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Maternal outcomes among pregnant mothers admitted at Abebech Gobena Mothers and Childrens Health and Saint Peter's Specialized Hospital, Addis Ababa, Ethiopia: The case of preeclampsia with severe features

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3 **Maternal outcomes among pregnant mothers admitted at Abebech Gobena Mothers and**
4 **Childrens Health and Saint Peter’s Specialized Hospital, Addis Ababa, Ethiopia: The case**
5 **of preeclampsia with severe features**
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9 Mesfin Tadese¹, Dr. Wogene Asefa Damesa², Gebeyehu Shumet Solomon³, Getu Engida Wakie¹,
10 Saba Desta Tessema¹, Agizew Endale⁴
11
12
13

14
15
16 **Affiliations:**
17

18
19 ¹Department of Midwifery, School of Nursing and Midwifery, Asrat Woldeyes Health Science
20 Campus, Debre Berhan University, Debre Berhan, Ethiopia.
21

22
23 ²Senior Obstetrician and Gynecologist, Abebech Gobena Mothers and Childrens Health Hospital,
24 Addis Ababa, Ethiopia
25

26
27 ³Department of Epidemiology, St. Peter Specialized Hospital, Addis Ababa, Ethiopia
28

29
30 ⁴Department of Nursing, Debre Berhan Health Science College, Amhara region, Ethiopia.
31

32
33 mesitad031@gmail.com (MT)

34 wogeneassefa@gmail.com (WAD)

35 gshumet866@gmail.com (GSS)

36 getuengida117@gmail.com (GEW)

37 sabadesta127@gmail.com (SDT)

38 agizewendale2018@gmail.com (AE)
39
40
41
42
43
44
45
46
47

48 **Corresponding author**
49

50 Mesfin Tadese

51 Email: mesitad031@gmail.com

52 Tel: +25915839921

53 Debre Berhan, Ethiopia
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Abstract

Objective: To determine the maternal outcome of preeclampsia with severity features (PEWSF) and associated factors among pregnant mothers admitted at Abebech Gobena Maternal and Children's Health and St. Peter's Hospital, Addis Ababa, Ethiopia, 2023.

Design: A hospital-based cross-sectional study was conducted from January 1, 2023 to July 2023. The data was collected using a structured and pre-tested questionnaire through face-to-face interviews and a review clinical chart. Data was entered using Epi-Data version 4.6 and analyzed using SPSS version 26.0 statistical software. Binary logistic regression analysis was run to identify predictors of maternal outcome.

Setting: Two hospitals in Addis Ababa, Ethiopia.

Participants: 348 pregnant women with PEWSF were included.

Outcome measures: Unfavorable maternal outcome was defined as mothers with preeclampsia with severe features that develop at least one complication, i.e., eclampsia, abruption placenta, HELLP syndrome, acute renal failure, disseminated intravascular coagulation, cardiac failure, stroke, postpartum hemorrhage, pulmonary edema, and death

Results: The overall prevalence of unfavorable maternal outcomes was 33.9% (N=118) (95% CI: 28.7–38.8). Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were common complications that occurred among mothers with PEWSF. Age above 35 years (AOR (CI)= 2.70 (1.31-5.59), rural residence (AOR (CI)= 1.94 (1.07-3.53), unemployment (AOR (CI)= 0.35 (0.20-0.62), severe blood pressure on admission (AOR (CI)= 2.32 (1.03-5.19), and complain of severe headache (AOR (CI)= 1.91 (1.16-3.16) were significant associates of unfavorable maternal outcomes.

Conclusions: The prevalence of unfavorable maternal outcomes was high compared to other studies in Ethiopia. Maternal age, residence, occupation, blood pressure on admission, and severe headache have shown a statistically significant association with unfavorable maternal outcomes. Socio-economic development and early identification of severe signs and symptoms of preeclampsia are needed to reduce unfavorable outcomes.

Strengths and limitations of this study

- Interviews and clinical chart reviews were conducted to collect data.
- One drawback was that, because the research was conducted in a hospital setting, the maternal outcome of home births was not assessed.
- Another limitation was that the study did not include unfavorable maternal outcomes after 24 hours of birth.

For peer review only

Background

Preeclampsia is a multisystem progressive illness distinguished by the new development of hypertension and either proteinuria or end-organ failure after 20 weeks of gestation, during pregnancy, labor, or postpartum (1). It complicates between 3% and 5% of pregnancies in high-income countries (2). A Zanzibar study found that preeclampsia with severe features (PEWSF) was prevalent in 26.3% of mothers (3). Besides, 19.5% of preeclampsia with severe features was reported in a prospective observational study done at Saint Paul's Hospital Millennium Medical College in Ethiopia (4).

In the United States, unfavorable maternal outcomes occurred in 10% of women with preeclampsia with severe features (5). According to a prospective cohort study in the Sidama region of Ethiopia, women with PEWSF had a 43% higher risk of unfavorable maternal outcomes (6). Similarly, unfavorable maternal outcomes of severe preeclampsia/eclampsia at Amhara region referral hospitals were determined to be 37.7% (7). Further, in Addis Ababa, Ethiopia, 36% of mothers with PEWSF reported having at least one maternal complication (8).

A cross-sectional study in the Amhara region Referral Hospitals, Ethiopia, reported a significant association between residence, level of education, monthly income, parity, history of abortion, booking status, time of drug given, and unfavorable maternal outcome (7). Women admitted at <34 weeks, age 16 – 24 years, lower wealth quintiles, and rural residence had also a positive association with unfavorable maternal outcomes (6).

Due to the progressive nature of the disease and the lack of a known medical management, delivery is always the definitive treatment, however, there is debate on the best time to deliver for both preterm and term gestations. Extending pregnancy carries a risk of exacerbating endothelial dysfunction in the mother and perpetuating inadequate perfusion of target organs, potentially leading to serious damage to the brain, liver, kidneys, placenta/fetus, hematologic and vascular systems (1). Thus, there is an increased chance of induction failure and subsequent cesarean birth in preeclamptic women (9). Other potential maternal sequelae include seizure, pulmonary edema, cerebral hemorrhage, renal detachment or cortical blindness, stroke, hepatic failure, heart failure,

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3 renal failure, postpartum hemorrhage, disseminated intravascular coagulation, placental abruption,
4 and death (1,10).
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8 Preeclampsia and eclampsia are one of the leading causes of maternal death and severe morbidity
9 (2). Ten to fifteen percent of all maternal deaths worldwide are attributed to preeclampsia and
10 eclampsia (11). In Ethiopia, on the other hand, the five primary direct causes of maternal death
11 were hemorrhage, obstructed labor, preeclampsia/eclampsia, unsafe abortion, and sepsis,
12 accounting for eighty-five percent of maternal deaths. Preeclampsia/eclampsia makes up 11% of
13 these five major causes of maternal mortality (12). Furthermore, the Lancet Regional Health
14 showed that a higher incidence of asthma and chronic obstructive lung diseases was associated
15 with hypertensive disorders during pregnancy (13). Long-term cardiovascular and renal disease
16 development is also more likely in patients with preeclampsia (1).
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24 Preeclampsia causes significant financial losses that affect not just the individual but also the next
25 generation because of the expense of prescription drugs, medical treatment, lost productivity and
26 hindered daily activities. According to a US study, preeclampsia during the first 12 months of life
27 is expected to cost \$2.18 billion (\$1.03 billion for moms and \$1.15 billion for infants). The cost
28 burden per infant varies with gestational age, starting at \$150,000 at 26 weeks and going up to
29 \$1311 at 36 weeks (14).
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35 Limited studies to date have been done to address the unfavorable maternal outcomes among
36 pregnant women with preeclampsia with severe features in developing countries including
37 Ethiopia. Hence, the study aimed to determine the prevalence and associated factors of unfavorable
38 maternal outcomes among pregnant women with preeclampsia with severe features in Ethiopia.
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43 **Research questions**

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- 46 1. What is the magnitude of unfavorable maternal outcomes among pregnant women
47 admitted with preeclampsia with severe features?
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- 49 2. What are the factors associated with unfavorable maternal outcomes?
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Methods

Study design, period, and area

This cross-sectional study was conducted at Abebech Gobena Mothers and Childrens Health (MCH) and St. Peter's Specialized Hospital from January 1, 2023, to July 30, 2023, in Addis Ababa, the capital city of Ethiopia. Abebech Gobena MCH Hospital is one of the tertiary referral hospitals directly under the Addis Ababa Health Bureau. Yekatit 12 Hospital Medical College uses it as a teaching hospital as well. The hospital gives service to more than 200,000 patients annually who were referred by about 18 catchment health centers in the Oromia regional state and Addis Ababa city, as well as one primary hospital. Whereas, St. Peter's Specialized Hospital is a government facility that served as the nation's first tuberculosis (TB) referral hospital. The hospital was founded in 1953. Currently providing care for over 100,000 people as a specialized hospital under the supervision of the Federal Ministry of Health (FMOH). The MCH center was established in 2006 E.C. and serves 15 catchment health centers and 3 primary hospitals from the Oromia region and Addis Ababa city.

Population and eligibility criteria

All pregnant mothers who were admitted with a diagnosis of preeclampsia with severe features in the study area were the source population. Mothers who were randomly selected and diagnosed with preeclampsia with severity features during the study period were the study population. All pregnant mothers who were diagnosed, admitted, and managed for PEWSF were included. Pregnant mothers who were diagnosed with preeclampsia but not with severe features and who were not giving birth at the study hospitals with unknown maternal outcomes were excluded.

Sample size and sampling technique

The sample size was determined using OpenEpi Version 3.03 statistical software with the assumption of 36% prevalence of unfavorable maternal outcomes in Addis Ababa, Ethiopia (8), 95% confidence interval, 5% marginal error, and 5% non-response rate. Considering, that the final sample size was 372. A total population sampling method was used to select the eligible study participants.

Variables

Maternal outcome was the dependent variable. Independent variables included sociodemographic factors (age, residence, marital status, occupation, educational level, and mode of admission), medical and reproductive history (gravidity, parity, history of abortion, antenatal care (ANC); history of pregnancy-induced hypertension, family history of hypertension, anemia, chronic hypertension, diabetes, and renal disease); clinical features and investigations on admission (headache, dizziness, epigastric pain, visual disturbance, nausea and/ or vomiting, convulsion, edema, hematocrit, liver function test, urea, creatinine, urine protein); and obstetric factors (onset of labor, mode of delivery, sex of the neonate, and duration of hospitalization).

Outcome measures

Preeclampsia with severe features: is a preeclampsia with one of the severity features; including altered mental status, severe headache, altered cerebral or visual disturbance, hepatic abnormality, renal abnormality, severe blood pressure ($\geq 160/110$), thrombocytopenia (platelet count $< 100,000/\mu\text{L}$), and pulmonary edema (1,2).

Severe headache: Incapacitating, "the worst headache I have ever had" or headache that persists and progresses despite analgesic therapy (1).

Hepatic abnormality: Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥ 2 times the upper limit of the normal range, or both (1).

Renal abnormality: Progressive renal insufficiency (serum creatinine > 1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease) (1).

Unfavorable maternal outcome: Mothers with preeclampsia with severe features that develop at least one complication, i.e., eclampsia, abruption placenta, HELLP syndrome, acute renal failure, disseminated intravascular coagulation, cardiac failure, stroke, postpartum hemorrhage, pulmonary edema, and death (6,7).

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3 **Favorable maternal outcome:** Mothers with preeclampsia with severe features managed and
4 improved without complications (7).
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7 **Data collection tool, procedure, quality control**

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10 The data was collected using a structured and pre-tested questionnaire through face-to-face
11 interviews and a review clinical chart. The questionnaire was adapted from similar studies (4–
12 7,10). The data collection team consisted of 2 supervisors and 4 data collectors. The principal
13 investigators gave the supervisors and data collectors a one-day training on the objectives,
14 methods, procedures, and data collection instrument. The questionnaire was translated back and
15 forth from English to Amharic and vice versa to make sure the questions remained true to their
16 original intent. Prior to the real data collection, a pre-test was done on 5% of the samples (19
17 mothers) at Debre Berhan Comprehensive Specialized Hospital and the necessary adjustments
18 were taken into account in light of the test results. Over the course of the data collection process,
19 the principal investigators and supervisors closely observed the clarity, consistency, and
20 completeness of the data.
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29 **Data management and analysis**

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32 Data was entered using Epi-Data version 4.6 and analyzed using SPSS version 26.0 statistical
33 software. The principal investigator randomly selected a questionnaire for quality control and
34 cross-checked it with the correspondingly entered data and clinical chart. We employed descriptive
35 statistics to describe the independent and dependent variables. The results were presented as
36 number, frequency, percentage, and comparison of maternal outcomes. Binary logistic regression
37 analysis was run to identify independent predictors of unfavorable maternal outcomes. Variables
38 with a p-value of less than 0.25 in the bivariable regression analysis were included in the final
39 multivariable logistic regression analysis model. Hosmer and Lemeshow's goodness-of-fit test was
40 employed to evaluate the fitness of the model. The multicollinearity of the explanatory components
41 was also investigated. With a two-sided 95% confidence interval (CI), adjusted odds ratios (AORs)
42 were used to interpret the strength of the association. A p-value of less than 0.05 was used to
43 declare the level of significance.
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Result

Socio-demographic characteristics of participants

A total of 348 mothers participated, giving the survey a 93.5% response rate. The age range of the participants was 18 to 42 years old, with a mean (SD) of 27.55 + 5.179 years. Of these, 272(78.2%) lived in urban, making up more than three-fourths. Furthermore, Table 1 shows that 324(93.1%) of the participants were married, and 134(38.5%) had completed secondary school.

