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Incidence of adverse perinatal outcomes and risk factors among women with pre-eclampsia, southern Ethiopia: a prospective open cohort study

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ABSTRACT

Background In Ethiopia, in 2021, more than 80% of all newborn deaths were caused by preventable and treatable conditions. This study aimed to measure the incidence of adverse perinatal outcomes and risk factors among women with pre-eclampsia in the Sidama region of southern Ethiopia.

Methods A prospective open cohort study was conducted from 8 August 2019 to 1 October 2020. We enrolled 363 women with pre-eclampsia and 367 normotensive women at ≥20 weeks of gestation and followed them until the 37th week. We then followed them until the seventh day after delivery up to the last perinatal outcome status was ascertained. A log-binomial logistic regression model was used to estimate the incidence of adverse perinatal outcomes and its risk factors among women with pre-eclampsia. Relative risk (RR) with a 95% CI was reported. A p<0.05 was considered statistically significant.

Results There were 224 adverse perinatal outcomes observed in the 363 women with pre-eclampsia compared with 136 adverse perinatal outcomes in the 367 normotensive women (p<0.001). There were 23 early neonatal deaths in the pre-eclampsia group compared with six deaths in the normotensive group (p<0.001). There were 35 perinatal deaths in the pre-eclampsia group compared with 16 deaths in the normotensive group (p<0.05). Women with severe features of pre-eclampsia had a 46% (adjusted RR 1.46, 95% CI 1.38 to 2.77) higher risk for adverse perinatal outcomes compared with women without severe features of pre-eclampsia.

Conclusions In this study, more adverse perinatal outcomes occurred among women with pre-eclampsia after controlling for confounders. A higher perinatal outcome observed among women with pre-eclampsia, especially among women with severe features of pre-eclampsia, and those admitted to hospital at <34 weeks. This paper highlights the significantly elevated perinatal risks associated with pre-eclampsia, especially when it has severe features.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Studies conducted in Ethiopia on maternal and perinatal outcomes related to pre-eclampsia have not generated evidence that could be used by policymakers or implemented in clinical practices because of study design. Most studies did not include control groups or measure the risk of outcomes of interest and there were missing sociodemographic variables such as maternal education level. A study in southern Ethiopia aiming to estimate the risk of pre-eclampsia on adverse perinatal outcomes did not include exposures and outcomes.

WHAT THIS STUDY ADDS

⇒ There were 224 adverse perinatal outcomes observed in the 363 women with pre-eclampsia compared with 136 adverse perinatal outcomes in the 367 normotensive women (p<0.001).
⇒ Women with severe features of pre-eclampsia had a 46% (adjusted relative risk, aRR 1.46, 95% CI 1.38 to 2.77) higher risk for adverse perinatal outcomes compared with women without severe features of pre-eclampsia.
⇒ Women without severe features of pre-eclampsia had a 39% (aRR 1.39, 95% CI 1.21 to 1.56) higher risk for adverse perinatal outcomes compared with women in the normotensive group.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study provides epidemiological evidence for the incidence of adverse perinatal outcomes and risk factors among women with pre-eclampsia. Early detection and management of pre-eclampsia may improve maternal and infant outcomes. So, this could support clinical and public health practitioners to be aware of early signs and symptoms of pre-eclampsia. A cohort study should be conducted to evaluate other types of hypertensive disorders of pregnancy on the incidence of adverse perinatal outcomes and its risk factors among pregnant women.

INTRODUCTION

Pre-eclampsia and eclampsia are two of the most common hypertensive disorders of pregnancy (HDPs).[1] It is the second-leading cause of direct maternal death and is directly responsible for 70 000 maternal deaths annually at the global level.[2] In low-income and middle-income countries, 10%–15% of direct maternal mortalities were associated

with pre-eclampsia and eclampsia in 2018.[1] In Ethiopia, in 2019, the pooled prevalence of maternal death was 4%.[3]

In Ethiopia, in 2018, the overall pooled prevalence of HDPs was 6.07%.[4] In the same study, a higher pooled prevalence of HDPs was observed in southern Ethiopia (10.13%), with the lowest prevalence observed in Addis Ababa, the capital city of Ethiopia (5.41%).[4]

Adverse perinatal outcomes include an overall <5 child mortality rate of 55 deaths per 1000 live births, and neonatal mortality was 30 deaths per 1000 live births[5] and the pooled prevalence of low birth weight was 17.3%[6] and stillbirths was 6.7%.[7] A study conducted in northwest Ethiopia in 2021 found that the overall prevalence of adverse perinatal outcomes was 19.4%.[8] According to a 2019 study in northwest Ethiopia, 46.5% of newborns delivered to women had unfavourable outcomes of severe pre-eclampsia and eclampsia, with 28.1% of those being stillbirths.[9]

A number of factors account for high rates of adverse perinatal outcomes, including poor infrastructure, scarcity of supplies and skilled labour, a weak referral system, poor quality of care, and lack of timely obstetric care, contributed to a higher proportion of adverse perinatal mortality in Ethiopia.[10]

