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Determinants of pre-eclampsia among pregnant women attending antenatal care and delivery services at Bahir Dar public hospitals, northwest Ethiopia: A case-control study

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Abstract

Background and Aims: Pre-eclampsia (PE) is a pregnancy-related syndrome that occurs after 20 weeks of pregnancy. The current study was designed to evaluate the determinants of PE in pregnant women following antenatal and delivery services.

Methods: An institution-based case-control study was performed in governmental hospitals of Bahir Dar city. The data were collected using an interview-administered questionnaire and analyzed by SPSS version 20 software. Bivariate and multivariable logistic regression models were utilized for the analysis of variables. A $p < 0.05$ was used to declare the level of significance.

Results: In this study, the mean ages (in years) of cases and controls were 28.20 ± 5.66 and 27.52 ± 4.70, respectively. Factors such as: being primiparous (adjusted odds ratio [AOR]: 3.19 at 95% confidence interval [CI]: 1.71, 5.97), family history of hypertension (HTN) (AOR: 4.14 at 95% CI: 1.71, 10.05), previous history of PE (AOR: 7.97 at 95% CI: 2.42, 26.63), number of antenatal care (ANC) visits (AOR: 5.43 at 95% CI: 2.86, 10.33), not taking iron and folic acid supplement (AOR: 4.46 at 95% CI: 1.59, 12.48), body mass index ≥25 kg/m^2 (AOR: 3.47 at 95% CI: 1.78, 6.77), not consuming vegetables (AOR: 1.99 at 95% CI: 1.07, 3.69) and not consuming egg, milk and milk products (AOR: 3.00 at 95% CI: 1.47, 6.11) were the determinants of PE.

Conclusion: In this study, different determinants of PE were identified. Hence, special attention should be given for primiparous women, women having previous history of PE and family history of HTN. Moreover, nutritional counseling should be given for pregnant women during ANC visits. Besides, higher officials should design an appropriate strategy to increase the number of mothers to complete their ANC

Abbreviations: ANC, antenatal care; AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; COR, crude odds ratio; DBP, diastolic blood pressure; DM, diabetes mellitus; GA, gestational age; HTN, hypertension; IUGR, intrauterine growth restriction; Kg/m^2, kilogram per meter square; PE, pre-eclampsia; SBP, systolic blood pressure; SD, standard deviation; UTI, urinary tract infection.

visits and to take iron and folic acid supplements. Furthermore, to verify the determinants of PE, community-based cohort studies are warranted.

KEYWORDS
Bahir Dar, case-control, determinants, Ethiopia, pre-eclampsia

1 | BACKGROUND

Pre-eclampsia (PE) is a pregnancy-related metabolic disorder characterized by hypertension (HTN) and proteinuria occurring ≥20 weeks of pregnancy.[1] Worldwide about 76,000 maternal deaths and 500,000 prenatal mortality are occurring due to PE annually.[2] Pregnancy related HTN is the second direct cause of maternal mortality globally next to hemorrhage,[3] which is highly pronounced in developing countries like; Ethiopia compared to developed nations.[3,4] According to the Ethiopian Demographic Health Survey report in 2016, 412 mothers died due to pregnancy-related causes.[5] In Ethiopia, a nation-wide representative data on the incidence and prevalence of PE are somewhat scarce. Nevertheless, previous systematic review reports showed the prevalence of PE to be 4.74%–5.47%.[6,7]

Even though there are remarkable improvements in the understanding of the pathophysiology of PE, the etiology of PE is not fully elucidated. It is known that the interplay between maternal and fetal or paternal aspects playing a pivotal role in the etiopathogenesis of the disease.[8] Abnormal placental blood vessel remodeling leads to placental hypo-perfusion which in turn results in placental necrosis and maternal disorder characterized by high blood pressure and proteinuria.[9,10] Placenta is the cornerstone for PE development which is associated with the presence of paternal genetic determinants leading to immune incompatibility.[11]