Table 1: Socio-demographic characteristics of participants admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Age in years	20 – 34	294	84.5%
	<20	13	3.7%
	≥35	41	11.8%
Residence	Urban	272	78.2%
	Rural	76	21.8%
Level of education	No formal education	45	12.9%
	Primary	97	27.9%
	Secondary	134	38.5%
	Higher education	72	20.7%
Marital status	Married	324	93.1%
	Others*	24	6.9%
Occupation	Employed	204	58.6%
	Unemployed	144	41.4%
Mode of admission	Self	52	14.9%
	Referral	296	85.1%

*Single, Divorced, and Widowed

PEWSF: Preeclampsia with severe features

Medical and obstetric history

More than half, 179(51.4%) of mothers, were primigravida and 69(19.8%) had previously experienced an abortion. Nearly all, 342(98.3%), of the participants had antenatal care (ANC) contact for the current pregnancy. However, only 22 (6.3%) of them had adequate ANC contact. Furthermore, 34(9.8%) of mothers had a history of pregnancy-induced hypertension. Twenty-seven (7.8%) of participants had a medical history. Of them, chronic hypertension and anemia were reported in 12(3.4%) and 8(2.3%) of cases, respectively (Table 2).

Table 2: Medical and obstetric history of mothers admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Gravidity	Primigravida	179	51.4%
	Multigravida	162	46.6%
	Grand multipara	7	2.0%
Parity	Nulliparous	12	3.4%
	1 – 3	322	92.5%
	≥4	14	4.0%
History of abortion	Null	279	80.2%
	1	61	17.5%
	≥2	8	2.3%
Antenatal care (ANC) contact	Yes	342	98.3%
	No	6	1.7%
Number of ANC contact	1 – 3	74	21.3%
	4 – 6	252	72.4%
	≥7 – 8	22	6.3%
Number of fetuses	Singleton	326	93.7%
	Twin/Multiple	22	6.3%
History of pregnancy-induced hypertension (PIH)	Yes	34	9.8%
	No	314	90.2%
Family history of hypertension	Yes	70	20.1%
	No	278	79.9%

Past medical history	Yes	27	7.8%
	No	321	92.2%
Anemia	Yes	8	2.3%
	No	340	97.7%
Chronic hypertension	Yes	12	3.4%
	No	336	96.6%
Diabetes mellitus	Yes	5	1.4%
	No	343	98.6%
Renal disease	Yes	2	0.6%
	No	346	99.4%

Clinical features and investigations on admission

In this study, 180(51.7%), 119(34.2%), and 87(25.0%) of mothers were admitted with a chief complaint of headache, epigastric pain, and edema, respectively. Whereas, on an investigation, 38(10.9%) of the women had deranged liver function tests and 53(15.2%) had protein 3+ upon admission. In addition, 196(56.3%) of mothers had induction of labor and 213(61.2%) of them spent more than three days in the hospital (Table 3).

Table 3: Clinical features of participants admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Headache	Yes	180	51.7%
	No	168	48.3%
Dizziness	Yes	45	12.9%
	No	303	87.1%
Epigastric pain	Yes	119	34.2%
	No	229	65.8%
Visual disturbance	Yes	59	17.0%
	No	289	83.0%
Nausea and/or vomiting	Yes	15	4.3%
	No	333	95.7%
Convulsion	Yes	33	9.5%
	No	315	90.5%
Edema	Yes	87	25.0%
	No	261	75.0%
Grade of edema (n=87)	Grade 1	46	52.9%
	Grade 2	38	43.7%
	Grade 3	3	3.4%
Blood pressure at admission	Severe range	297	85.3%
	Mild range	51	14.7%
Hematocrit	<33%	39	11.2%
	≥33%	309	88.8%
Liver function test	Normal	310	89.1%
	Deranged	38	10.9%
Urea	Normal	322	92.5%
	Deranged	26	7.5%
Creatinine	Normal	319	91.7%
	Deranged	29	8.3%

Urine protein (Dipstick)	Negative	105	30.2%
	1+	50	14.4%
	2+	140	40.2%
	3+	53	15.2%
Onset of labor	Spontaneous	104	29.9%
	Induction	244	70.1%
Mode of delivery	Spontaneous vaginal delivery	186	53.4%
	Instrumental	14	4.0%
	Cesarean section	148	42.5%
Sex of the neonate	Male	186	53.4%
	Female	162	46.6%
Duration of hospital stay	≤ 3 days	135	38.8%
	≥ 4 days	213	61.2%

Maternal outcomes

Overall, 33.9% (N=118) (95% CI: 28.7–38.8) of mothers had unfavorable maternal outcomes. Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were the most prevalent complications that occurred among mothers admitted with a diagnosis of preeclampsia with severe features (Figure 1).

Factor of unfavorable outcomes

Variables having a p-value of less than 0.25 in the bivariable analysis were chosen for the multivariable logistic regression analysis model. In the final model, age, residence, occupation, blood pressure upon admission, and complaints of headache were found to be statistically significantly associated with unfavorable maternal outcomes.

Mothers aged above 35 had approximately three-fold increased risk of developing unfavorable outcomes compared to those aged between 20 and 34 (AOR (CI)= 2.70 (1.31-5.59)). Rural residents had a 94% higher chance of experiencing unfavorable outcomes compared to their urban counterparts (AOR (CI)= 1.94 (1.07-3.53)). Unemployed mothers bore a 65% lower risk of unfavorable outcomes in comparison to those who were employed (AOR (CI)= 0.35 (0.20-0.62)). Severe blood pressure measurement upon admission increased the risk of unfavorable outcomes

by two-fold (AOR (CI)= 2.32 (1.03-5.19). Furthermore, women who were admitted with a headache as their chief complaint had a 91% higher likelihood of having unfavorable outcomes (AOR (CI)= 1.91 (1.16-3.16) (Table 4).

Table 4: Factors associated with unfavorable maternal outcome among mothers admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Maternal outcomes		COR (95% CI)	AOR (95% CI)
	Favorable	Unfavorable		
Age in years				
20 – 34	202 (87.8%)	92 (78.0%)	1	1
<20	8 (3.5%)	5 (4.2%)	1.37 (0.44-4.31)	1.33 (0.39-4.52)
≥35	20 (8.7%)	21 (17.8%)	2.31 (1.19-4.46)	2.70 (1.31-5.59)*
Residence				
Urban	188 (81.7%)	84 (71.2%)	1	1
Rural	42 (18.3)	34 (28.8%)	1.81 (1.08-3.05)	1.94 (1.07-3.53)*
Level of education				
No formal education	23 (10.0%)	22 (18.6%)	1.80 (0.84-3.84)	2.15 (0.89-5.17)
Primary	62 (27.0%)	35 (29.7%)	1.06 (0.56-2.01)	1.73 (0.82-3.67)
Secondary	98 (42.6%)	36 (30.5%)	0.69 (0.37-1.28)	1.00 (0.51-1.98)
Higher education	47 (20.4%)	25 (21.2%)	1	1
Occupation				
Employed	123 (53.5%)	81 (68.6%)	1	1
Unemployed	107 (46.5%)	37 (31.4%)	0.53 (0.33-0.84)	0.35 (0.20-0.62)*
Number of fetuses				
Singleton	220 (95.7%)	106 (89.8%)	1	1
Twin/Multiple	10 (4.3%)	12 (10.2%)	2.49 (1.04-5.95)	2.04 (0.79-5.24)
Sex of the neonate				
Male	116 (50.4%)	70 (59.3%)	1.43 (0.92-2.25)	1.43 (0.88-2.33)
Female	114 (49.6%)	48 (40.7%)	1	1
Blood pressure on admission				

Severe range	188 (81.7%)	109 (92.4%)	2.71 (1.27-5.77)	2.32 (1.03-5.19)*
Mild range	42 (18.3%)	9 (7.6%)	1	1
Headache complaint				
Yes	106 (46.1%)	74 (62.7%)	1.97 (1.25-3.10)	1.91 (1.16-3.16)*
No	124 (53.9%)	44 (37.3%)	1	1

*Statistically significant at p-value <0.05

Discussion

In this study, the overall prevalence of unfavorable maternal outcomes was 33.9% (95% CI: 28.7-38.8). Age, residence, occupation, blood pressure upon admission, and headache complaints have shown a statistically significant association with unfavorable outcomes among women of PEWSF admitted at Abebech Gobena MCH and St. Peter's Specialized Hospital, Addis Ababa, Ethiopia.

Unfavorable maternal outcomes occurred in 33.9% of mothers with preeclampsia with severe features. This is comparable with the study findings from Amhara region referral hospitals, where 37.7% of mothers with preeclampsia with severe features developed unfavorable outcomes (7). However, it was higher than 10% in the United States (5). This discrepancy could be the result of variations in the study population, time, setup, sample size, and quality and standard of care provided by contemporary, well-equipped maternity hospitals, as well as good prenatal and obstetric care. On the other hand, it was lower than 43% in the Sidama region of Ethiopia (6). Variations in the incidence proportion of unfavorable outcomes between the studies might be attributed to the severity of the disease, differences in clinical features (severity signs and symptoms) upon admission, and gestational age at diagnosis.

Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were the most prevalent complications. Similarly, in Thailand, postpartum hemorrhage, placental abruption, and heart failure occurred in 9.4%, 1.4%, and 0.4% of women with preeclampsia with severe features, respectively (10). Further, in the Sidama region, Ethiopia, a higher level of antepartum and postpartum hemorrhage was observed in the mothers of preeclampsia with severe features (6).

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3 It was discovered that older mothers were linked to a higher likelihood of unfavorable outcomes.
4 Mothers over 35 were almost three times more likely to experience an adverse outcome. In a
5 similar vein, poor maternal outcome was more common in Indonesia among mothers with
6 preeclampsia who were older than 35 (15). Because of increased endothelial injuries that lower
7 renal reserves and the incapacity to adapt to physiological changes during pregnancy, older people
8 may be more susceptible to developing renal insufficiency even if their pre-gestational kidney
9 functions are normal (16). It might also be connected to the extravascular space's increased fluid
10 accumulation during pregnancy. Additionally, older people are more likely to have additional risk
11 factors that increase their likelihood of developing preeclampsia, such as diabetes mellitus, obesity,
12 and chronic hypertension (1).

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21 The odds of unfavorable maternal outcomes were 94% higher among rural residents than their
22 urban counterparts. Similarly, in Ethiopia's Sidama region, women who lived in rural regions were
23 more likely to experience unfavorable maternal outcomes (6). This could be because women in
24 rural areas may have had a lower socioeconomic level, which may have resulted in a lesser
25 tendency to seek medical attention. Pregnant women with low health-seeking behavior are less
26 likely to visit antenatal care clinics, which delays the diagnosis and treatment of preeclampsia. In
27 addition, rural women faced significant challenges in getting to health facilities due to
28 transportation issues, which caused delays in receiving medical care. It is improbable that they are
29 aware of the risks and complications associated with pregnancy, labor, and delivery. In addition,
30 the cultural practices prevalent in rural areas greatly impact women's nutritional status by
31 preventing them from consuming necessary foods and/or beverages (17).

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41 Unemployed mothers had less risk of unfavorable outcomes compared to those employed. In the
42 Netherlands, when employed women worked longer hours (≥ 40 hrs/week), the mean birth weight
43 of kids decreased by 45 g (18). Similarly, in South Korea (19), higher risks of early abortive
44 outcomes and stillbirths were more frequent in employed women. The possible explanation might
45 be that unemployed mothers are more likely to have adequate time to care for themselves and listen
46 to updated information regarding pregnancy-induced hypertension via TV, Radio, or others. This
47 might help them to have a lower risk of unfavorable outcomes.

