Before the beginning of the data collection, this study was reviewed and approved by Addis Ababa University College of health science, Department of Obstetrics and Gynecology, research and publication committee. Official letter was provided to the study hospital administration. In order to keep confidentiality of any information provided by study subjects, the data collection procedure was anonymous. Participation was on voluntary basis after verbal consent and they could withdraw from the study at any time and the level of care provided won't be compromised.

4.14. Result dissemination plan

The result of this study will be presented for Addis Ababa University, College of health science, department of Obstetrics and Gynecology, and for other concerned bodies working on maternal and child health quality care including FMOH, Medias and NGOs working in this area. All possible effort will be made to publish the findings on peer reviewed journal.

5. Result

5.1 Socio demographic variable

We have found 274 participants; all of them were successfully interviewed making the response rate of 100%. Majority (90.5%) of the participants were in the age group of 20 to 34 years. The minimum age among the participants was 19 and the maximum was 40 with the mean age being 28 years, SD (4.89). A vast majority of respondents were from Addis Ababa (91.6%), married (95.6%), and 46.7% were private employer. About 34.7% of respondents attended higher education and 6.2% had no formal education. About 61.3% of participants were orthodox by religion and half (50.0%) of participants were Amhara in ethnicity. (Table 1)

TABLE 1. SOCIO DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANT WITH HYPERTENSIVE DISORDER IN PREGNANCY IN ADDIS ABABA UNIVERSITY TEACHING HOSPITAL, 2021 (N=274)

Variable	Frequency(N=274)	Percent (100%)
Place of delivery		
GMH	162	59.1
TASH	74	27.0
ZMH	38	13.9
Total	274	100
Residence		
Addis Ababa	251	91.6
Out of Addis Ababa	23	8.4
Age in years		
≤ 20	12	4.4
21-24	52	19.0
25-29	116	42.3
30-34	70	25.5
≥ 35	24	8.8
Marital status		
Married	262	95.6
Other (single, divorced, widowed)	12	4.4
Occupation		
House wife	94	34.3
Government employee	37	13.5
Private employee	128	46.7
Daily labor	15	5.5
Monthly family income (Birr)		

≤ 1650	7	2.6
1651-3200	67	24.5
3201-5250	143	52.2
5251-7800	36	13.1
≥ 7801	21	7.7
Education level		
Illiterate	17	6.2
Read and write	23	8.4
Primary	62	22.6
Secondary	77	28.1
Tertiary and above	95	34.7
Religion		
Orthodox	168	61.3
Muslim	57	20.8
Protestant	46	16.8
Catholic	3	1.1
Ethnicity		
Amhara	137	50.0
Oromo	64	23.4
Tigre	12	4.4
Gurage	47	17.2
Other	14	5.1

5.2 Obstetric characteristics

In this study, 270 (98.5%) of at participants least had one antenatal contact in the current pregnancy. Twenty five participants (9.1%) had history of preterm birth. From those 13 deliveries were before 34 weeks of gestation. (Table 2)

Among the 274 participants who gave birth in the three teaching hospitals, 150 (54.7%) of mothers were primigravida and 22 (8.0%) were grand multipara. The proportions of preeclampsia, eclampsia, superimposed preeclampsia and gestational hypertension were 232(84.7%), 10(3.6%), 14(5.1%) and 18(6.6%) respectively. Overall 117/274, 42.7% of these mothers were admitted in-patient care with hypertensive disorders of pregnancy. From all participants 108/274, 39.4% mothers were given corticosteroids and from those 98.1% took four doses. Among 274 newborns 191(69.7%) were delivered by C/S, 74 (27%) by SVD, 3 (1.1%) by assisted breech delivery (ABD) and the remaining 6 (2.2%) infants were delivered by assisted

vacuum delivery (AVD). From all cesarean sections majority, 118/274 (43.1%) were done before onset of labor for maternal or fetal indications. Majority of the infants 162 (59.1%) were delivered at GMH, 74 (27%) of infants at TASH and the remaining 38(13.9%) at ZMH. (Table 3)

More than two third (68%) of mothers were diagnosed with hypertensive disorders of pregnancy after 34 weeks of gestational age. Fifty five (20%) of mothers were diagnosed between 32-33+6 weeks and the rest 12% before 32 weeks of gestational age. (Table 3)

Nearly half(46.4%) of mothers delivered within 48 hours of the diagnosis of HDP and only ten mothers stayed more than 35 days. The maximum stay was 58 days with mean duration of stay being 5 days.

TABLE 2. THE OBSTETRIC CHARACTERISTICS OF PARTICIPANTS IN ADDIS ABABA UNIVERSITY TEACHING HOSPITALS, ETHIOPIA, 2021. (N=274)

Variable	Frequency(N=274)	Percent (100%)
Antenatal care follow-up		
Yes	270	98.5
No	4	1.5
History of chronic HTN		
Yes	21	7.7
No	253	92.3
History of preterm birth		
Yes	25	9.1
No	249	90.9
Gestational age in weeks(n=25)		
< 34	13	52.0
≥ 34	12	48.0
Reason for previous preterm birth(n=25)		
HTN	21	84.0
PROM	2	8.0
Previous still birth	2	8.0
Outcome of past preterm birth(n=25)		
Alive	17	68.0
Dead	8	32.0
Gravidity		
1	150	54.7
2-4	102	37.2
≥ 5	22	8.0