In Ethiopia, in 2021, more than 80% of all newborn deaths were caused by preventable and treatable conditions.[11] However, the reduction of mortality is still a challenge. The government of Ethiopia has taken steps to strengthen engagement with key local and international sectors and stakeholders to address determinants of health.[12] Ethiopia recently replaced the previous four-visit focused antenatal care (ANC) model with the new ANC eight-contacts model.[12]

Studies conducted in Ethiopia have poor in generating evidence that could be used by policy-makers and in clinical practices because they did not include control groups or measure the risk of outcomes of interest and did not include sociodemographic variables such as maternal education status.[9 13 14] A study in southern Ethiopia was limited in estimating the risk of pre-eclampsia on adverse perinatal outcomes because of poor ascertainment of exposures and outcomes using purposive sampling techniques.[15] Another study in Ethiopia did not include a non-exposed group that would have been important to controlling confounders like the quality of perinatal care associated with morbidity and mortality.[16] This study's findings will provide epidemiological evidence for policy-makers and implementers to reduce adverse perinatal outcomes among women with pre-eclampsia and normotensive women. This paper highlights the significantly elevated perinatal risks associated with pre-eclampsia, especially when it has severe features. We aimed to measure the incidence of adverse perinatal outcomes and risk factors among women with pre-eclampsia in Sidama region of southern Ethiopia.

METHODS

Study design and setting

A prospective open cohort study was conducted from 8 August 2019 to 1 October 2020 in the Sidama region of Ethiopia. In 2020, the population of the region was approximately 4 million. There were 13 public hospitals, 138 health centres and 540 health posts in the region that provided maternal, newborn and child health services. In 2020, approximately 132 031 pregnant women attended ≥4 ANC visits and 127 585 births were assisted by skilled birth attendants. Out of the 13 hospitals that are found in the region, we enrolled participants from 7 of the hospitals, including Adare, Hawassa, Yirgalem, Hula, Bona, Chuko and Daye hospitals.

Participants

The participants were women with pre-eclampsia and normotensive women who were enrolled at ≥20 weeks of gestation up until the 37th week. We followed them until the seventh day after delivery and waited for the last enrolled woman's perinatal outcome status to be ascertained. During the follow-up, 194 women with pre-eclampsia and normotensive women were admitted to the hospitals at <34 weeks of gestation, and 536 women with pre-eclampsia and normotensive women were admitted to the hospitals at 34–37 weeks of gestation. During the follow-up, eight normotensive women developed pre-eclampsia. We, thus, included these eight women in the exposed group. Pregnant women with hypertension plus proteinuria, mild hypertension and evidence of organ dysfunction, severe hypertensive without proteinuria and evidence of organ dysfunction were included in the study.[17 18] Pregnant women with pre-eclampsia and normotensive women were selected by healthcare providers: general medical practitioners, emergency surgical officers or obstetricians/gynaecologists during the follow-up.

Operational definitions

We ascertained exposure of interest supported by guidelines of the Obstetrics Management Protocol for Hospitals in Ethiopia in 2021 and on the recent International Society for the Study of Hypertension in Pregnancy.[17 18] Birth asphyxia was defined as the condition of a baby with trouble in breathing (gasping or breathing very irregularly or no breathing). Small for gestational age of pregnancy was defined as a birth weight of a newborn below the 10th percentile of weight distribution at the specified gestational age of pregnancy.[19] Stillbirth refers to a baby born with no sign of life at or after 28 weeks of gestation. Preterm delivery was defined as the delivery of a baby before 37 weeks gestation. Low birth weight describes a baby with a birth weight of less than 2.5 kg. A low Apgar score refers to a newborn baby with an Apgar score of less than seven at 1 and 5 min.

Perinatal death was defined as a stillbirth or an early neonatal death. Early neonatal death is defined as the death of a live newborn in the first 7 days of life.

Intrauterine growth restriction of newborn is defined as birth weight and/or birth length below the 10th percentile for their gestational age and whose abdominal circumference was below the 2.5th percentile with pathological restriction of fetal growth.[19] Gestational age at admission was defined as the time when the women were enrolled in the study. Skilled birth attendant was defined as a professionally trained health worker having the essential midwifery skills to manage normal labour and delivery, recognise complications early and perform any essential intervention including early referral.[17]

Sample size and sampling

The sample size was calculated using Epi Info V.7. We considered the following assumptions for sample size calculations: early neonatal death,[20] the ratio of exposed to unexposed group (1–1), the proportion of early neonatal death among women with pre-eclampsia (5%) and the proportion of early neonatal death among normotensive women (1%). The sample size was estimated to be 733 (366 women with pre-eclampsia and 367 normotensive women), accounting for a design effect of 2% and 10% lost to follow-up. We also assumed a two-sided confidence level of 95% with a power of 80%.

A two-stage cluster sampling technique was used to recruit study participants. In the first stage, 7 of 13 hospitals were selected using a simple random sampling technique. In the second stage, perinatal conditions were selected from women with pre-eclampsia and normotensive women using a simple random sampling technique.

