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Predictors of unfavorable perinatal outcomes among women with early-onset preeclampsia without severe features: a retrospective cohort study at Wachemo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital

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Abstract

Background

Although the prognosis of preeclampsia without severity features is favorable, its adverse forms are a major cause of perinatal and maternal morbidity and mortality. There is no data on predictors and survival time to develop maternal and perinatal unfavorable outcomes of preeclampsia without severity features and normotensive women in the study area.

Objective

To determine the incidence and predictors of unfavorable perinatal outcomes of early-onset preeclampsia without severity feature and normotensive pregnant women in Wachemo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital,2022 G.C.

Methods

Hospital-based retrospective cohort study was conducted among 132 exposed and 132 unexposed pregnant women at Wachemo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital from January 1/2019 to December 30/2021. The incidence of unfavorable perinatal outcomes was calculated from the total adverse outcome to the sample(population) time. Survival probabilities were shown in the Kaplan-Meier graph. Data were entered using the epi data version 4.6 and exported to STATA version 14. Variables having $P < 0.25$ in bivariate analysis were fitted for multivariate Cox.

Results

A total of 264 pregnant women were followed for 2305.96 person weeks for perinatal outcomes. The incidence of unfavorable perinatal outcomes was 19.1 per 1000 person-weeks. Gestational age at admission (AHR: 11.81 95%CI:5.94–23.46)), medical illness (AHR: 3.85 95%CI:2.00-7.40), exposure status (AHR:2.64 95%CI:1.20–5.79)) and maternal outcome (AHR: 5.15, 95%CI:2.67–9.92) were predictors of the unfavorable perinatal outcome.

Conclusion

The Kaplan-Meier survival function graph shows the cumulative survival proportion appears to be much higher in the unexposed group than in the exposed group. There were indicators that were significant for maternal and perinatal outcomes.

Introduction

Preeclampsia is defined as the new onset of hypertension and proteinuria in previously normotensive women after 20 weeks of gestational age (1). Recently the diagnostic criteria have been changed, and Fetal Growth Restriction (FGR) is included (2).

In the past 30 years pathogenesis, pathophysiology, treatment options, predictors of preeclampsia, and associations with risk factors like smoking, stroke, and cardiovascular disease have been the subject of extensive research. Preeclampsia can be divided into two distinct disease entities: early-onset and late-onset preeclampsia. Early onset preeclampsia (EOP) occurs before 34 weeks of pregnancy, whereas late-onset preeclampsia (LOP) occurs at or after 34 weeks of gestation. Even though the presenting characteristics are similar, they are associated with various maternal and fetal outcomes, biochemical markers, heritability, and clinical characteristics (3).

World Health Organisation (WHO) multicountry survey has shown perinatal mortality is three to five times higher in women with preeclampsia/eclampsia syndrome than in women without the disorders (4).

In Ethiopia, the incidence of early-onset preeclampsia without severity feature was 3%, and perinatal mortality was 42.6 per 1000. It was 5.22 and 25.9 times riskier to develop maternal and perinatal complications compared to late-onset preeclampsia (5).

EOP poses a management dilemma. Delivery may benefit the mother but may harm a premature fetus. Expectant management in women with EOP before 34 weeks' gestation may reduce neonatal complications and stay in a Neonatal Intensive Care Unit (NICU). Although this could aggravate the maternal condition (6, 7).

Before deciding on outpatient follow-up and management, the International Societ for the Study of Hypertension in Pregnancy (ISSHP) advises admitting all patients with preeclampsia; following assessment in the hospital some women may be managed in a specialized outpatient setting, such as day assessment units in a hospital with appropriate expertise (8, 9).

There is no data on predictors and survival time to develop maternal and perinatal unfavorable outcomes of preeclampsia without severity features and normotensive women in the study area.

Therefore the study aimed to investigate the incidence predictors and survival time of unfavorable perinatal outcomes among preeclampsia without severe features and normotensive pregnant women between the gestational age of 28 to 34 weeks at Wachemo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital (WCUNEMMCSH), Ethiopia.