Abortion		
Yes	70	25.5
No	204	74.5

TABLE 3.THE CURRENT OBSTETRIC CHARACTERISTICS OF PARTICIPANTS IN ADDIS ABABA UNIVERSITY TEACHING HOSPITALS, ETHIOPIA, 2021.(N=274)

variable	Frequency(N=274)	Percent (100%)
Admission to ward		
Yes	117	42.7
No	157	57.3
Antenatal corticosteroids		
Yes	108	39.4
No	166	60.6
Doses of corticosteroid(n=108)		
One	2	1.9
Four	106	98.1
Gestational age of HDP diagnosed		
28-31+6	33	12.0
32-33+6	55	20.1
34-35+6	84	30.7
≥ 36	102	37.2
Total	274	100
Medication use to prevent or manage HDP		
Yes	224	81.8
No	50	18.2
Types of HDP medication (n=224)		
Magnesium sulphate alone	9	4.0
Methyldopa + MgSO4	161	71.9
Methyldopa + Hydralazine +MgSO4	36	16.1
Methyldopa + Nifedipine + MgSO4	8	3.6
Nifedipine + MgSO4	10	4.5
Body mass index (BMI)		
< 18.5	8	2.9
18.5-24.9	220	80.3
≥ 25	46	16.8
Onset of labor		
Spontaneous	74	27.0
Induced	82	29.9

No labor	118	43.1
Total	274	100
If induced indication (n=82)		
Severe preeclampsia	32	39
HEELP syndrome	31	37.8
Preeclampsia with IUGR	6	7.3
Severe preeclampsia with APH	5	6.1
IUFD (Intrauterine Fetal Death)	1	1.2
Eclampsia	4	4.9
Mode of delivery		
Spontaneous Vertex Delivery	74	27.0
Assisted Vacuum Delivery	6	2.2
Assisted Breech Delivery	3	1.1
Cesarean Section	191	69.7
Total	274	100
Duration of labor (n=151)		
≤ 12 hours	80	53
Greater than 12 hours.	71	47
Duration of membrane rupture (n=145)		
Up to 8hrs	101	67.7
9-18hrs	39	26.9
>18hrs	5	3.4

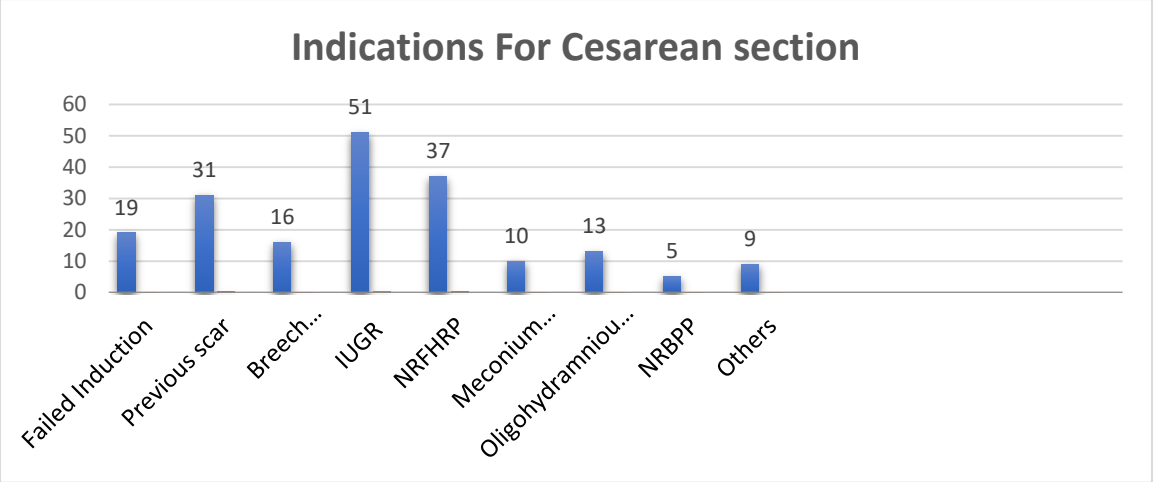


Figure 1.The indications of cesarean section of participants who delivered by c/S.