Exposure ascertainments

We ascertained exposure of interest supported by guidelines of the Obstetrics Management Protocol for Hospitals in Ethiopia in 2021 and on the recent International Society for the Study of Hypertension in Pregnancy.[17 18] The main exposure variable in this study was pre-eclampsia with or without severity features. Pre-eclampsia with severe features was defined as the presence of one or more of the following conditions: blood pressure (BP) of ≥160 mm Hg systolic or ≥110 mm Hg diastolic, ≥3+ protein on two urine samples taken 4 hours or more apart or 5 g of protein in a 24-hour urine sample.[18] Pre-eclampsia without severe features was defined as raised BP >140/90 mm Hg plus 24-hour urine protein >300 mg/24 hour or urine dipstick >+1 after 20 weeks of gestation in previously normotensive women.[18] Normotensive women were pregnant women having a (BP) <140/90 mm Hg with ≥20 weeks of gestation or who did not develop pre-eclampsia and proteinuria. Gestational age was calculated based on a woman's recall of her last menstrual period. However, an ultrasound scan was used for those women who could not remember their last menstrual period.[18]

Outcome variable

Adverse- perinatal outcomes were defined as a newborn with the occurrence of at least one of the following outcomes: birth asphyxia, low birth weight, small for gestational age, preterm delivery, admission to the neonatal intensive care unit and perinatal death.

Data collection

We validated the data collection tool before data collection.[21] Two bilingual translators (speakers of both Sidamic and English languages), who were capable of translating the original tool in the English version into the Sidamic version, were selected. Translations into the Sidamic language more accurately reflected the tones of the language. The translations were compared and discrepancies were noted during the translation process. The poorer wording choices were identified and resolved in a discussion between the translators.

The back translations were done by two experts of the source language (English). This was a validity checking process to ensure that the translated version reflected the same item content as the original version did. Face and content validation of the tool was done by a panel of experts (midwife experts, epidemiologists and gynaecologists). The panel of experts independently assessed the tool for readability, intelligibility, clarity and ease of use. The internal consistency for each dimension was checked using Cronbach's alpha (Cronbach's alpha=0.98).[21]

In the first pilot test, conducted in a non-study area, all participants responded to all items in the data collection tool and marked them correctly. No missing items were found. Data collectors also reported no difficulty in asking the questions, and no participant reported having any problem understanding the items. The tool was tested for the second time 2 weeks after the first measurement. The 2-week test–retest reliability result was shown to have a good correlation with reliable strategies to assess these point scores (intraclass correlation coefficients (ICC) for agreement 0.78; p<0.001) because the ICC value was found to be in the range of 0.75 to 0.9, indicating good reliability.[22] We also specified the kind of ICC was calculated we used the two-way mixed-effects model for calculating ICC as the model of choice for test–retest reliability measure.[21 22]

Trained midwives conducted face-to-face interviews at ANC clinics using the pretested validated tool. A checklist was used to collect information from the maternal and neonatal records of women with pre-eclampsia and normotensive women in each hospital. We collected sociodemographic information and clinical and laboratory variables linked to maternal and perinatal outcome status. The data collection procedures were supervised by three Maternal and Child Health maternity and reproductive health professionals.

Outcome ascertainment

Adverse perinatal outcomes were ascertained by obstetricians/gynaecologists and trained midwives. Client medical registration was also used to retrieve adverse perinatal outcome status. The perinatal condition was determined at the follow-up appointment for those who

were discharged, and a phone call was made for those who did not show up for this follow-up.

Statistical analysis

Data were cleaned, coded and analysed using Stata 14. We identified outliers and missing values and checked data consistency using the original questionnaire for the responses using participants' code numbers. Mean and SDs were computed for continuous variables. Frequencies and percentages were computed for categorical variables. An incidence proportion of adverse perinatal outcomes was conducted on women who had pre-eclampsia and normotensive women. Cross-tabulation was also performed to test the relationship of exposure variables with the outcome variable. A χ^2 test was used to compare categorical variables between women with pre-eclampsia and normotensive women.

Principal component analysis was computed and used for wealth index computation and was ranked in three groups as low, middle and high. It was a composite measure of household cumulative living standard, and calculated by using data on household ownership of selected assets, like various household assets and means of transportation. Different items for urban and rural areas were computed separately. We included 21 items for rural residents and 16 items for urban residents. The suitability of data was computed by using Bartlett's test of sphericity and the Kaiser-Meyer-Olkin (KMO) measure of sample adequacy.[23] The KMO >0.6 was used to confirm the sample adequacy for factor analysis.[23]

A multivariable log-binomial logistic regression model was performed to identify the risk factors for adverse perinatal outcomes. According to Hosmer and Lemeshow, a variable with a p<0.25 was recommended as a screening criterion for the selection of candidate variables used in a multivariable log-binomial logistic regression model.[24] This confirmed that insignificant variables from the first step were reanalysed in later steps.[24] Moreover, the candidate variables were also considered based on subject matter expertise, such as gynaecologists, obstetricians, epidemiologists and statisticians who were working as a supervisor, and who provided more subject matter expertise to improve the modelling process substantially. This insight from subject matter experts substantially improved the modelling process.[24] A variable with a p<0.05 was used to identify statistically significant risk factors for adverse perinatal outcomes. Maternal age was treated as a continuous variable and reported using the beta-coefficient with a 95% CI.