Methods And Materials

Study Setting

The study was conducted at WCUNEMMCSH from January 1/2019 to December 30/2021. The Hospital was established in 1984 G.C in Hadiya zone, Hossana town which is located 232 km from Addis Ababa

(capital city of Ethiopia) and 192 km from Hawassa (capital city of Southern Nation and Nationalities Regional State) and provides preventive, curative, and rehabilitative services for 3.4 million population with a total of 262917 and 10881 Outpatient Diagnosis (OPD) and Inpatient attendants in 2021 respectively. The hospital had a total of 1172 staff and among them, 588 of them are health professionals. Of 584 Technical staff,269 are administrative staff. The hospital provides different services like an adult Intensive Care Unit, Neonatal Intensive Care Unit, Psychiatry, Ophthalmology, Dental, Medical, Pediatrics, Surgical, Orthopedic, Gynecology, and Obstetrics services.

The gynecology and Obstetrics department had nine Gynecologists and Obstetricians, two were females, and 68 midwifery professionals. The department provided different services like delivery, outpatient, ANC, emergency, and inpatient services.

There were 15Gynecolgy and 12 Obstetric inpatient beds. The hospital had 4 Laboring coaches and 7Operation room tables.

In 2021 a total of 10167 mothers got delivery service.

Study Design and Period

Hospital-based retrospective cohort study was conducted from June,1/2022 to June,30/2022.

Inclusion and Exclusion Criteria

All delivered women managed in WUNEMMCSH with the diagnosis of early-onset preeclampsia without severity feature and normotensive pregnant women from January 1/2019 to December 30/2021. Pregnant mothers whose chart was not complete or lost and died on arrival.

Sample Size Determination and Sampling Technique

The required optimal sample size was determined by using the Epi Info version 7 double population formula with the assumptions of a 95% significance level (2-sided), 5% margin of error, power of 80%, and 1:1 Ratio.

Table 1
Sample size estimation of unfavorable perinatal outcome of early-onset preeclampsia and normotensive pregnant women in WUNEMMCSH,2022.

Variable	CI (%)	Power	Ratio	% Of Unexposed in Outcome	% Of Exposed in Outcome	Final sample size (10% data incompleteness)	Reference
Stillbirth	95	80	1	10.2	1.7	**268**	(10)
Low birth weight	95	80	1	6.1	37.7	59	(10)
Preterm delivery	95	80	1	5.6	40.8	51	(10)
Preterm labor	95	80	1	2.5	43.75	37	(11)

From January 1st, 2019, to December 30th, 2021G.C, there were 858 pregnant mothers managed for early onset preeclampsia without severity feature and 14,070normotensive women. From January 1st, 2019, to December 30th, 2021G.C, pregnant mothers managed for early onset preeclampsia without severity features (exposed group) and normotensives pregnant women (unexposed group) were obtained by simple random sampling technique using computer generated random numbers.

Four charts were excluded from the total sample size, two from exposed and unexposed.

Data Collection Technique and Tool

The data were collected from high-risk registration books, delivery registration books, and patient charts using a well-prepared checklist. The checklist incorporates socio-demographic characteristics, obstetrics history, laboratory results, and maternal and fetal outcomes. Data were collected by trained BSc Midwives under strict supervision.

Data Quality and Management

The data collection tool was adapted from prior research and adjusted to fit the context. The checklist was written in English. Data collectors and a supervisor received two-day training on the data abstraction checklist and collection method. The supervisor and principal investigator monitored and supervised the data collection process closely.

Data Processing and Analysis

All collected data were rechecked for completeness, coded, entered using Epi data version 4.6.0.2, and exported to STATA version 14 for analysis. The data was recoded, categorized, and sorted to facilitate

analysis. Descriptive statistics were analyzed and presented in tables. Kaplan-Meier survival function among the exposed and unexposed groups was used to compare survival probability between the groups. Then statistically significant difference was checked by the log-rank test. Bivariable analysis was done to see associations between the dependent and independent variables. Variables having a p-value of less than 0.25 were included in the multivariable Cox regression analysis. Those variables having a p-value < 0.05 were considered statistically significant.