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54 A severe blood pressure measurement upon admission doubled the likelihood of unfavorable
55 maternal outcomes. Severe blood pressure was also revealed to be a significant predictor of an

adverse outcome (eclampsia) among preeclamptic mothers in Morocco (20). Hypertension is one of the hallmarks of preeclampsia and severe hypertension, defined as a blood pressure of more than 160/110 mmHg, has been considered a warning indicator of the development of negative outcomes, such as eclampsia. Thus, severe blood pressure is a symptom of a severe condition, rapid disease progression, and a terrible prognosis.

Furthermore, women who were admitted with a chief complaint of headache had a 91% increased risk of unfavorable outcomes. In a retrospective chart review of preeclamptic patients treated at Ayder Comprehensive Specialized Hospital, Ethiopia, headache and blurring were associated with poor maternal outcomes (21). It has been noted that neurologic symptoms indicate an impending negative consequence (22).

Conclusion and recommendations

In this study, the prevalence of unfavorable maternal outcomes was high compared to other studies in Ethiopia. Maternal age, residence, occupation, blood pressure on admission, and severe headache have shown a statistically significant association with unfavorable maternal outcomes. Socio-economic development and early identification and treatment of severe signs and symptoms of preeclampsia are needed to reduce unfavorable outcomes. Further, longitudinal studies are recommended to investigate the outcome of mothers with preeclampsia with severe features.

Limitations

It shares the limitation of a cross-sectional study to draw a causal relationship. In addition, as this was done in the hospital setting, the maternal outcome of women delivered at home was not assessed. Further, this study does not include adverse maternal outcomes after 24 hours of birth.

Abbreviations and acronym

C/S: Cesarean Section

DIC: Disseminated Intravascular Coagulation

HDP: Pregnancy Induced Hypertension

HELLP: Hemolysis, Elevated Liver Enzymes, and Low Platelet Count

HTN: Hypertension

MCH: Maternal and Child Health

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3 PEWSF: Preeclampsia with Severe Features

4 PIH: Pregnancy Induced Hypertension

5
6 SVD: Spontaneous Vaginal Delivery

7 8 9 **Acknowledgement**

10
11 The authors would like to thank the administrators, data collectors, and study participants for
12 providing genuine data, as well as Yekatit 12 Hospital Medical College for approving the project's
13 ethical clearance.
14

15 16 17 **Contributions**

18
19 WAD drafted the topic, designed the proposal, and performed data collection. MT critically
20 revised, performed the analysis, and developed the manuscript. MT, WAD, GSS, GEW, SDT, and
21 AE reviewed the proposal, contributed to data collection and analysis, and critically revised the
22 manuscript. MT made basic adjustments to the final manuscript and processed publication. All
23 authors approved the manuscript for journal submission.
24

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28
29 There was no funding for the study.

30 31 32 **Competing interests**

33
34 None declared

35 36 37 **Patient consent for publication**

38
39 Not required

40 41 42 **Patient and public involvement**

43
44 Patients and/or the public were not involved in the design, or conduct, or reporting, or
45 dissemination plans of this research.
46

47 48 49 **Ethics approval**

50
51 The Institutional Review Board (IRB) of Yekatit 12 Hospital Medical College granted ethical
52 clearance (Protocol number 128/23). A formal letter of support was forwarded to the study
53

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3 hospitals. Participants gave their free and informed consent, and they participated willingly. Those
4 who were illiterate were asked to thumbprint the consent form once the content was read.
5 Confidentiality and anonymity were preserved and the client records were returned to their place
6 after the completion of data collection.
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10 **Data availability statement**

11 All relevant data set are incorporated within the paper.
12
13

14 **ORCID ID**

15 Mesfin Tadese [http:// orcid. org/ 0000- 0001- 6288- 9771](http://orcid.org/0000-0001-6288-9771)
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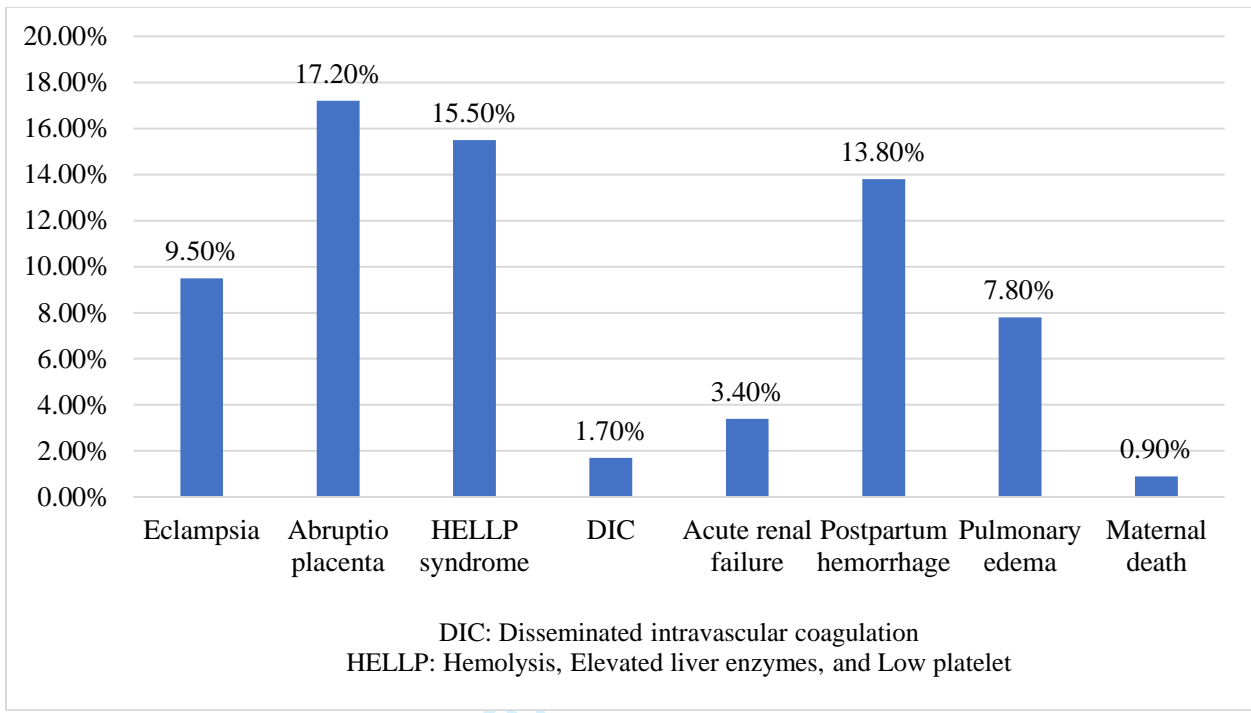
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STROBE Statement—checklist of items that should be included in reports of *cross-sectional studies*

	Item No.	Recommendation	Page No.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 & 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 1 & 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 6
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 7
Bias	9	Describe any efforts to address potential sources of bias	Page 7 & 8
Study size	10	Explain how the study size was arrived at	Page 6

Continued on next page

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2	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8
3				
4	Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 8
5			(b) Describe any methods used to examine subgroups and interactions	Page 8
6			(c) Explain how missing data were addressed	Page 8
7			(d) If applicable, describe analytical methods taking account of sampling strategy	Page 8
8			(e) Describe any sensitivity analyses	Page 8
9				
10				
11	Results			
12	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 9
13			(b) Give reasons for non-participation at each stage	Page 9
14			(c) Consider use of a flow diagram	
15	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9
16			(b) Indicate number of participants with missing data for each variable of interest	Page 9
17	Outcome data	15*	Report numbers of outcome events or summary measures	Page 17
18	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 13 and 14
19			(b) Report category boundaries when continuous variables were categorized	Page 9 – 12
20			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Maternal outcomes of preeclampsia with severe features and its determinants at Abebech Gobena Mothers and Childrens Health and Saint Peter's Specialized Hospital, Addis Ababa, Ethiopia: a cross-sectional study

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3 **Maternal outcomes of preeclampsia with severe features and its determinants at Abebech**
4 **Gobena Mothers and Childrens Health and Saint Peter's Specialized Hospital, Addis Ababa,**
5 **Ethiopia: a cross-sectional study**
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9 Mesfin Tadese¹, Wogene Asefa Damesa², Gebeyehu Shumet Solomon³, Getu Engida Wakie¹, Saba
10 Desta Tessema¹, Agizew Endale⁴
11
12
13
14
15

16
17 **Affiliations:**
18

19 ¹Department of Midwifery, School of Nursing and Midwifery, Asrat Woldeyes Health Science
20 Campus, Debre Berhan University, Debre Berhan, Ethiopia.
21
22

23 ²Department of Medicine, Obstetrician and Gynecologist, Abebech Gobena Mothers and
24 Childrens Health Hospital, Addis Ababa, Ethiopia
25
26

27 ³Department of Epidemiology, St. Peter Specialized Hospital, Addis Ababa, Ethiopia
28
29

30 ⁴Department of Nursing, Debre Berhan Health Science College, Debre Berhan, Ethiopia.
31
32

33 mesitad031@gmail.com (MT)
34

35 wogeneassefa@gmail.com (WAD)
36

37 gshumet866@gmail.com (GSS)
38

39 getuengida117@gmail.com (GEW)
40

41 sabadesta127@gmail.com (SDT)
42

43 agizewendale2018@gmail.com (AE)
44
45
46
47

48 **Corresponding author**
49

50 Mesfin Tadese

51 Email: mesitad031@gmail.com

52 Tel: +25915839921

53 Debre Berhan, Ethiopia
54
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Abstract

Objective: The main objective of this study was to determine the prevalence and factors associated with unfavorable maternal outcomes among pregnant women with preeclampsia with severity features (PEWSF) at Abebech Gobena Maternal and Children's Health and St. Peter's Hospital, Addis Ababa, Ethiopia, 2023.

Design: A hospital-based cross-sectional study was conducted from January 1, 2023 to July 2023. The data was collected using a structured and pre-tested questionnaire through face-to-face interviews and a review clinical chart. Data was entered using Epi-Data version 4.6 and analyzed using SPSS version 26.0 statistical software. Binary logistic regression analysis was run to identify predictors of maternal outcome.

Setting: Two hospitals in Addis Ababa, Ethiopia.

Participants: 348 pregnant women with PEWSF were included.

Outcome measures: Unfavorable maternal outcome was defined as mothers with preeclampsia with severe features that develop at least one complication, i.e., eclampsia, abruption placenta, HELLP syndrome, acute renal failure, disseminated intravascular coagulation, cardiac failure, stroke, postpartum hemorrhage, pulmonary edema, and death

Results: The overall prevalence of unfavorable maternal outcomes was 33.9% (N=118) (95% CI: 28.7–38.8). Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were common complications that occurred among mothers with PEWSF. Age above 35 years (AOR (CI)= 2.70 (1.31-5.59), rural residence (AOR (CI)= 1.94 (1.07-3.53), unemployment (AOR (CI)= 0.35 (0.20-0.62), severe blood pressure on admission (AOR (CI)= 2.32 (1.03-5.19), and complain of severe headache (AOR (CI)= 1.91 (1.16-3.16) were significant associates of unfavorable maternal outcomes.

Conclusions: The prevalence of unfavorable maternal outcomes was high compared to other studies in Ethiopia. Maternal age, residence, occupation, blood pressure on admission, and severe headache have shown a statistically significant association with unfavorable maternal outcomes.

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3 Socio-economic development and early identification of severe signs and symptoms of
4 preeclampsia are needed to reduce unfavorable outcomes.
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8 **Strengths and limitations of this study**

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- 10 ■ Interviews and clinical chart reviews were conducted to collect data.
- 11 ■ One drawback was that, because the research was conducted in a hospital setting, the
- 12 maternal outcome of home births was not assessed.
- 13 ■ Another limitation was that the study did not include unfavorable maternal outcomes after
- 14 24 hours of birth.
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Background

Preeclampsia is a multisystem progressive illness distinguished by the new development of hypertension and either proteinuria or end-organ failure after 20 weeks of gestation, during pregnancy, labor, or postpartum (1). A combination of maternal and fetal/placental factors is most likely the reason. Relative placental hypoxia, ischemia, or under-perfusion can be brought on by abnormalities in the placental vasculature early in pregnancy (2). This may then cause the mother's circulation to release antiangiogenic factors, altering the mother's systemic endothelium's function and causing hypertension in addition to other disease manifestations (hematologic, neurologic, cardiac, pulmonary, renal, and hepatic dysfunction). However, the reason behind abnormal placental development and the subsequent sequence of events is still unknown (3).

Preeclampsia complicates between 3% and 5% of pregnancies in high-income countries (4). In Africa, hypertension disorders during pregnancy affect 10% of pregnancies (5). A Zanzibar study found that preeclampsia with severe features (PEWSF) was prevalent in 26.3% of mothers (6). Besides, 19.5% of preeclampsia with severe features was reported in a prospective observational study done at Saint Paul's Hospital Millennium Medical College in Ethiopia (7).