We checked the multicollinearity among predictors using a variance inflation factor at a cut-off point of 10.[25] We confirmed that there was no collinearity among predictors. The goodness of the fit was tested using the Hosmer-Lemeshow test.[26] The predictor that was greater than the significance level (p>0.05) was accepted.[26] This indicates that the observed model did not significantly differ from the expected model.

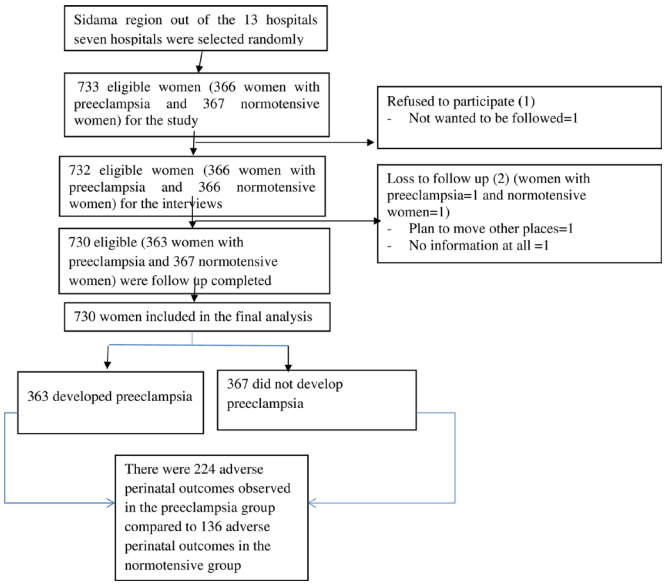

Figure 1 Flow diagram of the overall study process in Sidama region, southern Ethiopia, 8 August 2019 to 1 October 2020.

RESULTS

Sociodemographic and economic characteristics of study participants

Of the 733women eligible for this study, 730 were enrolled. Two (0.27%) of the participants were lost to follow-up. Of these two participants, one was from the pre-eclamptic group and one from the normotensive group. One participant refused to participate in the study. During the follow-up, eight normotensive women developed pre-eclampsia. We; thus, included these eight women in the exposed group (figure 1).

The mean gestational age at the diagnosis of pre-eclampsia was 32.85±3.25 weeks and that of normotensive women was (33.90±2.75) weeks. The mean duration of follow-up of women with pre-eclampsia was 6.51±3.15 weeks and that of normotensive women was 5.68±2.97 weeks (figure 1).

The mean age of the women with pre-eclampsia was 25.42±4.76 years, and 24.6±4.48 years for the normotensive group. Nearly half of the women had pre-eclampsia (45.2%, 164/363) were attended primary school education, compared with the normotensive group (39.5%, 145/367, p<0.05). A higher proportion of women with pre-eclampsia was observed (81%, 294/363) among women who resided in rural areas compared with urban residents (19%, 69/363), p<0.001) (table 1).

Obstetric characteristics of women with pre-eclampsia and normotensive

Compared with the normotensive group (35.7%, 131/367), a higher proportion of women with pre-eclampsia (40.8%, 148/363, p<0.001) was observed in Yirgalem hospital. A higher proportion of twins was reported in the pre-eclampsia group (7.2%, 26/363) compared with the normotensive group (4.6%, 17/367,

Table 1 Sociodemographic and economic characteristics of women with pre-eclampsia and normotensive women in Sidama region, Southern Ethiopia from 8 August 2019 to 1 October 2020

Variables	Women with pre-eclampsia (n=363)	Normotensive women (n=367)	Total (n=730)	P value
Maternal age (in year)	25.42±4.76	24.6±4.48	25.02±4.64	
Maternal education				
No formal education	33 (9.1)	16 (4.3)	49 (6.7)	<0.05
Primary education	164 (45.2)	145 (39.5)	309 (42.3)	
Secondary education	98 (27)	110 (30)	208 (28.5)	
College/university	68 (18.7)	96 (26.2)	164 (22.5)	
Husband education				
No formal education	15 (4.1)	7 (1.9)	22 (3)	<0.05
Primary education	122 (33.6)	87 (23.7)	209 (28.5)	
Secondary education	99 (27.3)	117 (31.9)	216 (29.6)	
College/university	127(35)	156 (42.5)	283 (38.8)	
Maternal occupation				
House wife	191 (52.6)	163 (44.4)	354 (48.5)	>0.05
Merchant	70 (19.3)	76 (20.7)	146 (20)	
Employed	64 (17.6)	88 (24)	152 (20.8)	
Student	23 (6.3)	21 (5.7)	44 (6)	
Farmer	10 (2.8)	10 (2.7)	20 (2.7)	
Daily labourer	5 (1.4)	9 (2.5)	14 (1.9)	
Husband occupation				
Employed	116 (32)	149 (40.6)	265 (36.3)	<0.05
Merchant	126 (34.7)	136 (37.1)	262 (35.9)	
Farmer	75 (20.7)	45 (12.3)	120 (16.4)	
Daily labourer	31 (8.5)	23 (6.3)	54 (7.4)	
Student	7 (1.9)	10 (2.7)	17 (2.3)	
Unemployed	8 (2.2)	4 (1.1)	12 (1.6)	
Place of residence				
Rural	294 (81)	331 (90.4)	104 (14.3)	<0.001
Urban	69 (19)	35 (9.6)	625 (85.7)	
Wealth Index				
Low	157 (43.3)	95 (26)	252 (34.6)	<0.001
Middle	105 (28.9)	139 (28)	244 (33.5)	
Rich	101 (27.8)	132 (36.1)	233 (32)	

A p<0.05 was considered statistically significant.

p>0.05). However, there was no significant difference between the two groups. A higher proportion of women with pre-eclampsia (28.4%, 103/363) was observed among women who were admitted at <34 weeks compared with the normotensive group (24.5%, 91/367, p<0.05) (table 2).