Proportional-hazard assumption test was used for selecting fitted proportional hazard models. Schoenfeld's residuals test was performed. The global tests were significant, with p > 0.05. The Cox regression model was fitted for analysis.

Results

Sociodemographic characteristics

Most of the women lived in urban 182 (68.9%) (Table 2).

Table 2
Sociodemographic characteristics among early-onset preeclampsia without severity feature and normotensive pregnant women in WCUNEMMCSH, 2022.

Variables		Status of Exposure		Total
		Yes(N = 132)	No(N = 132)	
Address	Rural	42(31.8%)	40(30.3%)	82(31.1%)
	Urban	90(68.2%)	92(69.7%)	182(68.9%)
Age	<=18	2(1.5%)	2(1.5%)	4(1.5%)
	18–35	125(94.7%)	128(97.0%)	253(95.8%)
	>=35	5(3.8%)	2(1.5%)	7(2.7%)

Maternal medical and obstetric factors

Multi-Gravidity among exposed and normotensive women was 98 (74.2%) and 83 (62.8%) respectively. Singleton pregnancy was the most common type of pregnancy, 247 (93.6%) of the total. Forty-four (33.3%) of preeclamptic women (exposed group) had a history of medical illness. Of these pre-existing hypertension, 30 (68.2%) and pregestational diabetes mellitus 7 (15.9%) were common comorbidities (Table 3).

Table 3
Obstetrical and medical history among early-onset preeclampsia without severity feature and normotensive pregnant women in WCUNEMMCSH, 2022.

Variables		Status of Exposure		Total
		Yes	No	
Gravidity	Primigravida	34(25.8%)	49(37.1%)	83(31.4%)
	Multigravida	98(74.2%)	83(62.9%)	181(68.6%)
Parity	Nulliparous	5(3.8%)	8(6.1%)	13(4.9%)
	Multiparous	80(60.6%)	66(50.0%)	146(55.3%)
	Grand Multiparous	47(35.6%)	58(43.9%)	105(39.8%)
Type of pregnancy	Singleton	117(88.6%)	130(98.5%)	247(93.6%)
	Twin	15(11.4%)	2(1.5%)	17(6.4%)
History of medical illness	Yes	44(33.3%)	2(1.5%)	46(17.4%)
	No	88(66.7%)	130(98.5%)	82.6%
Type of medical illness	Pre-existing hypertension	30(68.2%)	1(50%)	31(67.4%)
	History of Renal Disease	3(6.8%)	1(50%)	4(8.7%)
	History of Cardiovascular Disease	3(6.8%)	0	3(6.5%)
	Pre-gestational diabetes mellitus	7(15.9%)	0	7(15.2%)
	Toxic goiter	1(2.3%)	0	1(2.2%)
Were drugs given to decrease Blood Pressure	Yes	54(40.9%)	1(0.8%)	55(20.8%)
	No	78(59.1%)	131(99.2%)	209(79.2%)
If yes what was/were the drug/s?	Methyldopa	38(70.4%)	0	38(69.1%)
	Nifedipine	2(3.7%)	0	2(3.6%)
	Hydralazine	8(14.8%)	0	8(3.0%)
	MgSo4	4(7.4%)	1(100%)	5(14.5%)
	Aspirin	2(3.7%)	0	2(3.6%)

Perinatal unfavorable outcomes incidence rate

Perinatal unfavorable outcome a total of 264 pregnant women were enrolled and followed for a minimum and the maximum follow-up time of 2 and 14.4 weeks respectively giving 2305.96 person-

weeks observation. The mean follow-up time was 8.73 weeks. The overall incidence rate of the unfavorable outcome during the follow-up time among pregnant women was 19.1 out of 1000 observations. Of this, the total time at risk for preeclamptic women (exposed group) was 1071.3 and 1234.66 for the unexposed group with an incidence rate of 31.74 per 1000 and 8.12 per 1000 respectively (Table 4).

Table 4
The incidence rate in person per week of perinatal unfavorable outcome per 1000 among early onset preeclampsia without severity feature and normotensive pregnant women in WCUNEMMCSH,2022.