5.3 Maternal outcome with hypertensive disorder of pregnancy (N=274)

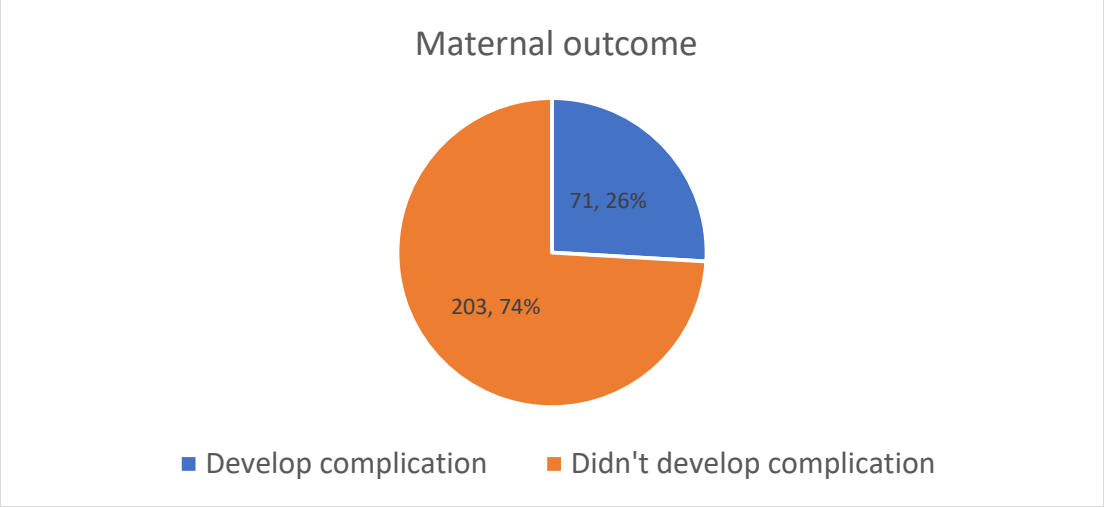


FIGURE 2. MATERNAL OUTCOME IN HYPERTENSIVE DISORDER IN PREGNANCY

In this study women who develop at list one complication were stated as "complicated outcome". Maternal complication was recorded in 71 (25.9%) of women with HDP; 48 (17.5%), 16(5.8%) 14 (5.1%) and 13 (4.7%) were Hemolysis Elevated Liver enzymes syndrome, Antepartum Hemorrhage, Postpartum Hemorrhage, Acute Kidney Injury respectively. And there was no maternal death report in the study. (See Table 4*)*

TABLE 4. THE MATERNAL OUTCOMES OF MOTHERS WITH HYPERTENSIVE DISORDER OF PREGNANCY (N=274)

Variable		Frequency (274)	Percent (100%)
Antepartum bleeding			
Yes		16	5.8
No		258	94.2
Causes of APH(n=16)	Abruption	15	93.8
	Placental Previa	1	6.2
Postpartum Bleeding			
Yes		14	5.1
No		260	94.9
Causes of PPH(n=14)			
Uterine atony		14	100

Blood transfusion		
Yes	15	5.5
No	259	94.5
Pulmonary edema		
Yes	2	0.7
No	272	99.3
AKI (Acute Kidney Injury)		
Yes	13	4.7
No	261	95.3
HELLP syndrome		
Yes	48	17.5
No	226	82.5

5.4 Neonatal characteristics

During the six months study period, among a total of 10,129 deliveries, the number of preterm deliveries were 952(9.4%), late preterm delivery were 680/952 (71.4%). The proportion of preterm delivery was 9.4%. From the 680 late preterm deliveries 274 fulfills the inclusion criteria, and the majority 146 (53.3%) were delivered at 36+0-36+6 weeks.

Among 274 newborns 173 (63.1%) had birth weight of 1500-2499 grams and 25 (9.1%) had very low birth weight. 155 (56.6%) were small for gestational age. 53.6% of the neonates was females and 127 (46.4%) were males. (Table 5)

TABLE 5. CHARACTERISTICS OF NEONATES WHO DELIVERED IN LATE PRETERM FROM HDP IN ADDIS ABABA UNIVERSITY TEACHING HOSPITAL, 2021.(N=274)

Variable	Frequency(N=274)	Percent (100%)
Gestational Age of at Delivery		
34-34+6	83	30.3
35-35+6	45	16.4
36-36+6	146	53.3
Total	**274**	**100**
Birth weight in gram		
<1500	25	9.1
1500-1999	88	32.1
2000-2499	85	31.0

2500-3999	76	27.8
Total	**274**	**100**
Condition of weight for GA		
SGA	155	56.6
AGA	119	43.4
Total	**274**	**100**
Sex of neonate		
Male	127	46.4
Female	147	53.6
Total	**274**	**100**

5.5 Outcomes of neonate delivered from mothers with HDP in late preterm

Among 270 neonates delivered alive, 227 (84.1%) of newborns had first minute Apgar score of seven and above, while the rest 43 (15.9%) of newborns had first minute Apgar score of less than seven, 2 of these newborns had Apgar scores of less than 3 and died at delivery room. At fifth minute 266 (98.5%) of newborns had Apgar score of seven and above. The success of resuscitation was 90.7%. Over half (55.2%) of neonates were referred to NICU for different reasons and 120 (44.8%) remain by mother side. Among all the referred newborns 102 (68.9%) of them required NICU admission with different diagnosis. (Table 6)

TABLE 6.OUTCOMES OF NEONATE DELIVERED FROM MOTHERS WITH HDP IN LATE PRETERM (N=274)

Variable		Frequency (N=274)	Percent (100%)
Fetal outcome			
Alive		270	98.5
Still birth		4	1.5
APGAR scores(270)			
At first minute	< 7	43	15.9
	≥ 7	227	84.1
At fifth minutes	<7	4	1.5
	≥ 7	266	98.5
Neonatal resuscitation(n=270)			
Yes		58	21.5
No		212	78.5
NICU Referral (n=268)			

Yes	148	55.2
No	120	44.8
NICU admission (n=148)		
Yes	102	68.9
No	46	31.1
Perinatal death (Total=21)		
Antepartum death	4	19.0
ENND	17	81.0
Cause of ENND (n=17)		
Sudden cardiac arrest	4	23.5
Respiratory failure	9	52.9
Unknown cause	4	23.6