Incidence of adverse perinatal outcomes women with pre-eclampsia

There were 224 adverse perinatal outcomes observed in the 363 pre-eclampsia women compared with 136 adverse perinatal outcomes in the 367 normotensive women (p<0.001). There were 23 early neonatal deaths reported in the pre-eclampsia group compared with 6 deaths in the normotensive group (p<0.001). Also, there were 96 preterm births observed in the pre-eclampsia group compared with 17 preterm births in the normotensive group (p<0.001). There were 35 perinatal deaths reported in the pre-eclampsia group compared with 16 deaths in the normotensive group (p<0.05) (table 3).

Women with or without severity features of pre-eclampsia on adverse perinatal outcomes and other risk factors

In the bivariable log-binomial logistic regression model, the following variables were identified as candidate variables for multivariable log-binomial logistic regression analysis: maternal age, maternal and husband's education, maternal and husband's occupation, parity,

Table 2 Obstetrics factors for women with pre-eclampsia and normotensive women in Sidama region, Southern Ethiopia from 1 August 2019 to 1 October 2020

Variables	Women with pre-eclampsia (n=363)	Normotensive women (n=367)	Total (n=730)	P value
Fetal sex				
Male	202 (55.6)	195 (53.1)	397 (54.4)	>0.05
Female	161 (44.4)	172 (46.9)	333 (45.6)	
No of neonates delivered				
Singleton	337 (92.8)	350 (95.4)	687 (95.4)	>0.05
Twin	26 (7.2)	17 (4.6)	43 (5.9)	
Gravida				
1	46 (12.7)	77 (21)	123 (16.8)	>0.05
2–3	253 (69.7)	208 (56.7)	461 (63.2)	
≥4	64 (17.6)	82 (22.3)	146 (20)	
Parity				>0.05
Nullipara	12 (3.3)	5 (1.4)	17 (2.3)	
1	37 (10.2)	94 (25.6)	131 (17.9)	
2–3	264 (72.4)	222 (60.5)	486 (66.6)	
≥4	50 (13.8)	46 (12.5)	96 (13.2)	
Interpregnancy Interval (IPI)				
<24 months (short (IPI)	8 (2.2)	4 (1.1)	12 (1.6)	<0.001
24–59 months (optimal IPI)	180 (49.6)	263 (71.7)	443 (60.7)	
60+ months (long IPI)	115 (31.7)	35 (9.5)	150 (20.5)	
Not applicable (prim)	60 (16.5)	65 (17.7)	125 (17.1)	
Gestational age at admission (week)				
<34	103 (28.4)	91 (24.5)	194 (26.6)	<0.05
34–37	260 (71.6)	276 (75.5)	536 (73.4)	
Maternal intensive care unit admission				
Yes	5 (1.4)	1 (0.3)	6 (0.8)	>0.05
No	358 (98.6)	366 (99.7)	724 (99.2)	
Gestational age at delivery (week)				
Extremely preterm (<28)	10 (2.8)	5 (1.4)	15 (2.1)	<0.001
Very preterm (28–32)	24 (6.6)	1 (0.3)	25 (3.4)	
Moderate to late preterm (32–37)	123 (33.9)	67 (18.3)	190 (26)	
Term+ (≥37)	206 (56.7)	294 (80)	500 (68.5)	
Hospitals				
Adare general hospital	60 (16.5)	109 (29.7)	169 (23.2)	
Hawassa referral hospital	53 (14.6)	47 (12.8)	100 (13.7)	
Yirgalem general hospital	148 (40.8)	131 (35.7)	279 (38.2)	<0.001
Hula primary hospital	7 (1.9)	7 (1.4)	12 (1.6)	
Bona general hospital	51 (14)	29 (7.9)	80 (11)	
Chuko primary hospital	11 (3)	6 (1.6)	17 (2.3)	
Daye primary hospital	33 (9.1)	40 (10.9)	73 (10)	

A p<0.05 was considered statistically significant.