Variables		Status of Exposure		Total
		Yes	No	Incidence Rate
Unfavorable perinatal outcomes	LBW	12.1	1.6	6.5
	IUGR	3.7	2.4	3.0
	Low APGAR score	4.7	0.8	2.6
	Preterm birth	2.8	0.8	1.7
	Stillbirth	3.7	0.8	1.3
	IUFD	4.7	0.8	2.6
	Death	1.9	0.8	1.3

Survival status of pregnant women for perinatal outcome

The Kaplan-Meier survival function graph shows the cumulative survival proportion appears to be much higher in the unexposed group than in the exposed (preeclamptic pregnant women) (Fig. 1). A log-rank test was run to determine if there were statistical differences in the survival distribution for the unexposed and exposed groups. The survival distributions were statistically significantly different, $\chi 2(2) = 24.93$, $p < .0005$. The median survival time of pregnant women with preeclampsia was 12.4 weeks. However, the median time for normotensive pregnant women was not reached.

predictors of unfavorable perinatal outcome among pregnant women

In Bivariable Cox proportional hazard regression type of pregnancy, Antenatal Care (ANC) follow-up, gestational age at admission, history of medical illness, proteinuria, exposure status, and the maternal outcome were a candidate for multivariable analysis (Table 5).

Table 5
Bivariable Cox regression analysis of predictors of unfavorable perinatal outcome at WCUNEMMCSH, 2022.

Variables	Category	Status		CHR (95%CI)	p-value
		Favorable outcome N (%)	Unfavorable outcome N (%)		
Residence	Rural	74 (90.2)	8 (9.8)	1.51(0.69, 3.33)	0.303
	Urban	155 (85.2)	27 (14.8)	1	
Maternal age	< 35	207 (84.1)	39 (15.9)	1	
	≥ 35	13 (72.2)	5 (27.8)	2.11(0.83, 5.36)	0.12
Gravidity	Primigravida	70 (84.3)	13 (15.7)	0.93(0.50, 1.72)	0.680
	Multigravida	159 (87.8)	22 (12.2)	1	
Parity	Nulliparous	76 (80.9)	18 (19.1)	0.93(0.58, 1.49)	0.75
	Multiparous	125 (85.0)	22 (15.0)	1	
	Grand Multiparous	19 (82.6)	4 (17.4)	0.96(0.54, 1.70)	
Type of pregnancy	Singleton	218 (88.3)	29 (11.7)	1	**0.005***
	Twin	11 (64.7)	6 (35.3)	3.52(1.45, 8.53)	
Number of ANC	< 3 visits	136 (80.0)	34 (20.0)	2.28(1.12, 4.62)	**0.023**
	>=3visits	84 (89.4)	10 (10.6)	1	
Gestational age at admission	< 37	1 (5.6)	17 (94.4)	12.06(6.49,22.42)	**0.000***
	>=37	219 (89.0)	27 (11.0)	1	
History of medical illness	Yes	31 (67.4)	15 (32.6)	3.34(1.78, 6.24)	**0.001***
	No	189 (86.7)	29 (13.3)	1	
Proteinuria	< 2	20 (64.5)	11 (35.5)	4.17(2.08, 8.34)	**0.000***
	>=2	200 (85.8)	33 (14.2)	1	
Exposure status	Exposed	98 (74.2)	34 (28.5)	5.00(2.46, 10.18)	**0.000***
	Unexposed	122 (92.4)	10 (7.6)	1	
Maternal outcome	Favorable	195 (91.1)	19 (8.9)	1	
	Unfavorable	25 (50.0)	25 (50.0)	7.99(4.37, 14.63)	**0.000***

In multivariable Cox regression analysis after adjusting the confounders' gestational age at admission (AHR: 11.81 CI:5.94, 23.46)), medical illness (AHR: 3.85 CI:2.00, 7.40), exposure status (AHR:2.64 CI:1.20, 5.79)) and maternal outcome (AHR: 5.15 CI:2.67, 9.92) were found predictors of unfavorable perinatal outcome (Table 6). Pregnant women admitted to the hospital before 37 weeks of gestation were 11.81 times hazard to develop unfavorable perinatal outcomes than termly admitted and delivered newborns. Similarly, pregnant women with a history of medical illness were 3.85 times the hazard of unfavorable perinatal outcomes than healthier pregnant women. Pregnant women with unfavorable outcomes were 5.15 times more likely to develop unfavorable perinatal outcomes than pregnant women with favorable outcomes. The hazard of newborns delivered from preeclamptic women was 2.64 times more than the normotensive pregnant women.