In the United States, unfavorable maternal outcomes occurred in 10% of women with preeclampsia with severe features (8). According to a prospective cohort study in the Sidama region of Ethiopia, women with PEWSF had a 43% higher risk of unfavorable maternal outcomes (9). Similarly, it was shown that 37.7% of mothers with severe preeclampsia/eclampsia in referral hospitals in the Amhara region had unfavorable maternal outcomes (10). Further, in Addis Ababa, Ethiopia, 36% of mothers with PEWSF reported having at least one maternal complication (11).

Due to the progressive nature of the disease and the lack of known medical management, delivery is always the definitive treatment, however, there is debate on the best time to deliver for both preterm and term gestations. Extending pregnancy carries a risk of exacerbating endothelial dysfunction in the mother and perpetuating inadequate perfusion of target organs, potentially leading to serious damage to the brain, liver, kidneys, placenta/fetus, hematologic and vascular systems (1). Thus, there is an increased chance of induction failure and subsequent cesarean birth in preeclamptic women(12). Other potential maternal sequelae include seizure, pulmonary edema,

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3 cerebral hemorrhage, renal detachment or cortical blindness, stroke, hepatic failure, heart failure,
4 renal failure, postpartum hemorrhage, disseminated intravascular coagulation, placental abruption,
5 and death (1,13). There was also a reported lifetime risk of hypertension (14). Furthermore,
6 research published in the Lancet Regional Health revealed that pregnant women with hypertensive
7 disorders have an increased risk of developing asthma and chronic obstructive pulmonary diseases
8 (15).
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15 Moreover, preeclampsia and eclampsia made a substantial contribution to maternal deaths and
16 severe morbidity (4,16). Ten to fifteen percent of all maternal deaths worldwide are attributed to
17 preeclampsia and eclampsia (11). In Ethiopia, the five primary direct causes of maternal death
18 were hemorrhage, obstructed labor, preeclampsia/eclampsia, unsafe abortion, and sepsis,
19 accounting for eighty-five percent of maternal deaths. Preeclampsia/eclampsia makes up 11% of
20 these five major causes of maternal mortality (17).
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27 A cross-sectional study in the Amhara region Referral Hospitals, Ethiopia, reported a significant
28 association between residence, level of education, monthly income, parity, history of abortion,
29 booking status, time of drug given, and unfavorable maternal outcome (10). Women admitted at
30 <34 weeks, age 16 – 24 years, lower wealth quintiles, and rural residence had also a positive
31 association with unfavorable maternal outcomes (9). Further, gestational age at admission (18),
32 onset of the disease, and low hemoglobin level (19) were predictors of maternal complication.
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39 Preeclampsia causes significant financial losses that affect not just the individual but also the next
40 generation because of the expense of prescription drugs, medical treatment, lost productivity, and
41 hindered daily activities. According to a US study, preeclampsia during the first 12 months of life
42 is expected to cost \$2.18 billion (\$1.03 billion for moms and \$1.15 billion for infants). The cost
43 burden per infant varies with gestational age, starting at \$150,000 at 26 weeks and going up to
44 \$1311 at 36 weeks (20).
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50 Limited studies to date have been done to address the unfavorable maternal outcomes among
51 pregnant women with preeclampsia with severe features in developing countries including
52 Ethiopia. The findings could have its own contribution to the local Ethiopian Health Sector
53 Transformation Plan-II (HSTP-II) targeted to lower maternal mortality ratio from 401 to 140 per
54 100,000 live births (21) and global Sustainable Development Goal (SDG) target plans of less than
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70 per 100,000 live births by 2030 (22). Hence, the study aimed to determine the prevalence and associated factors of unfavorable maternal outcomes among pregnant women with preeclampsia with severe features in Ethiopia.

Research questions

1. What is the magnitude of unfavorable maternal outcomes among pregnant women admitted with preeclampsia with severe features?
2. What are the factors associated with unfavorable maternal outcomes?

Methods

Study design, period, and area

This cross-sectional study was conducted at Abebech Gobena Mothers and Childrens Health (MCH) and St. Peter's Specialized Hospital from January 1, 2023, to July 30, 2023, in Addis Ababa, the capital city of Ethiopia. Abebech Gobena MCH Hospital is one of the tertiary referral hospitals directly under the Addis Ababa Health Bureau. Yekatit 12 Hospital Medical College uses it as a teaching hospital as well. The hospital gives service to more than 200,000 patients annually who were referred by about 18 catchment health centers in the Oromia regional state and Addis Ababa city, as well as one primary hospital. Whereas, St. Peter's Specialized Hospital is a government facility that served as the nation's first tuberculosis (TB) referral hospital. The hospital was founded in 1953. Currently providing care for over 100,000 people as a specialized hospital under the supervision of the Federal Ministry of Health (FMOH). The MCH center was established in 2006 E.C. and serves 15 catchment health centers and 3 primary hospitals from the Oromia region and Addis Ababa city.

Population and eligibility criteria

All pregnant mothers who were admitted with a diagnosis of preeclampsia with severe features in the study area were the source population. Participants were randomly selected from this source population. All pregnant mothers who were diagnosed, admitted, and managed for PEWSF were included. Pregnant mothers who were diagnosed with preeclampsia but not with severe features and who were not giving birth at the study hospitals with unknown maternal outcomes were excluded.

Sample size and sampling technique

The sample size was determined using OpenEpi Version 3.03 statistical software with the assumption of 36% prevalence of unfavorable maternal outcomes in Addis Ababa, Ethiopia (23), 95% confidence interval, 5% marginal error, and 5% non-response rate. Considering, that the final sample size was 372. A total population sampling method was used to select the eligible study participants.

Variables

Maternal outcome was the dependent variable. Independent variables included sociodemographic factors (age, residence, marital status, occupation, educational level, and mode of admission), medical and reproductive history (gravidity, parity, history of abortion, antenatal care (ANC); history of gestational hypertension, family history of hypertension, anemia, chronic hypertension, diabetes, and renal disease); clinical features and investigations on admission (headache, dizziness, epigastric pain, visual disturbance, nausea and/ or vomiting, convulsion, edema, hematocrit, liver function test, urea, creatinine, urine protein); and obstetric factors (onset of labor, mode of delivery, sex of the neonate, and duration of hospitalization).

Outcome measures

Preeclampsia with severe features: is a preeclampsia with one of the severity features; including altered mental status, severe headache, altered cerebral or visual disturbance, hepatic abnormality, renal abnormality, severe blood pressure ($\geq 160/110$), thrombocytopenia (platelet count $< 100,000/\mu\text{L}$), and pulmonary edema (1,4).

Blood pressure at admission: Severe hypertension if blood pressure measurement was $\geq 160/110$ and mild hypertension if 140-159/90-109 (4,11).

Severe headache: Incapacitating, "the worst headache I have ever had" or headache that persists and progresses despite analgesic therapy (1).

Hepatic abnormality: Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥ 2 times the upper limit of the normal range, or both (1).

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3 **Renal abnormality:** Progressive renal insufficiency (serum creatinine >1.1 mg/dL [97.2
4 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal
5 disease) (1).
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9 **Unfavorable maternal outcome:** Mothers with preeclampsia with severe features that develop at
10 least one complication, i.e., eclampsia, abruption placenta, HELLP syndrome, acute renal failure,
11 disseminated intravascular coagulation, cardiac failure, stroke, postpartum hemorrhage,
12 pulmonary edema, and death (9,10).
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16 **Favorable maternal outcome:** Mothers with preeclampsia with severe features managed and
17 improved without complications (10).
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20 21 **Data collection tool, procedure, quality control**

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23 The data was collected using a well-constructed case record form and procedure. The questionnaire
24 was adapted from similar studies (7–10,13). The data collection team consisted of 2 supervisors
25 and 4 data collectors. The principal investigators gave the supervisors and data collectors a one-
26 day training on the objectives, methods, procedures, and data collection instrument. The
27 questionnaire was translated back and forth from English to Amharic and vice versa to make sure
28 the questions remained true to their original intent. Prior to the real data collection, a pre-test was
29 done on 5% of the samples (19 mothers) at Debre Berhan Comprehensive Specialized Hospital
30 and the necessary adjustments were taken into account in light of the test results. Over the course
31 of the data collection process, the principal investigators and supervisors closely observed the
32 clarity, consistency, and completeness of the data.
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42 **Patient and public involvement**

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44 There was no patient and/ or public involvement in the design and planning of this study.
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47 **Data management and analysis**

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49 Data was entered using Epi-Data version 4.6 and analyzed using SPSS version 26.0 statistical
50 software. The principal investigator randomly selected a questionnaire for quality control and
51 cross-checked it with the correspondingly entered data and clinical chart. We employed descriptive
52 statistics to describe the independent and dependent variables. The results were presented as
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number, frequency, percentage, and comparison of maternal outcomes. Binary logistic regression analysis was run to identify independent predictors of unfavorable maternal outcomes. Variables with a p-value of less than 0.25 in the bivariable regression analysis were included in the final multivariable logistic regression analysis model. Hosmer and Lemeshow's goodness-of-fit test was employed to evaluate the fitness of the model. The multicollinearity of the explanatory components was also investigated. With a two-sided 95% confidence interval (CI), adjusted odds ratios (AORs) were used to interpret the strength of the association. A p-value of less than 0.05 was used to declare the level of significance.

Result

Socio-demographic characteristics of participants

A total of 348 mothers participated, giving the survey a 93.5% response rate. The age range of the participants was 18 to 42 years old, with a mean (SD) of 27.55 ± 5.18 years. Of these, 272(78.2%) lived in urban, making up more than three-fourths. Furthermore, Table 1 shows that 324(93.1%) of the participants were married, and 134(38.5%) had completed secondary school.

Table 1: Socio-demographic characteristics of participants admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Age in years	20 – 34	294	84.5%
	<20	13	3.7%
	≥35	41	11.8%
Residence	Urban	272	78.2%
	Rural	76	21.8%
Level of education	No formal education	45	12.9%
	Primary	97	27.9%
	Secondary	134	38.5%
	Higher education	72	20.7%
Marital status	Married	324	93.1%
	Others*	24	6.9%
Occupation	Employed	204	58.6%

	Unemployed	144	41.4%
Mode of admission	Self	52	14.9%
	Referral	296	85.1%

*Single, Divorced, and Widowed

PEWSF: Preeclampsia with severe features

Medical and obstetric history

More than half, 179(51.4%) of mothers, were primigravida and 69(19.8%) had previously experienced an abortion. Nearly all, 342(98.3%), of the participants had antenatal care (ANC) contact for the current pregnancy. However, only 22 (6.3%) of them had adequate ANC contact. Furthermore, 34(9.8%) of mothers had a history of gestational hypertension. Twenty-seven (7.8%) of participants had a medical history. Of them, chronic hypertension and anemia were reported in 12(3.4%) and 8(2.3%) of cases, respectively (Table 2).

Table 2: Medical and obstetric history of mothers admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Gravidity	Primigravida	179	51.4%
	Multigravida	162	46.6%
	Grand multipara	7	2.0%
Parity	Nulliparous	12	3.4%
	1 – 3	322	92.5%
	≥4	14	4.0%
History of abortion	Null	279	80.2%
	1	61	17.5%
	≥2	8	2.3%
Antenatal care (ANC) contact	Yes	342	98.3%
	No	6	1.7%
Number of ANC contact	1 – 3	74	21.3%
	4 – 6	252	72.4%
	≥7 – 8	22	6.3%
Number of fetuses	Singleton	326	93.7%
	Twin/Multiple	22	6.3%

History of chronic hypertension	Yes	34	9.8%
	No	314	90.2%
Family history of gestational hypertension	Yes	70	20.1%
	No	278	79.9%
Past medical history	Yes	27	7.8%
	No	321	92.2%
Anemia	Yes	8	2.3%
	No	340	97.7%
Chronic hypertension	Yes	12	3.4%
	No	336	96.6%
Diabetes mellitus	Yes	5	1.4%
	No	343	98.6%
Renal disease	Yes	2	0.6%
	No	346	99.4%

Clinical features and investigations on admission

In this study, 180(51.7%), 119(34.2%), and 87(25.0%) of mothers were admitted with a chief complaint of headache, epigastric pain, and edema, respectively. Whereas, on an investigation, 38(10.9%) of the women had deranged liver function tests and 53(15.2%) had protein 3+ upon admission. In addition, 196(56.3%) of mothers had induction of labor and 213(61.2%) of them spent more than three days in the hospital (Table 3).