On day seven neonatal assessment 72(26%) were still in the neonatal intensive care unit and the overall perinatal losses were 21(8%) as shown the figure below

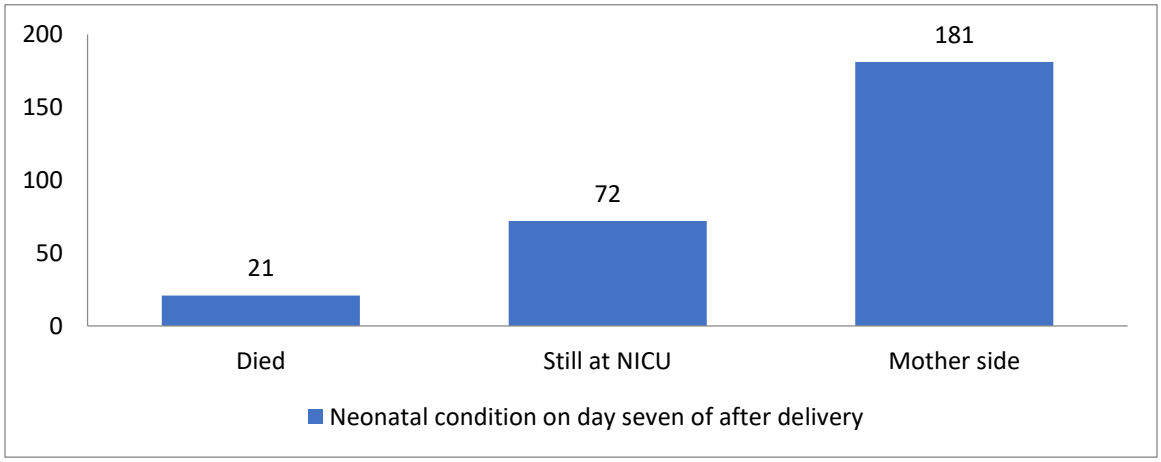


FIGURE 3.NEONATAL ASSESSMENT ON DAY SEVEN AFTER DELIVERY

From referred cases preterm birth with low birth weight accounts 36(24.3 %%) and the other admission diagnosis were IUGR and respiratory distress syndrome each 27(18%) as shown in the figure 4 below

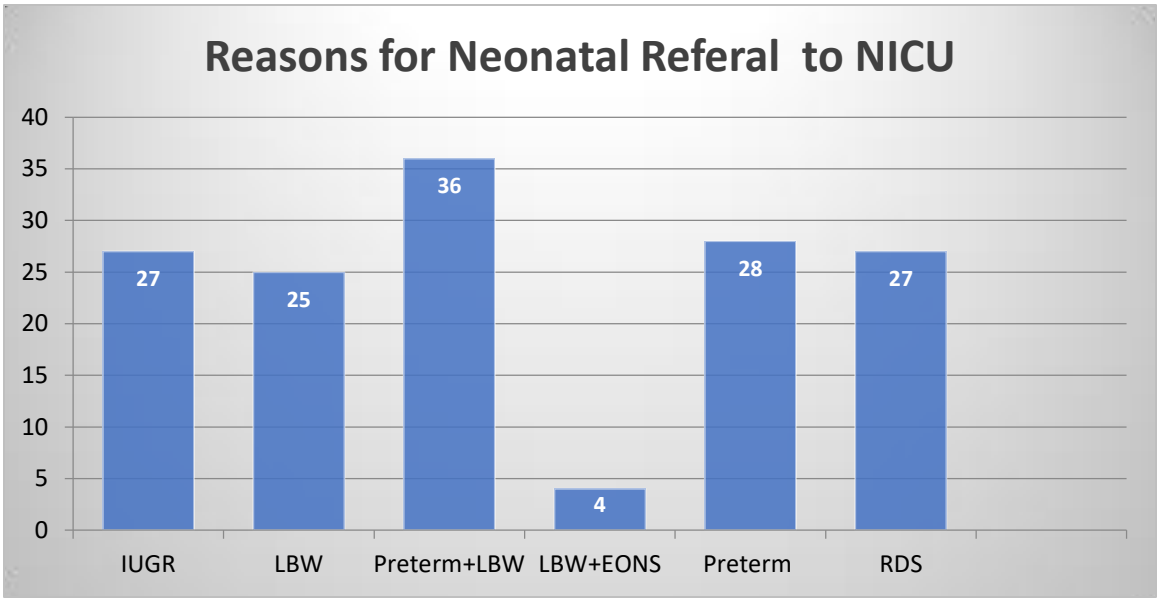


Figure 4.reasons of neonatal referral to neonatal intensive care unit.