Table 6
Multivariable Cox regression analysis of predictors of Unfavorable perinatal outcome at WCUNEMMCSH, 2022.

Variables	Category	Status		CHR (95%CI)	AHR	P value
		Favorable outcome N (%)	Unfavorable outcome N (%)			
Type of pregnancy	Singleton	218 (88.3)	29 (11.7)	1	1	0.183
	Twin	11 (64.7)	6 (35.3)	3.52(1.45–8.53)	1.82(0.75, 4.40	
Number of ANC	< 3 visits	136 (80.0)	34 (20.0)	2.28(1.12–4.62)	1.22(0.57, 2.63)	0.606
	>=3visits	84 (89.4)	10 (10.6)	1	1	
Gestational age at admission	< 37	1 (5.6)	17 (94.4)	12.06(6.49–22.42)	11.81 (5.94,23.46)	**0.000***
	>=37	219 (89.0)	27 (11.0)	1	1	
History of medical illness	Yes	31 (67.4)	15 (32.6)	3.34(1.78–6.24)	3.85(2.00, 7.40	**0.000***
	No	189 (86.7)	29 (13.3)	1	1	
Proteinuria	< 2	20 (64.5)	11 (35.5)	4.17(2.08–8.34)	1.65(0.78, 3.45)	0.183
	>=2	200 (85.8)	33 (14.2)	1	1	
Exposure status	Exposed	98 (74.2)	34 (28.5)	5.00(2.46–10.18)	2.64(1.20, 5.79)	**0.015***
	Unexposed	122 (92.4)	10 (7.6)	1	1	
Maternal outcome	Favorable	195 (91.1)	19 (8.9)	1	1	**0.000***
	Unfavorable	25 (50.0)	25 (50.0)	7.99(4.37–14.63)	5.15(2.67, 9.92)	

Discussion

Our study confirmed the presence of significant differences regarding unfavorable perinatal outcomes between preeclamptic and normotensive pregnant women. The overall incidence rate of unfavorable outcomes, LBW, IUGR, Low APGAR score, Preterm birth, stillbirth, IUFD, and Death, during the follow-up time among pregnant women, was 19.1. The incidence rate among the exposed group (preeclamptic women) was 31.74 and 8.12 among the unexposed group (normotensive pregnant women). In our study, the newborns delivered from preeclamptic women were around three times riskier than the

normotensive pregnant women. Unfavorable maternal and perinatal complications were reported by WHO multinational analysis using 29 Countries from Africa, Asia, Latin America, and the Middle East (12). A study in Sidama reported higher adverse perinatal outcomes in the pre-eclampsia group (61.7%) compared with the normotensive group (37.5%) (13). This finding was similar to another study conducted in southwest Ethiopia in 2021, which found a higher rate of adverse perinatal outcomes among women with HDPs (64.1%) compared with normotensive women (32.8%) (14). Another study conducted in the Tigray region in 2020 reported the overall incidence of adverse perinatal outcomes was higher among women with pregnancy-induced hypertension than among normotensive women (66.4% vs 22.2%) (10). Generally, the above studies confirmed the presence of significant perinatal outcome differences between pregnant women with preeclampsia and normotensive.

The incidence of perinatal complications was 24.7% in Ghana(15) and 40.9% at Saint Paul's Hospital Millennium Medical College (5). This might be due to the study including preeclamptic women with severity features and participants of Gestational age (28–36 weeks) at Paul's.

A higher low birthweight rate (12.1) was observed in the preeclampsia group compared with the normotensive group. This finding was lower than the findings of the Multicountry 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%) (16), even studies conducted in Tigray (37.7%), Ghana (24.7%), and India (22.2%) (10, 15, 17). The difference could be due to the study participants, the quality of antenatal care services, management in the study area, and the interventional delivery for preventing further maternal and perinatal morbidity and mortality irrespective of gestational age.