Table 3 Neonatal outcomes among women with pre-eclampsia and normotensive women in Sidama region Southern Ethiopia from 8 August 2019 to 1 October 2020

Variables	Women with pre-eclampsia (n=363)	Normotensive women (n=367)	Total (n=730)	P value
Birth weight of neonate (g)				
<1500	33 (9.1)	6 (1.6)	39 (5.3)	<0.001
1500–2499	103 (28.4)	31 (8.4)	134 (18.4)	
2500–3999	211 (58.1)	302 (82.3)	513 (70.3)	
≥4000	16 (4.4)	28 (7.6)	44 (6)	
Apgar score <7 at 1 min	64 (17.6)	52 (14.2)	116 (15.9)	<0.05
Apgar score <7 at 5 min	62 (17.1)	54 (14.7)	116 (15.9)	>0.05
Intrauterine growth restriction	22 (6.1)	4 (1.1)	26 (3.6)	<0.001
Stillbirth	21 (5.8)	11 (3)	32 (4.4)	<0.05
Early neonatal death	23 (6.3)	6 (1.6)	29 (4)	<0.001
Preterm birth	96 (26.4)	17 (4.6)	113 (15.5)	<0.001
Perinatal death	35 (9.6)	16 (3.8)	49 (6.7)	<0.05
Low birth weight	98 (27)	73 (19.9)	171 (23.4)	<0.05
Small for gestational age	66 (18.2)	30 (8.2)	96 (13.2)	<0.001
Birth asphyxia	39 (10.7)	15 (4.1)	54 (7.4)	<0.05
Admission to NICU	88 (24.2)	39 (10.6)	127 (17.4)	<0.001
Adverse perinatal outcomes	224 (61.7)	136 (37.1)	360 (49.3)	<0.001

A p<0.05 was considered statistically significant.
NICU, neonatal intensive care unit.

gravidity, wealth index, women without severe features of pre-eclampsia, mode of delivery, women with severe features of pre-eclampsia, maternal ICU admission, systolic and diastolic BP.

After controlling for confounders, we identified significant risk factors for adverse perinatal outcomes as women with severe features of pre-eclampsia, those admitted to hospital at <34 weeks, women without severe features of pre-eclampsia, maternal age, women with no formal education or with only primary school education and women with high systolic BP.

Women with severe feature of pre-eclampsia had a 46% (adjusted relative risk, aRR 1.46, 95% CI 1.38 to 2.77) higher risk for adverse perinatal outcomes compared with women without severe features of pre-eclampsia. Women without severe features of pre-eclampsia had a 39% (aRR 1.39, 95% CI 1.21 to 1.56) higher risk for adverse perinatal outcomes compared with women in the normotensive group. Maternal age was found to have a significantly higher risk on adverse perinatal outcomes of women with pre-eclampsia (β=1.9, 95% CI 1.5 to 3.3) compared with normotensive women, while other factors were kept constant. Women who were admitted to the hospital at <34 weeks had a 15% (aRR 1.15, 95% CI: 1.03 to 1.28) higher risk for adverse perinatal outcomes compared with women who were admitted between 34 and 37 weeks (table 4).

DISCUSSION

In this study, more adverse perinatal outcomes occurred among women with pre-eclampsia compared with normotensive women after controlling for confounders. Perinatal death, stillbirth, small for gestational age, preterm birth, birth asphyxia and low birth weight were higher in the pre-eclampsia group compared with the normotensive group. We identified significant risk factors for adverse perinatal outcomes such as women with severe feature of pre-eclampsia and women who were admitted to the hospital at <34 weeks.

A higher adverse perinatal outcome was observed in the pre-eclampsia group compared with the normotensive group. This finding was similar to another study conducted in southwest Ethiopia in 2021, which found that a higher rate of adverse perinatal outcomes was observed among women with HDPs (64.1%) compared with normotensive women (32.8%).[27] This finding was lower than the finding of a study conducted in Tigray Ethiopia in 2020 (66.4% vs 22.2%).[20] A reduction in the utilisation gaps of ANC practice is needed to end preventable deaths of newborns.[28] Women who had not had ANC attendance were three times more likely to have unfavourable perinatal outcomes as compared with women who had attended ANC.[14]

A higher perinatal death rate was reported in the pre-eclampsia group compared with the normotensive group. This finding was consistent with another study

Table 4 A multivariable log-binomial logistic regression model for risk factors for adverse perinatal outcomes among women with pre-eclampsia in Sidama region southern Ethiopia from 8 August 2019 to 1 October 2020