Genetic factors,[12] advanced maternal age,[13] being primiparous,[14,15] being overweight or obese,[14] previous history of PE,[14] family history of chronic HTN,[14,16] family history of diabetes mellitus (DM),[16] family history of PE,[14,16] maternal anemia,[14] multiple pregnancies, partner change, lack of antenatal care (ANC) follow-up,[14] inadequate consumption of fruits and vegetables[17,18] are among the characters known to increase the risk of PE development in different populations. In Ethiopia, some epidemiological studies were conducted and showed the prevalence and risk factors associated with PE.[15,16,19,20] Moreover, two independent systematic literature reviews on pregnancy related HTN identified potential determinants of hypertensive disorders of pregnancy.[6,7] Neverthless, PE-focused researches were limited; a few studies lacked operationalization while others used small sample size for analysis. To fill this gap, we designed a case-control study to evaluate the determinants of PE in pregnanat women attending ANC and delivery services in governmental hospitals of Bahir Dar city. The outcomes of the study will enable to healthcare providers and higher officials to engage in preventing maternal and fetal complications.

2 | MATERIALS AND METHODS

2.1 | Study design and period

A facility-based retrospective unmatched case-control study was conducted from September, 2020 to August, 2021. The unmatched case-control study design allowed us to study the possible determinants of PE and multivariable logistic regression model was used to control the effects of confounding variables.

2.2 | Study setting

This study was implemented in Bahir Dar city public hospitals. Bahir Dar city is found at the distance of 565 km from Addis Ababa, the capital city of Ethiopia. Currently, Bahir Dar city serves as the capital city of Amhara Regional State and is surrounded by lake "*Tana*" and Blue Nile River ("*Abay*"). According to the Finance and Economic Development Bureau of Amhara regional state projection in 2020, the populations of Bahir Dar city including satellite Kebeles (Meshenti, Zenzelma, Zegie, and Tiss Abay) were estimated to be 389,177 of which 13,115 women were expected to be pregnant.[21] In the city, three governmental hospitals are found that provide different health services. Tibebe Ghion specialized Hospital is the only governmental Hospital that treat advanced referral cases. Therefore, to avoid redundancy of the study participants we selected two public Hospitals.

2.3 | Study population and eligibility criteria

Source population included all pregnant women attending ANC and delivery services in Felege Hiwot Referral Hospital and Addis Alem Primary Hospital. Pregnant women attending ANC and delivery services in both hospitals fulfilling the inclusion criteria were our study populations. The diagnosis of the cases and controls were performed by physicians by taking the medical history of study participants physical examination and laboratory investigations.

Those pregnant women having HTN plus proteinuria ≥20 weeks of gestation in previously normotensive women were selected as cases. In the absence of proteinuria, PE has been diagnosed as HTN plus presence of severe features of the disease like: severe HTN (BP ≥160/110 mmHg or more in two occasions), low platelet count (<100,000 μL), signs of renal failure (serum creatinine value >1.1 mg/dL or twice of serum creatinine value without other renal pathology), elevated liver

enzymes (increased twice the normal range), signs of pulmonary edema and neurological involvement.[22]

Those normotensive pregnant women attending ANC and delivery services in both hospitals with the gestational age of ≥20 weeks during the study period were selected as controls. The study subjects were selected by simple random sampling techniques. For every case, a control was selected from the same health facility in women coming for ANC and delivery services until we got the required samples. Those pregnant women having chronic HTN, gestational HTN, gestational age <20 weeks and severely ill women who couldn't give consent were exclude from the study.

2.4 | Sample size and sampling procedure

Epi-Info version 7 statistical software was used to calculate the sample size with double population formula by assuming 80% study power at 95% confidence interval (CI). The proportion of controls with exposure was 10.1% and the proportion of cases with exposure would be 22.6% from the previous studies with 1:1 cases to controls ratio.[16] Factors such as: primigravidity, previous history of PE, family history of HTN and multiple pregnancies were significantly related with PE.[15,16,23] Family history of HTN is the commonest predisposing factor of PE with the lowest odds ratio 2.60 and it is utilized for the calculation of the sample size.[16] The total calculated sample size including 10% nonresponse rate was 336 (168 cases and 168 controls). Finally the study participants were proportionally allocated to both hospitals based on their patient load (196 study participants were selected from Felege Hiwot Referral Hospital whereas 140 study participants from Addis Alem Primary Hospital).