The magnitude of the Low APGAR score (4.7) among preeclamptic pregnant women without severity features was higher than the incidence in Public Hospitals in Addis Ababa (2.27%), and lower than the incidence in Yekatit 12 Hospital (22.4%)(5, 18). This difference may be due to the difference in service provision, and better management of laboring mothers' and professionals' skills.

The incidence rate of Preterm Birth and Stillbirth were 3.7 and 4.7 person week respectively. Preterm Birth is lower than the incidence in Tigray, Ethiopia 40.8%, Ghana (21.7%), India (24.6%) (10, 15, 17), Still Birth (Tigray, Ethiopia 10%, Mettu, Ethiopia 10%, Jimma University medical center 14.4) (10, 19, 20) and even less than (Zimbabwe 5.4%, Ghana 6.8%) (15, 21). The difference could be due to better counseling and obstetrical management provision.

In our study, Early Neonatal Death (END) was (1.5%). The incidence of early neonatal death was 2.27% at Paul's (5),3.6% at Tigray (10), and 3.8% in Ghana(15). This might be due to skilled professionals' presence and instrumental fulfillment of the NICU.

The most plausible argument for the emergence of preeclampsia is the defective remodeling of spiral arteries, even though the precise mechanisms underlying the perinatal problems are not yet fully understood. Preterm delivery, LBW, and IUGR are all issues brought on by defective placentation, which impairs uteroplacental blood flow(22, 23).

Based on our study the hazard of developing unfavorable perinatal outcomes of pregnant women admitted to the hospital before 37 weeks of gestation were around 12 times riskier to termly admitted and delivered newborns.

Similarly, pregnant women with a history of medical illness were around 4 times the hazard of unfavorable perinatal outcomes than healthier pregnant women. Additionally, pregnant women with unfavorable outcomes were around five times more likely to develop unfavorable perinatal outcomes than pregnant women with favorable outcomes.

Similar to our finding a study in Sidama reported that women who were admitted to a hospital early had a higher risk of adverse perinatal outcomes compared with women who were admitted term and near term (13). 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 (24).

Conclusion

The incidence of unfavorable perinatal outcomes among preeclamptic pregnant women was higher than among normotensive pregnant women. Preterm gestational age at admission, having a history of medical illness, being preeclamptic, and unfavorable maternal outcomes were found predictors of unfavorable perinatal outcomes.

Abbreviations

AHR, Adjusted Hazard Ratio; ANC**,** Antenatal Care; APGAR, Appearance, Pulse, Grimace, Activity, Respiration; CHR, Crude Hazard Ratio; EOP, Early Onset Preeclampsia; HDP, Hypertensive Disorders of Pregnancy; ICU, Intensive Care Unit; ISSHP, International Society for the Study of Hypertension in Pregnancy; IUFD, Intra Uterine Fetal Death; IUGR, Intra Uterine Growth Restriction; Km, Kilometer; LOP, Late Onset Preeclampsia

Declarations

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Authors' contribution

Mellese Tsehay wrote the proposal, participated in data collection, analyzed the data, and drafted the paper. Markos Selamu, Binalfew Tsehay, Dessalegn Shegute, Endale Fikre, Mekdes Folla and Tadele

Yohannes approved the proposal, participated in data analysis, and revised the subsequent draft of the paper. All authors read and approved the final manuscript**.**

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest: None declared

Ethical Consideration

Ethical approval for the study was obtained in accordance with the principles of th Declaration of Helsinki. A formal letter of support was secured from Wachemo University, and ethical clearance was granted by Wachemo University Nigist Elleni Mohammed Memorial Comprehensive Specialized Hospital Ethical Review Committee.

The study was based on a retrospective review of medical records, and that the requirement for informed consent to participate was waived by the Ethical Review Committee.