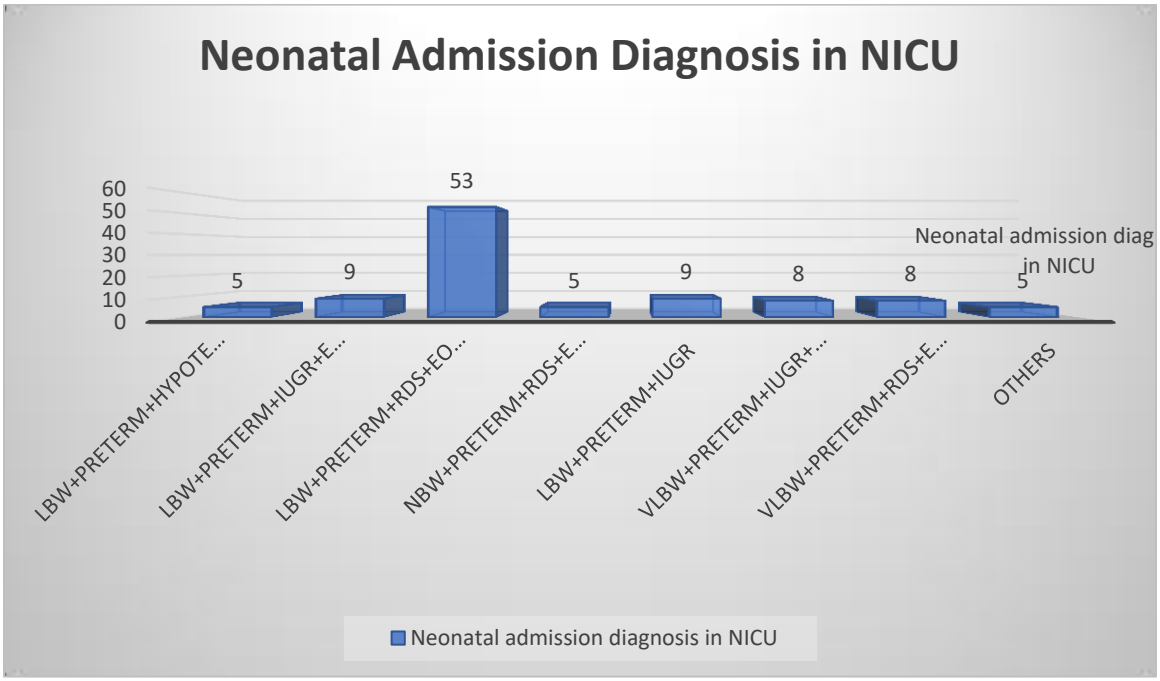


Figure 5. The Neonatal Admission Diagnosis in the Neonatal Intensive Care Unit

Among 270 newborns alive at delivery 253 (93.7%) of newborns were survived to 7th day and 17 (6.3%) neonates died. Majority 9/17 (52.9%) of neonatal deaths occurs within the first 48 hours and four of the deaths occurred on third day, two deaths occurred on fourth and the

remaining two on the fifth and sixth days after delivery. (Table 7). The perinatal mortality rate in late preterm pregnancy in hypertensive disorders of pregnancy in this study was 76.6/1000 live births.

Generally, about 41.2% of the perinatal losses occurred in those who delivered within 48 hours of the diagnosis of HDP between 34-36+6 weeks of gestational age, while 10/17 (58.8%) of perinatal loss occurred in those who delivered within three days of diagnosis. There were seven losses in those who stayed more than 10 days.

TABLE 7.SURVIVAL OF LATE PRETERM NEONATES DELIVERED FROM MOTHERS WITH HDP AT THREE TEACHING HOSPITALS FOR GA, ADDIS ABABA, 2021, (N=270).

Gestational age (In weeks)	Total delivery	Total death (ENND)	Survived	
			Number	Percent
34-34+6	81	10	71	87.7%
35-35+6	44	4	40	90.9%
36-36+6	145	3	142	97.9%
Overall	**270**	**17**	**253**	**93.7%**

TABLE 8.SURVIVAL AND BIRTH WEIGHT OF LATE PRETERM NEONATES DELIVERED AT THREE TEACHING HOSPITALS, ADDIS ABABA, 2021, (N=270).

Birth weight (in grams)	Total delivery	Total death (ENND)	Survived	
		Number	Number	Percent
<1500	25	4	21	84%
1500-1999	88	12	76	86.4%
2000-2499	85	1	84	98.8%
≥ 2500	76	0	76	100%
Overall	**270**	**17**	**253**	**93.7%**

In this study GA is the most important predictor of neonatal survival and neonatal survival significantly increase when GA increases. Increment of GA by one week improves the survival rate 20% and decreases rate neonatal morbidity and mortality of late preterm infants. (Figure 6).