Table 3: Clinical features of participants admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Headache	Yes	180	51.7%
	No	168	48.3%
Dizziness	Yes	45	12.9%
	No	303	87.1%
Epigastric pain	Yes	119	34.2%
	No	229	65.8%
Visual disturbance	Yes	59	17.0%
	No	289	83.0%
Nausea and/or vomiting	Yes	15	4.3%
	No	333	95.7%
Convulsion	Yes	33	9.5%
	No	315	90.5%
Edema	Yes	87	25.0%
	No	261	75.0%
Grade of edema (n=87)	Grade 1	46	52.9%
	Grade 2	38	43.7%
	Grade 3	3	3.4%
Blood pressure at admission	Severe range	297	85.3%
	Mild range	51	14.7%
Hematocrit	<33%	39	11.2%
	≥33%	309	88.8%
Liver function test	Normal	310	89.1%
	Deranged	38	10.9%
Urea	Normal	322	92.5%
	Deranged	26	7.5%
Creatinine	Normal	319	91.7%
	Deranged	29	8.3%

Urine protein (Dipstick)	Negative	105	30.2%
	1+	50	14.4%
	2+	140	40.2%
	3+	53	15.2%
Onset of labor	Spontaneous	104	29.9%
	Induction	244	70.1%
Mode of delivery	Spontaneous vaginal delivery	186	53.4%
	Instrumental	14	4.0%
	Cesarean section	148	42.5%
Sex of the neonate	Male	186	53.4%
	Female	162	46.6%
Duration of hospital stay	≤ 3 days	135	38.8%
	≥ 4 days	213	61.2%

Maternal outcomes

Overall, 33.9% (N=118) (95% CI: 28.7–38.8) of mothers had unfavorable maternal outcomes. Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were the most prevalent complications that occurred among mothers admitted with a diagnosis of preeclampsia with severe features (Figure 1).

Factor of unfavorable outcomes

Variables having a p-value of less than 0.25 in the bivariable analysis were chosen for the multivariable logistic regression analysis model. A crude odds ratio (COR) is an odds ratio of univariable analysis; one independent variable for predicting the dependent variable. Accordingly, age, residence, level of education, occupation, number of fetuses, sex of neonate, blood pressure on admission, and headache complaint were selected. In the final model, age, residence, occupation, blood pressure upon admission, and complaints of headache were found to be statistically significantly associated with unfavorable maternal outcomes.

Mothers aged above 35 had approximately three-fold increased risk of developing unfavorable outcomes compared to those aged between 20 and 34 (AOR (CI)= 2.70 (1.31-5.59)). Rural residents had a 94% higher chance of experiencing unfavorable outcomes compared to their urban

counterparts (AOR (CI)= 1.94 (1.07-3.53). Unemployed mothers bore a 65% lower risk of unfavorable outcomes in comparison to those who were employed (AOR (CI)= 0.35 (0.20-0.62). Severe blood pressure measurement upon admission increased the risk of unfavorable outcomes by two-fold (AOR (CI)= 2.32 (1.03-5.19). Furthermore, women who were admitted with a headache as their chief complaint had a 91% higher likelihood of having unfavorable outcomes (AOR (CI)= 1.91 (1.16-3.16) (Table 4).

Table 4: Factors associated with unfavorable maternal outcome among mothers admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Maternal outcomes		COR (95% CI)	AOR (95% CI)
	Favorable	Unfavorable		
Age in years				
20 – 34	202 (87.8%)	92 (78.0%)	1	1
<20	8 (3.5%)	5 (4.2%)	1.37 (0.44-4.31)	1.33 (0.39-4.52)
≥35	20 (8.7%)	21 (17.8%)	2.31 (1.19-4.46)	2.70 (1.31-5.59)*
Residence				
Urban	188 (81.7%)	84 (71.2%)	1	1
Rural	42 (18.3)	34 (28.8%)	1.81 (1.08-3.05)	1.94 (1.07-3.53)*
Level of education				
No formal education	23 (10.0%)	22 (18.6%)	1.80 (0.84-3.84)	2.15 (0.89-5.17)
Primary	62 (27.0%)	35 (29.7%)	1.06 (0.56-2.01)	1.73 (0.82-3.67)
Secondary	98 (42.6%)	36 (30.5%)	0.69 (0.37-1.28)	1.00 (0.51-1.98)
Higher education	47 (20.4%)	25 (21.2%)	1	1
Occupation				
Employed	123 (53.5%)	81 (68.6%)	1	1
Unemployed	107 (46.5%)	37 (31.4%)	0.53 (0.33-0.84)	0.35 (0.20-0.62)*
Number of fetuses				
Singleton	220 (95.7%)	106 (89.8%)	1	1
Twin/Multiple	10 (4.3%)	12 (10.2%)	2.49 (1.04-5.95)	2.04 (0.79-5.24)
Sex of the neonate				
Male	116 (50.4%)	70 (59.3%)	1.43 (0.92-2.25)	1.43 (0.88-2.33)

Female	114 (49.6%)	48 (40.7%)	1	1
Blood pressure on admission				
Severe range	188 (81.7%)	109 (92.4%)	2.71 (1.27-5.77)	2.32 (1.03-5.19)*
Mild range	42 (18.3%)	9 (7.6%)	1	1
Headache complaint				
Yes	106 (46.1%)	74 (62.7%)	1.97 (1.25-3.10)	1.91 (1.16-3.16)*
No	124 (53.9%)	44 (37.3%)	1	1

COR: Crude Odds Ratio; p-value ≤ 0.25 AOR: Adjusted Odds Ratio *Statistically significant at p-value < 0.05

Discussion

In this study, the overall prevalence of unfavorable maternal outcomes was 33.9% (95% CI: 28.7-38.8). Age, residence, occupation, blood pressure upon admission, and headache complaints have shown a statistically significant association with unfavorable outcomes among women of PEWSF admitted at Abebech Gobena MCH and St. Peter's Specialized Hospital, Addis Ababa, Ethiopia.

Unfavorable maternal outcomes occurred in 33.9% of mothers with preeclampsia with severe features. This is comparable with the study findings from Amhara region referral hospitals, where 37.7% of mothers with preeclampsia with severe features developed unfavorable outcomes (10). However, it was higher than 10% in the United States (8). This discrepancy could be the result of variations in the study population, time, setup, sample size, and quality and standard of care provided by contemporary, well-equipped maternity hospitals, as well as good prenatal and obstetric care. On the other hand, it was lower than 43% in the Sidama region of Ethiopia (9). Variations in the incidence proportion of unfavorable outcomes between the studies might be attributed to the severity of the disease, differences in clinical features (severity signs and symptoms) upon admission, and gestational age at diagnosis.

Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were the most prevalent complications. Similarly, in Thailand, postpartum hemorrhage, placental abruption, and heart failure occurred in 9.4%, 1.4%, and 0.4% of women with preeclampsia with severe features, respectively (13). Further, in the Sidama region, Ethiopia, a higher level of

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3 antepartum and postpartum hemorrhage was observed in the mothers of preeclampsia with severe
4 features (9).
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8 It was discovered that older mothers were linked to a higher likelihood of unfavorable outcomes.
9 Mothers over 35 were almost three times more likely to experience an adverse outcome. In a
10 similar vein, poor maternal outcome was more common in Indonesia among mothers with
11 preeclampsia who were older than 35 (24). Because of increased endothelial injuries that lower
12 renal reserves and the incapacity to adapt to physiological changes during pregnancy, older people
13 may be more susceptible to developing renal insufficiency even if their pre-gestational kidney
14 functions are normal (25). It might also be connected to the extravascular space's increased fluid
15 accumulation during pregnancy. Additionally, older people are more likely to have additional risk
16 factors that increase their likelihood of developing preeclampsia, such as diabetes mellitus, obesity,
17 and chronic hypertension (1).
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21 The odds of unfavorable maternal outcomes were 94% higher among rural residents than their
22 urban counterparts. Similarly, in Ethiopia's Sidama region, women who lived in rural regions were
23 more likely to experience unfavorable maternal outcomes (9). This could be because women in
24 rural areas may have had a lower socioeconomic level, which may have resulted in a lesser
25 tendency to seek medical attention. Pregnant women with low health-seeking behavior are less
26 likely to visit antenatal care clinics, which delays the diagnosis and treatment of preeclampsia. In
27 addition, rural women faced significant challenges in getting to health facilities due to
28 transportation issues, which caused delays in receiving medical care. It is improbable that they are
29 aware of the risks and complications associated with pregnancy, labor, and delivery. In addition,
30 the cultural practices prevalent in rural areas greatly impact women's nutritional status by
31 preventing them from consuming necessary foods and/or beverages (26).
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35 Unemployed mothers had less risk of unfavorable outcomes compared to those employed. In the
36 Netherlands, when employed women worked longer hours (≥ 40 hrs/week), the mean birth weight
37 of kids decreased by 45 g (27). Similarly, in South Korea (28), higher risks of early abortive
38 outcomes and stillbirths were more frequent in employed women. The possible explanation might
39 be that unemployed mothers are more likely to have adequate time to care for themselves and listen
40 to updated information regarding gestational hypertension via TV, Radio, or others. This might
41 help them to have a lower risk of unfavorable outcomes.
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3 A severe blood pressure measurement upon admission doubled the likelihood of unfavorable
4 maternal outcomes. Severe blood pressure was also revealed to be a significant predictor of an
5 adverse outcome (eclampsia) among preeclamptic mothers in Morocco (29). Hypertension is one
6 of the hallmarks of preeclampsia and severe hypertension, defined as a blood pressure of more
7 than 160/110 mmHg, has been considered a warning indicator of the development of negative
8 outcomes, such as eclampsia (4). Thus, severe blood pressure is a symptom of a severe condition,
9 rapid disease progression, and a terrible prognosis.

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12 Furthermore, women who were admitted with a chief complaint of headache had a 91% increased
13 risk of unfavorable outcomes. In a retrospective chart review of preeclamptic patients treated at
14 Ayder Comprehensive Specialized Hospital, Ethiopia, headache and blurring were associated with
15 poor maternal outcomes (30). It has been noted that neurologic symptoms indicate an impending
16 negative consequence(2).

17 18 19 20 21 22 23 24 25 **Conclusion and recommendations**

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28 In this study, the prevalence of unfavorable maternal outcomes was high compared to other studies
29 in Ethiopia. Maternal age, residence, occupation, blood pressure on admission, and severe
30 headache have shown a statistically significant association with unfavorable maternal outcomes.
31 Socio-economic development and early identification and treatment of severe signs and symptoms
32 of preeclampsia are needed to reduce unfavorable outcomes. Prenatal screening and specialized
33 care for women who are at high risk, such as older mothers, are also recommended. Further,
34 longitudinal studies are recommended to investigate the outcome of mothers with preeclampsia
35 with severe features.

36 37 38 39 40 41 42 **Limitations**

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45 It shares the limitation of a cross-sectional study to draw a causal relationship. Since this study
46 was conducted in referral hospitals, we are unable to ascertain whether these women delayed
47 visiting the primary health facilities or whether there were delays in referring them. In addition, as
48 this was done in the hospital setting, the maternal outcome of women delivered at home was not
49 assessed. Further, this study does not include adverse maternal outcomes after 24 hours of birth.
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Abbreviations and acronym

AOR: Adjusted Odds Ratio

COR: Crude Odds Ratio

CI: Confidence Interval

C/S: Cesarean Section

DIC: Disseminated Intravascular Coagulation

HDP: Hypertensive Disorder of Pregnancy

HELLP: Hemolysis, Elevated Liver Enzymes, and Low Platelet Count

HTN: Hypertension

MCH: Maternal and Child Health

PEWSF: Preeclampsia with Severe Features

SVD: Spontaneous Vaginal Delivery

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Contributions

WAD drafted the topic, designed the proposal, and performed data collection. MT critically revised, performed the analysis, and developed the manuscript. MT, WAD, GSS, GEW, SDT, and AE reviewed the proposal, contributed to data collection and analysis, and critically revised the manuscript. MT made basic adjustments to the final manuscript and processed publication. All authors approved the manuscript for journal submission.

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Competing interests

None declared

Patient consent for publication

Not required

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Ethics approval

The Institutional Review Board (IRB) of Yekatit 12 Hospital Medical College granted ethical clearance (Protocol number 128/23). A formal letter of support was forwarded to the study hospitals. Participants gave their free and informed consent, and they participated willingly. Those who were illiterate were asked to thumbprint the consent form once the content was read. Confidentiality and anonymity were preserved and the client records were returned to their place after the completion of data collection.

Data availability statement

All relevant data set are incorporated within the paper.