	Adverse perinatal outcomes			
Variables	**Yes (n=360)**	**No (n=370)**	**Unadjusted RR (95% CI)**	**Adjusted RR (95% CI†)**
Maternal age (in year)	25.42±4.76	24.6±4.48	2.2** (1.8 to 3.9)	1.9* (1.5 to 3.3)
Parity				
Nullipara	11 (64.7)	6 (35.3)	0.94 (0.64 to 1.78)	0.86 (0.65 to 1.78)
1	139 (43.7)	179 (56.3)	0.68*** (0.57 to 0.80)	0.86 (0.60 to 1.22)
2–3	148 (51.7)	138 (48.3)	0.83* (0.70 to 0.97)	0.93 (0.72 to 1.19)
≥4	62 (56.9)	47 (43.1)	1	1
Maternal education				
No formal education	32 (63.3)	17 (34.7)	1.52** (1.19 to 1.93)	1.41** (1.14 to 1.73)
Primary education	175 (56.6)	134 (43.4)	1.30** (1.08 to 1.57)	1.22* (1.06 to 1.46)
Secondary education	84 (40.4)	124 (59.6)	0.99 (0.79 to 1.23)	0.56 (0.44 to 1.25)
College/university	69 (42.1)	95 (57.9)	1	1
Husband education				
No formal education	17 (77.3)	5 (22.7)	1	1
Primary education	123 (58.9)	86 (41.1)	0.76* (0.59 to 0.98)	0.92 (0.76 to 1.97)
Secondary education	105 (48.6)	111 (51.4)	0.62** (0.48 to 0.81)	0.83 (0.67 to 1.04)
College/university	115 (40.6)	168 (59.4)	0.52*** (0.40 to 0.68)	0.74 (0.57 to 2.97)
Wealth Index				
Low	176 (69.6)	77 (30.4)	1.77*** (1.48 to 2.12)	1.72 (0.44 to 2.06)
Middle	98 (40.2)	146 (59.8)	1.03 (0.83 to 1.29)	1.02 (0.82 to 1.28)
Rich	86 (36.9)	147 (63.1)	1	1
Gravidity				
1	127 (42.6)	171 (57.4)	0.81 (0.91 to 1.96)	0.84 (0.72 to 1.97)
2–3	154 (52.4)	140 (47.6)	0.96 (0.80 to 1.15)	0.95 (0.81 to 1.11)
≥4	79 (57.2)	59 (42.8)	1	1
Mode of delivery				
Spontaneous vaginal delivery	205 (51.5)	193 (48.5)	0.89 (0.77 to 1.04)	0.12 (0.78 to 1.16)
Caesarean section	143 (46.3)	166 (53.7)	1.01 (0.67 to 1.561)	1.32 (0.85 to 2.34)
Vacuum assisted delivery	12 (52.2)	11 (47.8)	1	1
Gestational age at admission (week)				
<34	113 (58.2)	81 (41.8)	1.11 (0.97 to 1.28)	1.15* (1.03 to 1.28)
34–47	247 (46.1)	289 (53.9)	1	1
Maternal ICU admission				
Yes	4 (80)	1 (20)	1.67**(1.16 to 2.41)	1.22 (0.75 to 3.19)
No	356 (49.1)	369 (50.9)	1	1
Women without severe feature of pre-eclampsia				
Yes	159 (66.8)	79 (33.2)	1.67*** (1.39 to 1.93)	1.39*** (1.21 to 1.56)
No	201 (40.9)	291 (59.1)	1	1
Women with severe feature of pre-eclampsia				
Yes	99 (79.2)	26 (20.8)	1.58*** (1.25 to 1.85)	1.46*** (1.38 to 2.77)
No	261 (43.1)	344 (56.9)	1	1
Eclampsia				
Yes	32 (82.1)	7 (17.9)	1.61*** (1.38 to 1.92)	1.34 (0.41 to 1.83)
No	328 (47.5)	363 (52.5)	1	1

Continued

Table 4 Continued

Variables	Adverse perinatal outcomes		Unadjusted RR (95% CI)	Adjusted RR (95% CI†)
	Yes (n=360)	No (n=370)		
Systolic blood pressure (mm Hg)				
<140	136 (37.1)	231 (62.9)	1	1
140–159	162 (62.3)	98 (37.7)	1.55*** (1.35 to 1.85)	1.37*** (1.19 to 1.59)
≥160	62 (60.2)	41 (39.8)	1.60*** (1.33 to 1.92)	1.34** (1.13 to 1.58)
Diastolic blood pressure (mm Hg)				
<90	136 (37.1)	231 (62.9)	1	1
90–109	180 (62.3)	109 (37.7)	1.68*** (1.43 to 1.97)	1.12 (0.21 to 2.03)
≥110	44 (59.5)	30 (40.5)	1.60*** (1.27 to 2.02)	1.43 (0.96 to 2.43)
Magnesium sulfate treatment				
Yes	74 (43.8)	95 (56.2)	0.65*** (0.57 to 0.74)	0.56 (0.36 to 1.23)
No	286(51)	275(49)	1	1
Antihypertensive drug treatment				
Yes	124 (33.5)	178 (49.4)	0.64*** (0.56 to 0.73)	0.84 (0.40 to 1.75)
No	246 (66.5)	182 (50.6)	1	1
Dexamethasone treatment				
Yes	56 (48.7)	59 (51.3)	0.54 (0.34 to 1.81)	0.45 (0.23 to 1.98)
No	304 (49.4)	311 (50.6)	1	1

*P<0.05, **p<0.01, ***p<0.001.
ICU, intensive care unit; RR, relative risk.

conducted in southwest Ethiopia in 2021, which found that a higher perinatal death rate occurred in women with HDPs (21.2%) compared with normotensive women (6.2%).[27] This finding of this study was also lower than a study conducted in Ethiopia in 2020 (15.0% vs 2.5%).[20] Women who attended at least one ANC were found to have a 58% lower risk of perinatal mortality as compared with women who did not receive any ANC follow-up in Ethiopia.[29]

A higher stillbirth rate was observed in the pre-eclampsia group compared with the normotensive group. This finding was slightly lower than the findings of another study conducted in Ghana in 2015, which found that a higher stillbirth rate was observed among women with pre-eclampsia (6.2%) compared with normotensive women (1.3%).[30] Similarly, this finding was lower than the finding of a study conducted in Multicounty survey in 2014 (6.4% vs 1.9%).[31] Women who attended at least one ANC session were found to have a 66% lower risk of stillbirth rate as compared with mothers who did not receive any ANC follow-up in Ethiopia.[29]