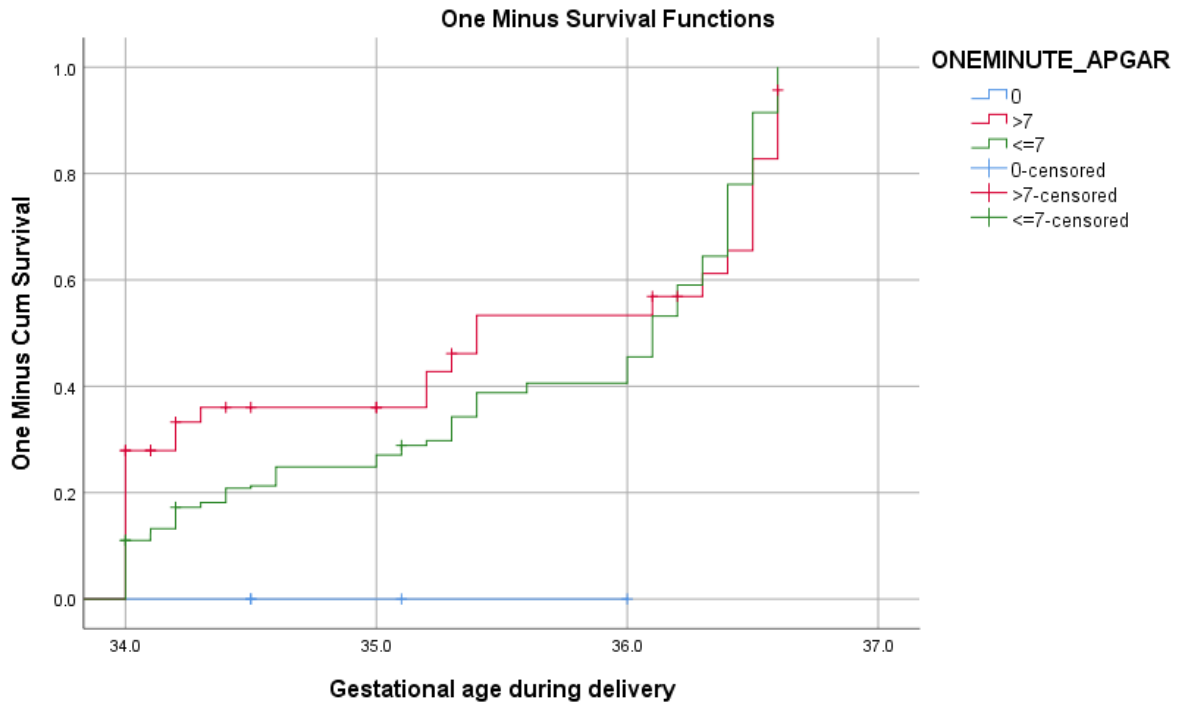


FIGURE 6.THE SURVIVAL TRENDS OF LATE PRETERM NEONATE BORN TO MOTHERS WITH HDP WITH REGARD TO GESTATIONAL AGE. (N=270)

5.5 Factor Associated with Neonatal Health

Binary Logistic regression was performed to assess the association of each independent variable with dependent variable (neonatal health condition). The factors that showed a p-value of 0.2 and less were added to multivariate regression model to detect the statistically significance variable.

In this study participants whose birth weight 2000-2499 grams had 16.3 times chance of survival (AOR=16.3, 95% CI=1.42, 187.32) than those with birth weight less than 1500 gram. One-minute Apgar score was also another significant variable for neonatal survival. Neonate having

1st minute APGAR score less than seven had increase neonatal mortality by 96% than APGAR of greater than or equal to seven (AOR=0.04, 95% CI=0.006, 0.26).

TABLE 9. BIVARIATE AND MULTIVARIATE LOGISTICS REGRESSION ANALYSIS OF THE DEPENDENT AND INDEPENDENT VARIABLE (N=274)

Variable	Neonatal status at day seven		p-value	COR	p-value	AOR
	Alive	Died				
Maternal BMI						
<18.5	5	3	0.023	**0.12(0.02, 0.74)**	0.149	0.07(0.002,2.53)
18.5-24.9	205	15	0.942	0.95(0.26, 3.44)	0.477	0.40(0.03, 4.92)
≥25	43	3	1		1	
Number of pregnancy						
primigravida	135	15	1		1	
multigravida	98	4	0.083	2.7(0.88, 8.45)	0.130	3.7(0.68,19.71)
grand multiparous	20	2	0.894	1.1(0.24, 5.23)	0.485	0.37(0.023, 5.96)
Neonatal birth weight						
<1500	20	5	1		1	
1500-1999	73	15	0.733	1.2(0.39, 3.75)	0.269	2.4(.50,11.6)
2000-2499	84	1	0.007	**21(2.32, 189.8)**	0.025	**16.3(1.42, 187.32)**
2500-3999	76	0	0.997	*	*	
APGAR at one minute						
<7	30	13	0.000	**0.04(.013, 0.135)**	0.001	**0.04(0.006, 0.26)**
≥7	223	4	1		1	
APGAR at five minute						
<7	1	2	0.004	**0.03(.002, 0.325)**	*	
≥7	252	14	1			
Neonatal resuscitation						
Yes	47	11	0.000	**0.13(.04, 0.353)**	0.435	2.1(0.34,13.4)
No	206	6	1		1	
Maternal complication						
No	190	13	1			
Yes	63	8	0.190	0.54(0.21, 1.36)	0.199	0.37(.08, 1.69)

5. Discussion

Hypertensive disorder of pregnancy is considered to be a major worldwide health problem running an increased risk of perinatal and maternal morbidity and mortality. There seems to be confusion about the terminology and classification of these disorders. Not only the etiology and pathophysiology still remain to be unclear, but also effective prevention and treatment modalities are limited.

In our study from classes of HDP preeclampsia was the most common reason for late preterm delivery, 232 (84.7%). In the study done on perinatal outcomes of HDP at Wolayita referral hospital, Southern Ethiopia (2019) preeclampsia accounts about 70%, whereas eclampsia was 26%.[**41**] This is probably majority of mothers were referred from neighboring health facilities showing that there might be some degree of complication before arrival unlike ours where 91.6% of mothers were from Addis Ababa. In this study 71.4% of preterm births were late preterm, which is almost comparable to most international studies where late preterm birth accounts greater than 75% of preterm birth. [**42**]

Majority of the women affected by the hypertensive disorders were primigravida (54.7%) and 91.2% of mothers were below 35 years of age. This is similar with the findings of other studies conducted in Ethiopia [**43-46**]. However, there was no statistically significant association between age of mothers and unfavorable perinatal outcomes.