Respect for participants' privacy and confidentiality was strictly maintained throughout the study. Personal identifiers, including mothers' names were not recorded; instead, unique codes were assigned to each record to ensure anonymity.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

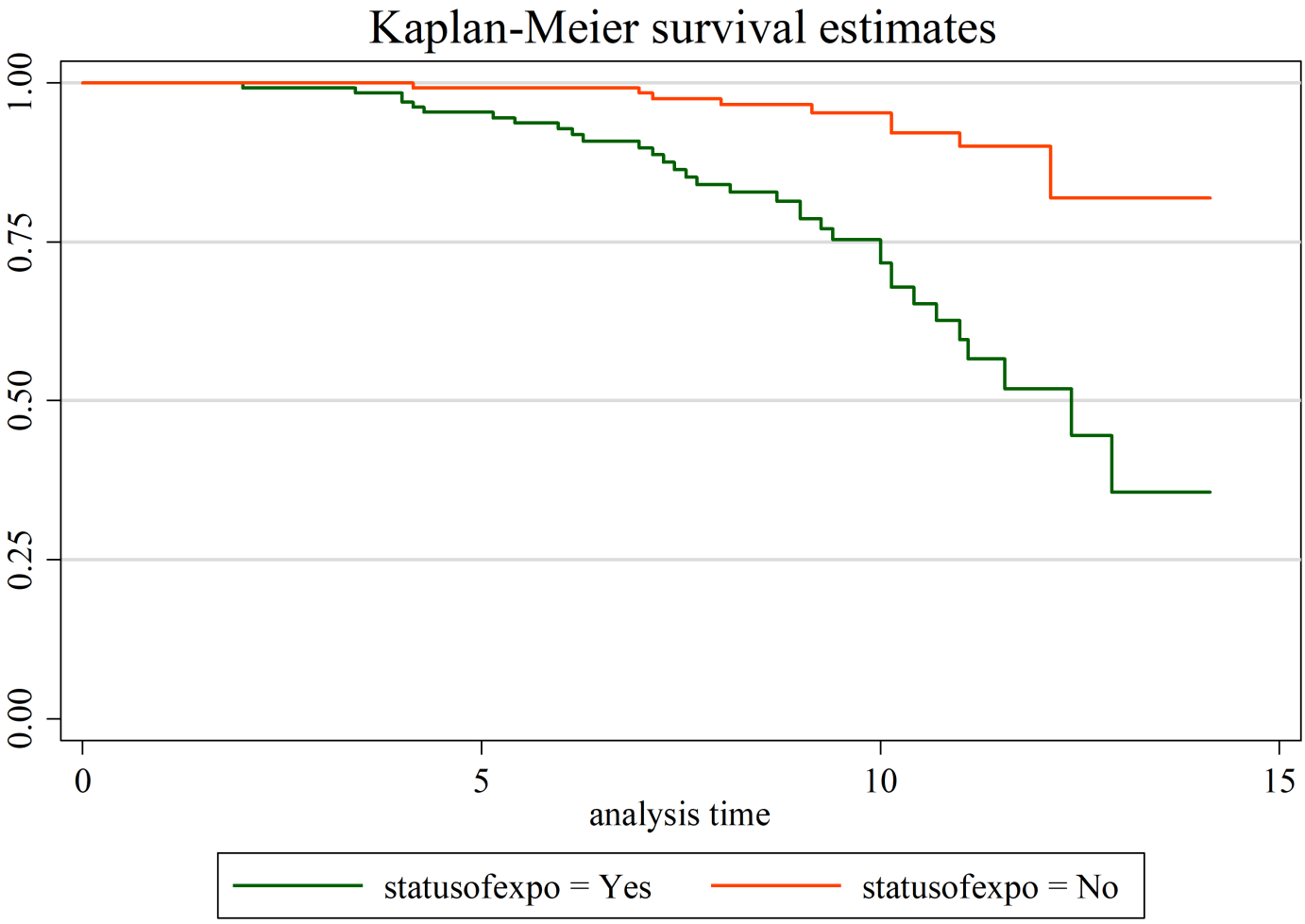


Figure 1

Kaplan-Meier survival curve of perinatal outcome for pregnant women by the status of exposure to early onset preeclampsia WUNEMMCSH, 2022, n = 264.