A higher small for gestational age rate was observed in the pre-eclampsia group compared with the normotensive group. This finding was higher than another study conducted in Ghana in 2015, which found that a small for gestational age rate was observed among more women with pre-eclampsia (14.3%) compared with normotensive women (2.3%)[30] and in Southwest Ethiopia in 2021 (9.3% vs 2.3%).[27] This finding was lower than the finding of another study conducted in Ethiopia in 2020 (36.7% vs 10.7%).[20] Early detection and management of pre-eclampsia may reduce small for gestational age rate among newborns.

A higher preterm birth rate was observed in the pre-eclampsia group compared with the normotensive group. This finding was lower than a study conducted in Ethiopia, which found that a higher preterm birth rate was observed among women with pregnancy-induced hypertension (PIH) (40.8%) compared with normotensive women (5.6%).[20] This finding was also lower than the findings of a study conducted in southwest Ethiopia in 2021 (39.4% vs 10.6%).[27] Furthermore, this finding was slightly lower than a study conducted in Haiti in 2019 (27.9% vs 9.9%).[32] The difference in incidence of preterm birth across the studies might be due to the difference in quality of ANC services and the difference in guidelines used for the management of pre-eclampsia.

A higher birth asphyxia rate was reported in the pre-eclampsia group compared with the normotensive group. This finding was higher than the finding of another study conducted in Ethiopia in 2020, particularly in the Tigray region, which found that the birth asphyxia rate was higher among women with PIH (39.6%) compared with normotensive women (10.9%).[20] This finding was slightly higher than the birth asphyxia rate reported (10.7%), compared with the study conducted in North West Ethiopia in 2018 (10.1%).[9] Monitoring the fetus for signs of asphyxia, usually by assessing the fetal heart rate either

during prenatal care for fetuses at risk or during labour, can determine which fetuses are at risk of stillbirth.[33]

A higher low birthweight rate was observed in the pre-eclampsia group compared with the normotensive group. This finding was higher than findings of the Multicounty Survey in 2014, which found that a higher low birth weight rate was reported among women with pre-eclampsia (26.1%) compared with normotensive women (9.4%)[31] and a study conducted in southwestern Ethiopia in 2021, which found that a higher low birth weight rate was observed among women with HDP (39.8% vs 12.7%).[27] This finding was lower than the findings of another study conducted in Ghana in 2015 (46.2% vs 6.8%).[30] One study in Ethiopia found that women who did not attend ANC follow-up were three times more likely to deliver low birth weight babies compared with those who had at least one ANC follow-up.[34]

Women with severe features of pre-eclampsia had a higher risk for adverse perinatal outcomes compared with women without severe features of pre-eclampsia. A study from Brazil in 2018 found that in terms of pre-eclampsia with severity, severe pre-eclampsia was associated with birth weight <2500 g in 59% of cases, and mild PE was associated with birth weight ≥2500 g in 85.5% of cases.[1] In 2015, one study from India found that those women with severe pre-eclampsia had a higher perinatal mortality when compared with those with mild pre-eclampsia.[35]

Women who were admitted to a hospital at <34 weeks had a higher risk of adverse perinatal outcomes compared with women who were admitted between 34 and 37 weeks. This finding was similar to another study conducted in Ethiopia in 2020 that patients with early onset of pre-eclampsia without severe feature were 25.9 times more likely to develop perinatal complication as compared with late-onset pre-eclampsia after 34 weeks.[16] These increased perinatal complications might be explained by the progression of pre-eclampsia to severe diseases in those women who developed pre-eclampsia before 34 weeks, which is associated with high preterm birth.[36]

Limitations of the study

One limitation could be recall bias linked to gestational age, which was calculated based on the women's recall of their last menstrual period. However, women who could not remember the approximate gestational age were given an ultrasound scan. Social desirability could have been present because data were collected in face-to-face interviews, which could have led to socially acceptable answers. This study is not generalisable as it was limited to one region of the country, and it was limited to women who received hospital care. It also only measured short-term morbidity in infants, so it did not assess the risk of pre-eclampsia on later mortality, growth, neurodevelopment or other important health outcomes. One strength that could be linked to this study was based on a prospective cohort, which minimised the risk of selection and recall bias.

CONCLUSION

In this study, more adverse perinatal outcomes occurred among women with pre-eclampsia after controlling for confounders. Early detection and management of pre-eclampsia may improve maternal and infant outcomes. We identified significant risk factors for adverse perinatal outcomes as women with severe features of pre-eclampsia, those admitted to hospital at <34 weeks, women without severe features of pre-eclampsia, maternal age, women with no formal education or with only primary school education, and women with high systolic BP. This paper highlights the significantly elevated perinatal risks associated with pre-eclampsia, especially when it has severe features.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This study was reviewed and ethically approved by the Institutional Review Board of the University of Gondar R.No: (O/V/P/RCS/044/2019 in March 2019). Participants gave informed consent to participate in the study before taking part.

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