More than 53% of neonates were delivered after 36 weeks of GA, 30.3% from 34 to 34+6 weeks and 16.4% delivered 35 to 35+6 weeks. This finding is in line with the study conducted in Nigeria,[**24**] Nepal[**25**] and Thailand,[**26**] Onyiriuka and Okolo.[**27**] This may be many of the physicians tend to deliver the baby than conservative management after 36 weeks of gestational age due to the relative fetal maturity at this gestational age than at 34-35 weeks of gestation.

In our study among 274 infants 191 (69.7%) were delivered by C/S, where 118/191 (43.1%) were done before the onset of labor for maternal or fetal indications. This figure is much higher than other local studies like in Yekatit 12(44.2%) [**43**]Jimma (34%) [**44**], Mettu(16.2%) [**45**], and Debre birhan (6.3%) [**46**]. The reason might be in this study, 56.6% neonates were small for gestational age. So, the presence of appropriate professionals in better number in our setting and the presence of maternal fetal medicine specialty might has increased the detection and diagnosis

of these growth restricted fetus which in turn have contributed to the higher cesarean delivery rate in the present study area.

On the final model, birth weight and first and fifth minutes Apgar score were found to be independent predictors of favorable perinatal outcome. According to the finding of this study perinatal outcome on day seven neonatal assessment, 181(66%) neonates were by mother side 72(26%) of neonates were still in neonatal intensive care unit and 7.6% of them were died. There is no study was congruent with this finding. Because most of the literature assessed immediate neonatal outcome rather than the seven-day neonatal assessment.

The finding of the study also showed that the major fetal complication, which is diagnosed during neonatal admission in intensive care units were intra uterine growth restriction, low birth weight, preterm, early onset of neonatal sepsis, respiratory distress, and hypothermia. This finding was in line with the study conducted in Aga Khan University Hospital, Karachi, Pakistan [**47**]. This similarity is may be due to in hypertensive women there is a reduction of nutritional flow to the fetus and that is the way to develop IUGR and preterm birth in fact that, may lead to fetal distress, hypothermia, and early onset of sepsis. The other significant findings in our study was that 56.6% were small for gestational age which is slightly higher than a multicenter prospective study done on women with HDP and singleton pregnancies between 34 and 37 weeks where the prevalence of SGA was 47%[**48**]

In this study finding there were 4 still births and 17 early neonatal deaths. The perinatal mortality rate in late preterm pregnancy in hypertensive disorders of pregnancy in this study was 76.6/1000 live births. This finding was in line with the study conducted in sub-Saharan Africa [**29**]. The high perinatal mortality in women with HDP is mainly due to premature delivery and growth restriction [**49**]. This is may be due to preterm neonate is high risk for Sudden cardiac arrest, EONS, Respiratory failure, Hypothermia.

Neonates who born at gestational age of 36 up to 36+6weeks had a better chance of survival than neonates those delivered with gestational age of 34 up to 34+6. This is similar with the findings of study conducted in Addis Ababa university teaching hospitals [**35**] where every one week increment of GA, increases neonatal survival by 2.5 folds (COR-2.45, 95% CI 2.04-2.9, P<0.01). This is the fact that neonatal survival increases as the gestational increase due to neonatal lung maturity.

In this study almost three fourth (76.5%) of neonatal deaths occurs within the first 72 hours of delivery. Nearly two third (64.7%) of these neonates were delivered by emergency cesarean sections for non-reassuring fetal status (7 neonates for non-reassuring fetal heart pattern in labor and 4 for stage II IUGR) and 94% of lost neonates were growth restricted at time of delivery. The most common cause of death was respiratory failure. In general this indicates that the need for proper antepartum and intrapartum surveillances, and intensive cares and vigilance in the first 72 hours of life are crucial for the survival of late preterm infants. This figure shows that initial care for the newborn infants is still suboptimal like in other developing countries.

As strength this study clearly answered the study objectives and proposed solutions for the identified problems. The study can also be generalized to other Public Hospitals of Addis Ababa as it was conducted in public hospitals providing antenatal care in Addis Ababa.

There are important limitations of this study that need to be taken into account when interpreting the findings reported. Neonatal survival analysis was limited to early neonatal period. Inadequate literature in Ethiopia to discuss with Ethiopian context.

6. Conclusion

Late preterm neonates are a higher risk for neonatal morbidities and mortality contrary to the belief that they are nearly mature. The high perinatal loss in late preterm deliveries needs attention and investigation into the underlying cause. This study shows preeclampsia as the most common cause for late preterm birth. The most common cause of neonatal death was respiratory failure. The weights of neonate and Apgar score during delivery were the important independent predictors for the neonatal survival. Our study showed higher perinatal mortality in a tertiary hospital where emergency obstetric and newborn care is set and quality obstetric care is expected. However, it is worth to note that tertiary facilities manage difficult cases which can explain the high perinatal mortality rate. But it is high which means there is enough room for improvement.

7. Recommendation

Deliveries prior to 37 weeks of GA have higher rate of neonatal morbidity and mortality and lower survival rate**.** Critical attention should be paid on the first 72 hours of newborn life to reduce factors contributing to high neonatal loss at this particular time.