ORCID ID

Mesfin Tadese [http:// orcid. org/ 0000- 0001- 6288- 9771](http://orcid.org/0000-0001-6288-9771)

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17 of maternal and perinatal outcome of preeclampsia at a tertiary hospital In Ethiopia. *Ethiop*
18 *J Reprod Heal.* 2019;11(4):8.
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Figure 1: Outcomes of pregnant women admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

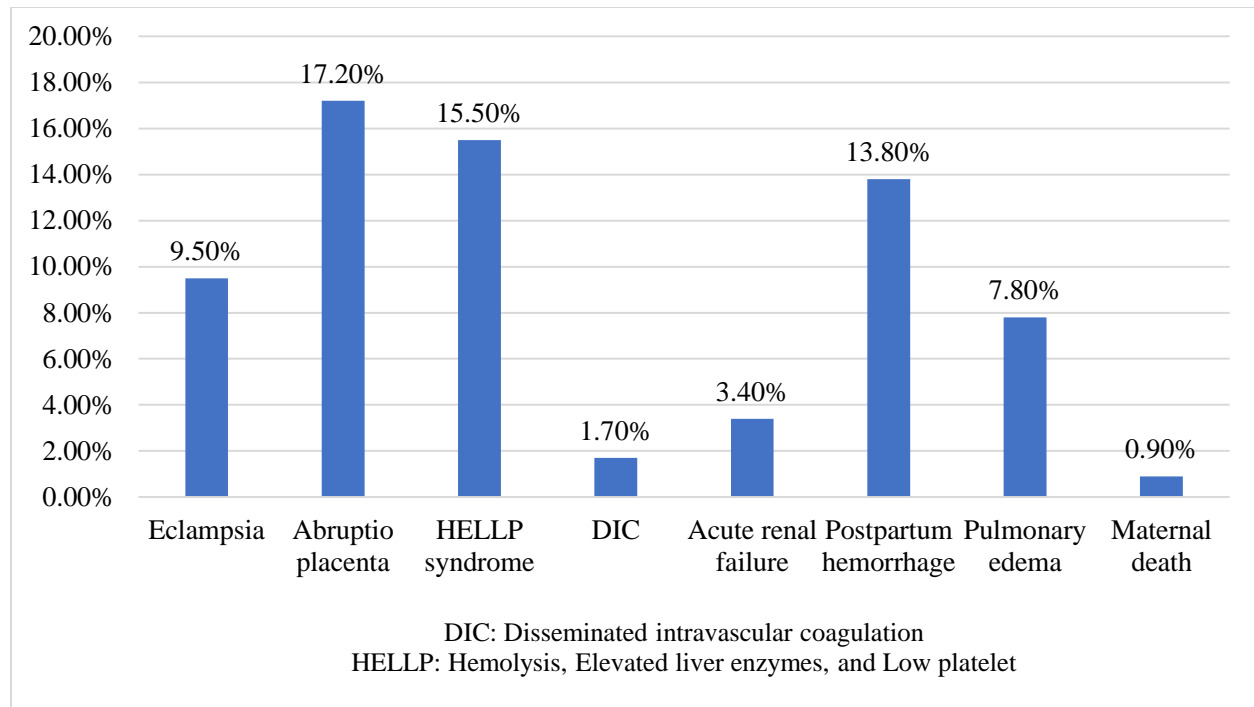


Figure 1: Outcomes of pregnant women admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

STROBE Statement—checklist of items that should be included in reports of *cross-sectional studies*

	Item No.	Recommendation	Page No.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 & 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 1 & 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 6
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 7
Bias	9	Describe any efforts to address potential sources of bias	Page 7 & 8
Study size	10	Explain how the study size was arrived at	Page 6

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 8
		(b) Describe any methods used to examine subgroups and interactions	Page 8
		(c) Explain how missing data were addressed	Page 8
		(d) If applicable, describe analytical methods taking account of sampling strategy	Page 8
		(e) Describe any sensitivity analyses	Page 8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 9
		(b) Give reasons for non-participation at each stage	Page 9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9
		(b) Indicate number of participants with missing data for each variable of interest	Page 9
Outcome data	15*	Report numbers of outcome events or summary measures	Page 17
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 13 and 14
		(b) Report category boundaries when continuous variables were categorized	Page 9 – 12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Continued on next page			

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Maternal outcomes of preeclampsia with severe features and its determinants at Abebech Gobena Mothers and Childrens Health and Saint Peter's Specialized Hospital, Addis Ababa, Ethiopia: a cross-sectional study

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3 **Maternal outcomes of preeclampsia with severe features and its determinants at Abebech**
4 **Gobena Mothers and Childrens Health and Saint Peter's Specialized Hospital, Addis Ababa,**
5 **Ethiopia: a cross-sectional study**
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9 Mesfin Tadese¹, Wogene Asefa Damesa², Gebeyehu Shumet Solomon³, Getu Engida Wakie¹, Saba
10 Desta Tessema¹, Agizew Endale⁴
11
12
13
14
15

16
17 **Affiliations:**
18

19 ¹Department of Midwifery, School of Nursing and Midwifery, Asrat Woldeyes Health Science
20 Campus, Debre Berhan University, Debre Berhan, Ethiopia.
21
22

23 ²Department of Medicine, Obstetrician and Gynecologist, Abebech Gobena Mothers and
24 Childrens Health Hospital, Addis Ababa, Ethiopia
25
26

27 ³Department of Epidemiology, St. Peter Specialized Hospital, Addis Ababa, Ethiopia
28
29

30 ⁴Department of Nursing, Debre Berhan Health Science College, Debre Berhan, Ethiopia.
31
32

33 mesitad031@gmail.com (MT)
34

35 wogeneassefa@gmail.com (WAD)
36

37 gshumet866@gmail.com (GSS)
38

39 getuengida117@gmail.com (GEW)
40

41 sabadesta127@gmail.com (SDT)
42

43 agizewendale2018@gmail.com (AE)
44
45
46
47

48 **Corresponding author**
49

50 Mesfin Tadese

51 Email: mesitad031@gmail.com

52 Tel: +25915839921
53

54 Debre Berhan, Ethiopia
55
56
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Abstract

Objective: The main objective of this study was to determine the prevalence and factors associated with unfavorable maternal outcomes among pregnant women with preeclampsia with severity features (PEWSF) at Abebech Gobena Maternal and Children's Health and St. Peter's Hospital, Addis Ababa, Ethiopia, 2023.

Design: A hospital-based cross-sectional study was conducted from January 1, 2023 to July 2023. The data was collected using a structured and pre-tested questionnaire through face-to-face interviews and a review clinical chart. Data was entered using Epi-Data version 4.6 and analyzed using SPSS version 26.0 statistical software. Binary logistic regression analysis was run to identify predictors of maternal outcome.

Setting: Two hospitals in Addis Ababa, Ethiopia.

Participants: 348 pregnant women with PEWSF were included.

Outcome measures: Unfavorable maternal outcome was defined as mothers with preeclampsia with severe features that develop at least one complication, i.e., eclampsia, abruption placenta, HELLP syndrome, acute renal failure, disseminated intravascular coagulation, cardiac failure, stroke, postpartum hemorrhage, pulmonary edema, and death

Results: The overall prevalence of unfavorable maternal outcomes was 33.9% (N=118) (95% CI: 28.7–38.8). Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were common complications that occurred among mothers with PEWSF. Age above 35 years (AOR (CI)= 2.70 (1.31-5.59), rural residence (AOR (CI)= 1.94 (1.07-3.53), unemployment (AOR (CI)= 0.35 (0.20-0.62), severe blood pressure on admission (AOR (CI)= 2.32 (1.03-5.19), and complain of severe headache (AOR (CI)= 1.91 (1.16-3.16) were significant associates of unfavorable maternal outcomes.

Conclusions: The prevalence of unfavorable maternal outcomes was high compared to other studies in Ethiopia. Maternal age, residence, occupation, blood pressure on admission, and severe headache have shown a statistically significant association with unfavorable maternal outcomes.

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3 Socio-economic development and early identification of severe signs and symptoms of
4 preeclampsia are needed to reduce unfavorable outcomes.
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7 **Strengths and limitations of this study**

- 10 ■ Interviews and clinical chart reviews were conducted to collect data.
- 11 ■ One drawback was that, because the research was conducted in a hospital setting, the
- 12 maternal outcome of home births was not assessed.
- 13 ■ Another limitation was that the study did not include unfavorable maternal outcomes after
- 14 24 hours of birth.
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Background

Preeclampsia is a multisystem progressive illness distinguished by the new development of hypertension and either proteinuria or end-organ failure after 20 weeks of gestation, during pregnancy, labor, or postpartum (1). A combination of maternal and fetal/placental factors is most likely the reason. Relative placental hypoxia, ischemia, or under-perfusion can be brought on by abnormalities in the placental vasculature early in pregnancy (2). This may then cause the mother's circulation to release antiangiogenic factors, altering the mother's systemic endothelium's function and causing hypertension in addition to other disease manifestations (hematologic, neurologic, cardiac, pulmonary, renal, and hepatic dysfunction). However, the reason behind abnormal placental development and the subsequent sequence of events is still unknown (3).

Preeclampsia complicates between 3% and 5% of pregnancies in high-income countries (4). In Africa, hypertension disorders during pregnancy affect 10% of pregnancies (5). A Zanzibar study found that preeclampsia with severe features (PEWSF) was prevalent in 26.3% of mothers (6). Besides, 19.5% of preeclampsia with severe features was reported in a prospective observational study done at Saint Paul's Hospital Millennium Medical College in Ethiopia (7).

In the United States, unfavorable maternal outcomes occurred in 10% of women with preeclampsia with severe features (8). According to a prospective cohort study in the Sidama region of Ethiopia, women with PEWSF had a 43% higher risk of unfavorable maternal outcomes (9). Similarly, it was shown that 37.7% of mothers with severe preeclampsia/eclampsia in referral hospitals in the Amhara region had unfavorable maternal outcomes (10). Further, in Addis Ababa, Ethiopia, 36% of mothers with PEWSF reported having at least one maternal complication (11).

Due to the progressive nature of the disease and the lack of known medical management, delivery is always the definitive treatment, however, there is debate on the best time to deliver for both preterm and term gestations. Extending pregnancy carries a risk of exacerbating endothelial dysfunction in the mother and perpetuating inadequate perfusion of target organs, potentially leading to serious damage to the brain, liver, kidneys, placenta/fetus, hematologic and vascular systems (1). Thus, there is an increased chance of induction failure and subsequent cesarean birth in preeclamptic women(12). Other potential maternal sequelae include seizure, pulmonary edema,

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3 cerebral hemorrhage, renal detachment or cortical blindness, stroke, hepatic failure, heart failure,
4 renal failure, postpartum hemorrhage, disseminated intravascular coagulation, placental abruption,
5 and death (1,13). There was also a reported lifetime risk of hypertension (14). Furthermore,
6 research published in the Lancet Regional Health revealed that pregnant women with hypertensive
7 disorders have an increased risk of developing asthma and chronic obstructive pulmonary diseases
8 (15).
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15 Moreover, preeclampsia and eclampsia made a substantial contribution to maternal deaths and
16 severe morbidity (4,16). Ten to fifteen percent of all maternal deaths worldwide are attributed to
17 preeclampsia and eclampsia (11). In Ethiopia, the five primary direct causes of maternal death
18 were hemorrhage, obstructed labor, preeclampsia/eclampsia, unsafe abortion, and sepsis,
19 accounting for eighty-five percent of maternal deaths. Preeclampsia/eclampsia makes up 11% of
20 these five major causes of maternal mortality (17).
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27 A cross-sectional study in the Amhara region Referral Hospitals, Ethiopia, reported a significant
28 association between residence, level of education, monthly income, parity, history of abortion,
29 booking status, time of drug given, and unfavorable maternal outcome (10). Women admitted at
30 <34 weeks, age 16 – 24 years, lower wealth quintiles, and rural residence had also a positive
31 association with unfavorable maternal outcomes (9). Further, gestational age at admission (18),
32 onset of the disease, and low hemoglobin level (19) were predictors of maternal complication.
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39 Preeclampsia causes significant financial losses that affect not just the individual but also the next
40 generation because of the expense of prescription drugs, medical treatment, lost productivity, and
41 hindered daily activities. According to a US study, preeclampsia during the first 12 months of life
42 is expected to cost \$2.18 billion (\$1.03 billion for moms and \$1.15 billion for infants). The cost
43 burden per infant varies with gestational age, starting at \$150,000 at 26 weeks and going up to
44 \$1311 at 36 weeks (20).
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50 Limited studies to date have been done to address the unfavorable maternal outcomes among
51 pregnant women with preeclampsia with severe features in developing countries including
52 Ethiopia. The findings could have its own contribution to the local Ethiopian Health Sector
53 Transformation Plan-II (HSTP-II) targeted to lower maternal mortality ratio from 401 to 140 per
54 100,000 live births (21) and global Sustainable Development Goal (SDG) target plans of less than
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70 per 100,000 live births by 2030 (22). Hence, the study aimed to determine the prevalence and associated factors of unfavorable maternal outcomes among pregnant women with preeclampsia with severe features in Ethiopia.

Research questions

1. What is the magnitude of unfavorable maternal outcomes among pregnant women admitted with preeclampsia with severe features?
2. What are the factors associated with unfavorable maternal outcomes?