Further study is needed to assess the quality of care in both obstetrics and neonatal intensive care units and cause of low survival rate of preterm infants. Also cause of intra uterine growth restriction should be studied.

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Annex 1: Consent Form

My name is _____. I am working as data collector for the study being conducted in this hospital by Dr. Getinet Girma who is studying for specialty of Obstetrics and Gynecology at Addis Ababa University, College of Health Sciences. I kindly request you to give me your attention to explain you about the study and being selected as the study participant. The study will be about perinatal outcomes of pregnancies complicated by hypertensive disorders of pregnancy in late preterm in two government teaching hospitals found in Addis Ababa Ethiopia(TASH &GMH) which is this hospital is one of the hospital selected. The findings of this study will have a paramount importance for women having HDP and neonates delivered from these mothers in late preterm.

I will be interviewing you using questionnaire, there are few questions to answer where I will fill the questionnaire by interviewing you. Also your neonate status will be checked every other day through phone call till 7 days from delivery date. The risk of being participated in this study is minimal, but only taking 30-45 minutes from your time. The data you will provide us will be confidential. There will be no information that will identify you. The findings of the study will be general for the study population and will not reflect anything particular of individual person. The questionnaire will be coded to exclude showing names. No reference will be made in oral or written reports that could link participants to the research.

Annex 2: Questionnaire and data collection tools

Questionnaire no_____ Date_____

Hospital_____

Data collector name _____ Signature _____

Supervisor Name _____ Phone No_____

Part-I: Socio Demographic Characteristics

CardNo_____phoneNo:1)……..……..

2)……..

1. Address: 1) Addis Ababa 2) Outside Addis Ababa

2. Age _____

3. Marital Status: 1) Single 2) Married 3) Widowed 4) Divorced 5) Separated

4. Occupation: 1) Housewife 2) Government employee 3) Private employee 4) Daily laborer 5) other (specify) _____

5. Monthly income:

6. Educational level: 1) Illiterate 2) Read and Write 3) Primary education 4) Secondary education 5) Tertiary and above

7. Religion: 1) Orthodox 2) Muslim 3) protestant 4) Catholic 5) Others (Specify)…….

8. Ethnicity: 1) Amhara 2) Oromo 3) Tigre 4) Gurage 5) Others (specify)……..

Part-II: Reproductive and Obstetric History

1**.** Height (in cm): ….. Pre-pregnancy weight at booking (in kg): ……. BMI: ……

2. History of chronic hypertension: Yes☐ No☐

3. History of preterm birth: Yes☐ No☐

4. If yes, GA and any identified reason: ……

5. Outcome of the past preterm birth: ……

6. Any medical comorbidities: Yes☐ No☐, If yes specify; ----------

7. Gravidity_____ Parity_____ Abortion_____

8. ANC follow up …….... Yes ☐ No ☐

9. Admission to ward .....Yes ☐ No ☐

10. Antenatal corticosteroids (Dexamethasone): yes☐ No☐

11. If yes to Question to no.10 how many doses? 1. One 2.Two 3.Three 4. Four or more

12.Any rescue dose?

13. Gestational Age HDP is diagnosed 1. Prepregnancy 2. GA in months or weeks if in the medical chart

14. Medication use during this pregnancy to prevent or manage HDP……

15. GA in Weeks at delivery for the current pregnancy ……..

16. Complications of HPD identified in the index pregnancy.

List: 1. ……. 2. …….. 3. ……

4. …… 5. …… 6. ……...

17. Onset of Labor: Spontaneous ☐Induced☐No labor ☐

If induced, Indication ----------

If CS, indication …….

18. Mode of delivery: SVD ☐Vacuum ☐Forceps☐ABD ☐CS ☐

19. Duration of labor: ---------, Duration of Rupture or membranes: ----------

Part-III: Neonatal outcome

1. Birth weight (in grams) ----------

2.SGA …… AGA …… LGA …….

3. Sex: M☐ F☐; Live birth or still birth

4. GA at birth From LMP/Early USG/Ballard score -------

5. If live birth; Apgar score: 1^{st} Minute ------- 5^{th} Minute-------- 10^{th} Minute……

6. Was the neonate resuscitated? Yes☐ No☐

7. Neonate referred to neonatal ICU: Yes☐ No☐

8. If yes to question number 7 specify the reason for referral----------
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9. NICU admission, Yes☐ No☐

10. If Yes, Admission diagnosis …….

11. Neonatal death, Yes☐ No☐ ,

12. If yes, cause of death, ……..

13. Age at death…….

14. Still at the ICU at day 7, Yes☐ No☐

15. Neonate alive by day 7 , Yes☐ No☐

Part-IV: Maternal outcome

1. APH: if identified cause specifiy

2. PPH: Yes☐ No☐: if identified cause specifiy……

3. Need for Blood and Blood product transfusion: Yes☐ No☐

4. DIC: Yes☐ No☐

5. ARF: Yes☐ No☐

6. HELLP syndrome: Yes☐ No☐

7. ICU admission: Yes☐ No☐ Indication----------

8. Pulmonary edema: Yes☐ No☐

9. Maternal collapse: Yes☐ No☐

10. Intracranial hemorrhage:Yes☐ No☐

11. Maternal Death: Yes☐ No☐

12. If yes/ Antepartum… Intraprtum …… Postpartum ……

13. If yes to question number 9 specify the cause ----------