Methods

Study design, period, and area

This cross-sectional study was conducted at Abebech Gobena Mothers and Childrens Health (MCH) and St. Peter's Specialized Hospital from January 1, 2023, to July 30, 2023, in Addis Ababa, the capital city of Ethiopia. Abebech Gobena MCH Hospital is one of the tertiary referral hospitals directly under the Addis Ababa Health Bureau. Yekatit 12 Hospital Medical College uses it as a teaching hospital as well. The hospital gives service to more than 200,000 patients annually who were referred by about 18 catchment health centers in the Oromia regional state and Addis Ababa city, as well as one primary hospital. Whereas, St. Peter's Specialized Hospital is a government facility that served as the nation's first tuberculosis (TB) referral hospital. The hospital was founded in 1953. Currently providing care for over 100,000 people as a specialized hospital under the supervision of the Federal Ministry of Health (FMOH). The MCH center was established in 2006 E.C. and serves 15 catchment health centers and 3 primary hospitals from the Oromia region and Addis Ababa city.

Population and eligibility criteria

All pregnant mothers who were admitted with a diagnosis of preeclampsia with severe features in the study area were the source population. Participants were randomly selected from this source population. All pregnant mothers who were diagnosed, admitted, and managed for PEWSF were included. Pregnant mothers who were diagnosed with preeclampsia but not with severe features and who were not giving birth at the study hospitals with unknown maternal outcomes were excluded.

Sample size and sampling technique

The sample size was determined using OpenEpi Version 3.03 statistical software with the assumption of 36% prevalence of unfavorable maternal outcomes in Addis Ababa, Ethiopia (23), 95% confidence interval, 5% marginal error, and 5% non-response rate. Considering, that the final sample size was 372. A total population sampling method was used to select the eligible study participants.

Variables

Maternal outcome was the dependent variable. Independent variables included sociodemographic factors (age, residence, marital status, occupation, educational level, and mode of admission), medical and reproductive history (gravidity, parity, history of abortion, antenatal care (ANC); history of gestational hypertension, family history of hypertension, anemia, chronic hypertension, diabetes, and renal disease); clinical features and investigations on admission (headache, dizziness, epigastric pain, visual disturbance, nausea and/ or vomiting, convulsion, edema, hematocrit, liver function test, urea, creatinine, urine protein); and obstetric factors (onset of labor, mode of delivery, sex of the neonate, and duration of hospitalization).

Outcome measures

Preeclampsia with severe features: is a preeclampsia with one of the severity features; including altered mental status, severe headache, altered cerebral or visual disturbance, hepatic abnormality, renal abnormality, severe blood pressure ($\geq 160/110$), thrombocytopenia (platelet count $< 100,000/\mu\text{L}$), and pulmonary edema (1,4).

Blood pressure at admission: Severe hypertension if blood pressure measurement was $\geq 160/110$ and mild hypertension if 140-159/90-109 (4,11).

Severe headache: Incapacitating, "the worst headache I have ever had" or headache that persists and progresses despite analgesic therapy (1).

Hepatic abnormality: Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥ 2 times the upper limit of the normal range, or both (1).

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3 **Renal abnormality:** Progressive renal insufficiency (serum creatinine >1.1 mg/dL [97.2
4 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal
5 disease) (1).
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9 **Unfavorable maternal outcome:** Mothers with preeclampsia with severe features that develop at
10 least one complication, i.e., eclampsia, abruption placenta, HELLP syndrome, acute renal failure,
11 disseminated intravascular coagulation, cardiac failure, stroke, postpartum hemorrhage,
12 pulmonary edema, and death (9,10).
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16 **Favorable maternal outcome:** Mothers with preeclampsia with severe features managed and
17 improved without complications (10).
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20 21 **Data collection tool, procedure, quality control**

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23 The data was collected using a well-constructed case record form and procedure. The questionnaire
24 was adapted from similar studies (7–10,13). The data collection team consisted of 2 supervisors
25 and 4 data collectors. The principal investigators gave the supervisors and data collectors a one-
26 day training on the objectives, methods, procedures, and data collection instrument. The
27 questionnaire was translated back and forth from English to Amharic and vice versa to make sure
28 the questions remained true to their original intent. Prior to the real data collection, a pre-test was
29 done on 5% of the samples (19 mothers) at Debre Berhan Comprehensive Specialized Hospital
30 and the necessary adjustments were taken into account in light of the test results. Over the course
31 of the data collection process, the principal investigators and supervisors closely observed the
32 clarity, consistency, and completeness of the data.
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42 **Patient and public involvement**

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44 There was no patient and/ or public involvement in the design and planning of this study.
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47 **Data management and analysis**

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49 Data was entered using Epi-Data version 4.6 and analyzed using SPSS version 26.0 statistical
50 software. The principal investigator randomly selected a questionnaire for quality control and
51 cross-checked it with the correspondingly entered data and clinical chart. We employed descriptive
52 statistics to describe the independent and dependent variables. The results were presented as
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number, frequency, percentage, and comparison of maternal outcomes. Binary logistic regression analysis was run to identify independent predictors of unfavorable maternal outcomes. Variables with a p-value of less than 0.25 in the bivariable regression analysis were included in the final multivariable logistic regression analysis model. Hosmer and Lemeshow's goodness-of-fit test was employed to evaluate the fitness of the model. The multicollinearity of the explanatory components was also investigated. With a two-sided 95% confidence interval (CI), adjusted odds ratios (AORs) were used to interpret the strength of the association. A p-value of less than 0.05 was used to declare the level of significance.

Results

Socio-demographic characteristics of participants

A total of 348 mothers participated, giving the survey a 93.5% response rate. The age range of the participants was 18 to 42 years old, with a mean (SD) of 27.55 ± 5.18 years. Of these, 272(78.2%) lived in urban, making up more than three-fourths. Furthermore, Table 1 shows that 324(93.1%) of the participants were married, and 134(38.5%) had completed secondary school.

Table 1: Socio-demographic characteristics of participants admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Age in years	20 – 34	294	84.5%
	<20	13	3.7%
	≥35	41	11.8%
Residence	Urban	272	78.2%
	Rural	76	21.8%
Level of education	No formal education	45	12.9%
	Primary	97	27.9%
	Secondary	134	38.5%
	Higher education	72	20.7%
Marital status	Married	324	93.1%
	Others*	24	6.9%
Occupation	Employed	204	58.6%

	Unemployed	144	41.4%
Mode of admission	Self	52	14.9%
	Referral	296	85.1%

*Single, Divorced, and Widowed

PEWSF: Preeclampsia with severe features

Medical and obstetric history

More than half, 179(51.4%) of mothers, were primigravida and 69(19.8%) had previously experienced an abortion. Nearly all, 342(98.3%), of the participants had antenatal care (ANC) contact for the current pregnancy. However, only 22 (6.3%) of them had adequate ANC contact. Furthermore, 34(9.8%) of mothers had a history of gestational hypertension. Twenty-seven (7.8%) of participants had a medical history. Of them, chronic hypertension and anemia were reported in 12(3.4%) and 8(2.3%) of cases, respectively (Table 2).

Table 2: Medical and obstetric history of mothers admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Gravidity	Primigravida	179	51.4%
	Multigravida	162	46.6%
	Grand multipara	7	2.0%
Parity	Nulliparous	12	3.4%
	1 – 3	322	92.5%
	≥4	14	4.0%
History of abortion	Null	279	80.2%
	1	61	17.5%
	≥2	8	2.3%
Antenatal care (ANC) contact	Yes	342	98.3%
	No	6	1.7%
Number of ANC contact	1 – 3	74	21.3%
	4 – 6	252	72.4%
	≥7 – 8	22	6.3%
Number of fetuses	Singleton	326	93.7%
	Twin/Multiple	22	6.3%

History of gestational hypertension	Yes	34	9.8%
	No	314	90.2%
Family history of gestational hypertension	Yes	70	20.1%
	No	278	79.9%
Past medical history	Yes	27	7.8%
	No	321	92.2%
Anemia	Yes	8	2.3%
	No	340	97.7%
Chronic hypertension	Yes	12	3.4%
	No	336	96.6%
Diabetes mellitus	Yes	5	1.4%
	No	343	98.6%
Renal disease	Yes	2	0.6%
	No	346	99.4%

Clinical features and investigations on admission

In this study, 180(51.7%), 119(34.2%), and 87(25.0%) of mothers were admitted with a chief complaint of headache, epigastric pain, and edema, respectively. Whereas, on an investigation, 38(10.9%) of the women had deranged liver function tests and 53(15.2%) had protein 3+ upon admission. In addition, 196(56.3%) of mothers had induction of labor and 213(61.2%) of them spent more than three days in the hospital (Table 3).

Table 3: Clinical features of participants admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Category	Frequency	Percent (%)
Headache	Yes	180	51.7%
	No	168	48.3%
Dizziness	Yes	45	12.9%
	No	303	87.1%
Epigastric pain	Yes	119	34.2%
	No	229	65.8%
Visual disturbance	Yes	59	17.0%
	No	289	83.0%
Nausea and/or vomiting	Yes	15	4.3%
	No	333	95.7%
Convulsion	Yes	33	9.5%
	No	315	90.5%
Edema	Yes	87	25.0%
	No	261	75.0%
Grade of edema (n=87)	Grade 1	46	52.9%
	Grade 2	38	43.7%
	Grade 3	3	3.4%
Blood pressure at admission	Severe range	297	85.3%
	Mild range	51	14.7%
Hematocrit	<33%	39	11.2%
	≥33%	309	88.8%
Liver function test	Normal	310	89.1%
	Deranged	38	10.9%
Urea	Normal	322	92.5%
	Deranged	26	7.5%
Creatinine	Normal	319	91.7%
	Deranged	29	8.3%

Urine protein (Dipstick)	Negative	105	30.2%
	1+	50	14.4%
	2+	140	40.2%
	3+	53	15.2%
Onset of labor	Spontaneous	104	29.9%
	Induction	244	70.1%
Mode of delivery	Spontaneous vaginal delivery	186	53.4%
	Instrumental	14	4.0%
	Cesarean section	148	42.5%
Sex of the neonate	Male	186	53.4%
	Female	162	46.6%
Duration of hospital stay	≤ 3 days	135	38.8%
	≥ 4 days	213	61.2%

Maternal outcomes

Overall, 33.9% (N=118) (95% CI: 28.7–38.8) of mothers had unfavorable maternal outcomes. Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were the most prevalent complications that occurred among mothers admitted with a diagnosis of preeclampsia with severe features (Figure 1).

Factor of unfavorable outcomes

Variables having a p-value of less than 0.25 in the bivariable analysis were chosen for the multivariable logistic regression analysis model. A crude odds ratio (COR) is an odds ratio of univariable analysis; one independent variable for predicting the dependent variable. Accordingly, age, residence, level of education, occupation, number of fetuses, sex of neonate, blood pressure on admission, and headache complaint were selected. In the final model, age, residence, occupation, blood pressure upon admission, and complaints of headache were found to be statistically significantly associated with unfavorable maternal outcomes.

Mothers aged above 35 had approximately three-fold increased risk of developing unfavorable outcomes compared to those aged between 20 and 34 (AOR (CI)= 2.70 (1.31-5.59)). Rural residents had a 94% higher chance of experiencing unfavorable outcomes compared to their urban

counterparts (AOR (CI)= 1.94 (1.07-3.53)). Unemployed mothers bore a 65% lower risk of unfavorable outcomes in comparison to those who were employed (AOR (CI)= 0.35 (0.20-0.62)). Severe blood pressure measurement upon admission increased the risk of unfavorable outcomes by two-fold (AOR (CI)= 2.32 (1.03-5.19)). Furthermore, women who were admitted with a headache as their chief complaint had a 91% higher likelihood of having unfavorable outcomes (AOR (CI)= 1.91 (1.16-3.16)) (Table 4).

Table 4: Factors associated with unfavorable maternal outcome among mothers admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

Variables	Maternal outcomes		COR (95% CI)	AOR (95% CI)
	Favorable	Unfavorable		
Age in years				
20 – 34	202 (87.8%)	92 (78.0%)	1	1
<20	8 (3.5%)	5 (4.2%)	1.37 (0.44-4.31)	1.33 (0.39-4.52)
≥35	20 (8.7%)	21 (17.8%)	2.31 (1.19-4.46)	2.70 (1.31-5.59)*
Residence				
Urban	188 (81.7%)	84 (71.2%)	1	1
Rural	42 (18.3)	34 (28.8%)	1.81 (1.08-3.05)	1.94 (1.07-3.53)*
Level of education				
No formal education	23 (10.0%)	22 (18.6%)	1.80 (0.84-3.84)	2.15 (0.89-5.17)
Primary	62 (27.0%)	35 (29.7%)	1.06 (0.56-2.01)	1.73 (0.82-3.67)
Secondary	98 (42.6%)	36 (30.5%)	0.69 (0.37-1.28)	1.00 (0.51-1.98)
Higher education	47 (20.4%)	25 (21.2%)	1	1
Occupation				
Employed	123 (53.5%)	81 (68.6%)	1	1
Unemployed	107 (46.5%)	37 (31.4%)	0.53 (0.33-0.84)	0.35 (0.20-0.62)*
Number of fetuses				
Singleton	220 (95.7%)	106 (89.8%)	1	1
Twin/Multiple	10 (4.3%)	12 (10.2%)	2.49 (1.04-5.95)	2.04 (0.79-5.24)
Sex of the neonate				
Male	116 (50.4%)	70 (59.3%)	1.43 (0.92-2.25)	1.43 (0.88-2.33)

Female	114 (49.6%)	48 (40.7%)	1	1
Blood pressure on admission				
Severe range	188 (81.7%)	109 (92.4%)	2.71 (1.27-5.77)	2.32 (1.03-5.19)*
Mild range	42 (18.3%)	9 (7.6%)	1	1
Headache complaint				
Yes	106 (46.1%)	74 (62.7%)	1.97 (1.25-3.10)	1.91 (1.16-3.16)*
No	124 (53.9%)	44 (37.3%)	1	1

COR: Crude Odds Ratio; p-value ≤ 0.25 AOR: Adjusted Odds Ratio *Statistically significant at p-value < 0.05

Discussion

In this study, the overall prevalence of unfavorable maternal outcomes was 33.9% (95% CI: 28.7-38.8). Age, residence, occupation, blood pressure upon admission, and headache complaints have shown a statistically significant association with unfavorable outcomes among women of PEWSF admitted at Abebech Gobena MCH and St. Peter's Specialized Hospital, Addis Ababa, Ethiopia.

Unfavorable maternal outcomes occurred in 33.9% of mothers with preeclampsia with severe features. This is comparable with the study findings from Amhara region referral hospitals, where 37.7% of mothers with preeclampsia with severe features developed unfavorable outcomes (10). However, it was higher than 10% in the United States (8). This discrepancy could be the result of variations in the study population, time, setup, sample size, and quality and standard of care provided by contemporary, well-equipped maternity hospitals, as well as good prenatal and obstetric care. On the other hand, it was lower than 43% in the Sidama region of Ethiopia (9). Variations in the incidence proportion of unfavorable outcomes between the studies might be attributed to the severity of the disease, differences in clinical features (severity signs and symptoms) upon admission, and gestational age at diagnosis.

Abruptio placenta (17.2%), HELLP syndrome (15.5%), and postpartum hemorrhage (13.8%) were the most prevalent complications. Similarly, in Thailand, postpartum hemorrhage, placental abruption, and heart failure occurred in 9.4%, 1.4%, and 0.4% of women with preeclampsia with severe features, respectively (13). Further, in the Sidama region, Ethiopia, a higher level of

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3 antepartum and postpartum hemorrhage was observed in the mothers of preeclampsia with severe
4 features (9).
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8 It was discovered that older mothers were linked to a higher likelihood of unfavorable outcomes.
9 Mothers over 35 were almost three times more likely to experience an adverse outcome. In a
10 similar vein, poor maternal outcome was more common in Indonesia among mothers with
11 preeclampsia who were older than 35 (24). Because of increased endothelial injuries that lower
12 renal reserves and the incapacity to adapt to physiological changes during pregnancy, older people
13 may be more susceptible to developing renal insufficiency even if their pre-gestational kidney
14 functions are normal (25). It might also be connected to the extravascular space's increased fluid
15 accumulation during pregnancy. Additionally, older people are more likely to have additional risk
16 factors that increase their likelihood of developing preeclampsia, such as diabetes mellitus, obesity,
17 and chronic hypertension (1).
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25 The odds of unfavorable maternal outcomes were 94% higher among rural residents than their
26 urban counterparts. Similarly, in Ethiopia's Sidama region, women who lived in rural regions were
27 more likely to experience unfavorable maternal outcomes (9). This could be because women in
28 rural areas may have had a lower socioeconomic level, which may have resulted in a lesser
29 tendency to seek medical attention. Pregnant women with low health-seeking behavior are less
30 likely to visit antenatal care clinics, which delays the diagnosis and treatment of preeclampsia. In
31 addition, rural women faced significant challenges in getting to health facilities due to
32 transportation issues, which caused delays in receiving medical care. It is improbable that they are
33 aware of the risks and complications associated with pregnancy, labor, and delivery. In addition,
34 the cultural practices prevalent in rural areas greatly impact women's nutritional status by
35 preventing them from consuming necessary foods and/or beverages (26).
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45 Unemployed mothers had less risk of unfavorable outcomes compared to those employed. In the
46 Netherlands, when employed women worked longer hours (≥ 40 hrs/week), the mean birth weight
47 of kids decreased by 45 g (27). Similarly, in South Korea (28), higher risks of early abortive
48 outcomes and stillbirths were more frequent in employed women. The possible explanation might
49 be that unemployed mothers are more likely to have adequate time to care for themselves and listen
50 to updated information regarding gestational hypertension via TV, Radio, or others. This might
51 help them to have a lower risk of unfavorable outcomes.
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3 A severe blood pressure measurement upon admission doubled the likelihood of unfavorable
4 maternal outcomes. Severe blood pressure was also revealed to be a significant predictor of an
5 adverse outcome (eclampsia) among preeclamptic mothers in Morocco (29). Hypertension is one
6 of the hallmarks of preeclampsia and severe hypertension, defined as a blood pressure of more
7 than 160/110 mmHg, has been considered a warning indicator of the development of negative
8 outcomes, such as eclampsia (4). Thus, severe blood pressure is a symptom of a severe condition,
9 rapid disease progression, and a terrible prognosis.

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12 Furthermore, women who were admitted with a chief complaint of headache had a 91% increased
13 risk of unfavorable outcomes. In a retrospective chart review of preeclamptic patients treated at
14 Ayder Comprehensive Specialized Hospital, Ethiopia, headache and blurring were associated with
15 poor maternal outcomes (30). It has been noted that neurologic symptoms indicate an impending
16 negative consequence(2).

17 18 19 20 21 22 23 24 25 **Conclusion and recommendations**

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28 In this study, the prevalence of unfavorable maternal outcomes was high compared to other studies
29 in Ethiopia. Maternal age, residence, occupation, blood pressure on admission, and severe
30 headache have shown a statistically significant association with unfavorable maternal outcomes.
31 Socio-economic development and early identification and treatment of severe signs and symptoms
32 of preeclampsia are needed to reduce unfavorable outcomes. Prenatal screening and specialized
33 care for women who are at high risk, such as older mothers, are also recommended. Further,
34 longitudinal studies are recommended to investigate the outcome of mothers with preeclampsia
35 with severe features.

36 37 38 39 40 41 42 **Limitations**

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45 It shares the limitation of a cross-sectional study to draw a causal relationship. Since this study
46 was conducted in referral hospitals, we are unable to ascertain whether these women delayed
47 visiting the primary health facilities or whether there were delays in referring them. In addition, as
48 this was done in the hospital setting, the maternal outcome of women delivered at home was not
49 assessed. Further, this study does not include adverse maternal outcomes after 24 hours of birth.
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Abbreviations and acronym

AOR: Adjusted Odds Ratio

COR: Crude Odds Ratio

CI: Confidence Interval

C/S: Cesarean Section

DIC: Disseminated Intravascular Coagulation

HDP: Hypertensive Disorder of Pregnancy

HELLP: Hemolysis, Elevated Liver Enzymes, and Low Platelet Count

HTN: Hypertension

MCH: Maternal and Child Health

PEWSF: Preeclampsia with Severe Features

SVD: Spontaneous Vaginal Delivery

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Contributions

WAD drafted the topic, designed the proposal, and performed data collection. MT critically revised, performed the analysis, and developed the manuscript. MT, WAD, GSS, GEW, SDT, and AE reviewed the proposal, contributed to data collection and analysis, and critically revised the manuscript. MT made basic adjustments to the final manuscript and processed publication. All authors approved the manuscript for journal submission.

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Competing interests

None declared

Patient consent for publication

Not required

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Ethics approval

The Institutional Review Board (IRB) of Yekatit 12 Hospital Medical College granted ethical clearance (Protocol number 128/23). A formal letter of support was forwarded to the study hospitals. Participants gave their free and informed consent, and they participated willingly. Those who were illiterate were asked to thumbprint the consent form once the content was read. Confidentiality and anonymity were preserved and the client records were returned to their place after the completion of data collection.

Data availability statement

All relevant data set are incorporated within the paper.

ORCID ID

Mesfin Tadese [http:// orcid. org/ 0000- 0001- 6288- 9771](http://orcid.org/0000-0001-6288-9771)

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Figure 1: Outcomes of pregnant women admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

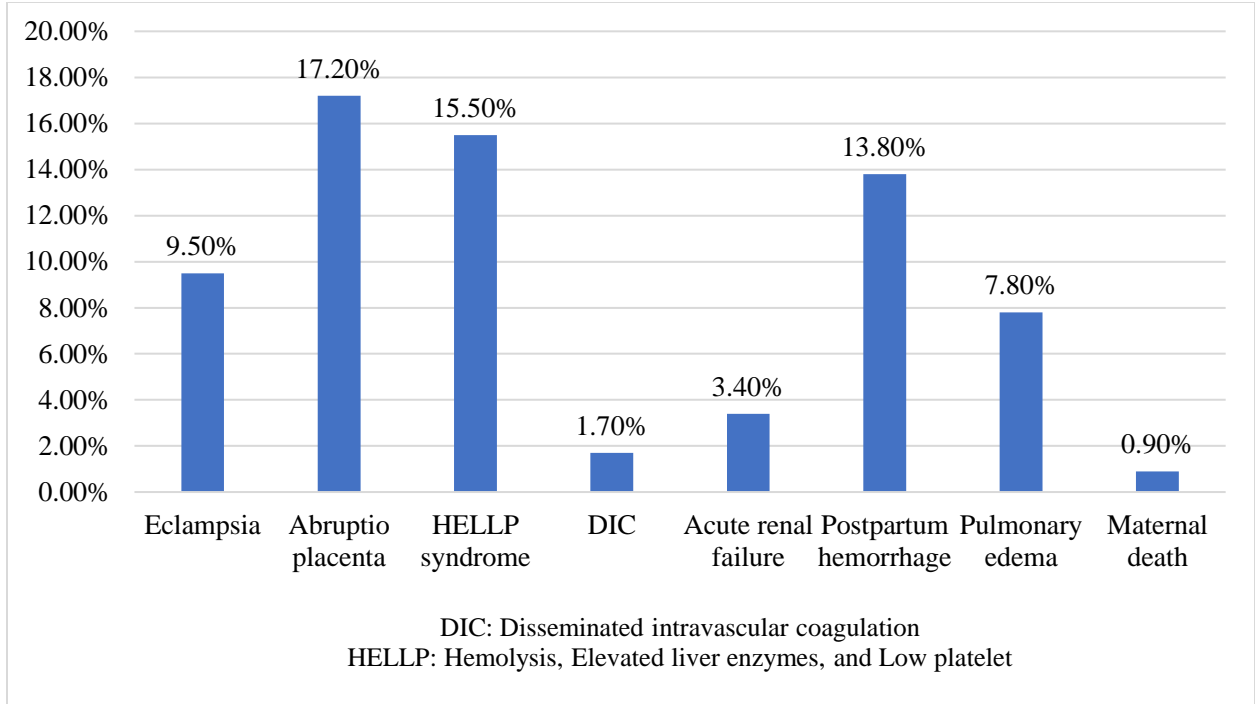


Figure 1: Outcomes of pregnant women admitted with PEWSF at Abebech Gobena MCH and St. Petros Specialized Hospital, Ethiopia, 2023.

STROBE Statement—checklist of items that should be included in reports of *cross-sectional studies*

	Item No.	Recommendation	Page No.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 & 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 1 & 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 6
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 7
Bias	9	Describe any efforts to address potential sources of bias	Page 7 & 8
Study size	10	Explain how the study size was arrived at	Page 6

Continued on next page

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2	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
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4			
5	Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
6			(b) Describe any methods used to examine subgroups and interactions
7			(c) Explain how missing data were addressed
8			(d) If applicable, describe analytical methods taking account of sampling strategy
9			(e) Describe any sensitivity analyses
10			
11	Results		
12	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
13			(b) Give reasons for non-participation at each stage
14			(c) Consider use of a flow diagram
15			
16	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
17			(b) Indicate number of participants with missing data for each variable of interest
18			
19	Outcome data	15*	Report numbers of outcome events or summary measures
20			
21	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
22			(b) Report category boundaries when continuous variables were categorized
23			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.