2.5 | Study variables

2.5.1 | Dependent variable

Pre-eclampsia.

2.5.2 | Independent variables

Demographic variables

Age of the women, residence, marital status, educational status, occupation, and monthly income.

Nutritional and behavioral variables

For the purpose of this study, intake of fruits, vegetables and egg, milk and milk product consumption were evaluated by asking the women whether she took the foodstuffs in daily basis, 3 days or weekly basis. And it is considered as adequate if the woman had been taking the foodstuffs at the time of data collection or within the past 3 days. Body mass index (BMI) was calculated by the formula weight in kilogram divided by height in meter square.

Obstetric history

Gravidity, parity, history of abortion, frequency of ANC visit, nutritional counseling, Iron and folic acid supplement, previous history of PE, desire of the current pregnancy and partner change within the past 6 months. The sex of the fetus was determined through ultrasonographically by radiologist or obstetrician.

Medical history

Family history of twin pregnancies, family history of HTN, family history of PE, family history of DM and history of UTI were considered as the explanatory variables.

2.6 | Definition of terms

1. HTN is defined as blood pressure of ≥140/90 mmHg measured on two occasions at least 4 h apart whereas severe HTN is defined as blood pressure of ≥160/110 mmHg.[10]
2. Proteinuria is defined as urinary protein excretion of ≥300 mg/24 h urine samples or ≥1+ on qualitative dipstick reading and protein/creatinine ratio of ≥0.3 or more in the absence of urinary tract infections.[2,22]
3. Gestational HTN is defined as HTN occurred ≥20 weeks of pregnancy in the absence of urinary protein.
4. PE is defined as new-onset of HTN plus proteinuria which diagnosed after 20 weeks of gestation.[2,24]

2.7 | Data collection and quality assurance

The questionnaire was adopted from various PE-related literatures. First the questionnaire were prepared in English then translated into Amharic the local language of the study area and later translated back into English by the language expert to ensure the data quality. Data collection was performed using an interviewer-administered questionnaire after we obtained an informed written consent from each study participants. Four BSc degree midwives were recruited to conduct the data collection under the supervision of the principal investigator. The data collection was conducted after confirming the diagnosis through physical examination and laboratory investigations. The interview was made by selecting comfortable place and time especially for those women identified in delivery services. To maintain the data quality, 1-day training was given to the data collectors and the questionnaire was pre-tested in another nearby health institution. The principal investigator verified the consistency, transparency and completeness of the data. When missing values existed in the questionnaire the principal investigator immediately communicated the data collectors to correct the questionnaire before discharging the study participants.

2.8 | Data management and analysis

Data were entered into Microsoft excel sheet and exported to SPSS version 20 statistical software for analysis. Further data cleaning and frequency run was performed to check the accuracy, consistencies, missed values, normality and outliers. First we checked the associations between independent and dependent variables by binary logistic regression model. Then, those independent variables having a $p \leq 0.145$ in bivariate logistic regression model were further analyzed through multivariable logistic regression model to control the effects of confounders. Before we performed the logistic regression model analysis Multicollinearity was checked between explanatory variables using variance inflation factor. In addition, all possible assumptions of logistic regression model were checked and also the model fitness was assessed by Hosmer and Lemeshow test with the p value of 0.338. In multivariable logistic regression model variables having $p < 0.05$ in two-tail were considered as statistically significant. The adjusted odds ratio (AOR) with 95% CI was calculated to measure the strengths of association between explanatory and outcome variables.

2.9 | Ethical approval

The study protocol was reviewed and approved by the Ethical Review Committee of Bahir Dar University (Ref. no: PGRCSVD/143/2012) and Amhara Public Health Institute (APHI with the Ref. no: /3/851/2012). Before the actual data collection the principal investigator described the purpose, significance, benefit, risk, confidentiality and withdrawal of the study for the hospital managers and the study participants. Then, the data collection was initiated after we ensured a written informed consent from each study subjects. The study was conducted according to the ethical principles of Helsinki declaration of studies conducted in human subjects.[25]

3 | RESULTS

3.1 | Sociodemographic characteristics of study participants

In this study, a total of 336 study participants were involved (168 pre-eclamptic and 168 normotensive). The mean ages (±*SD*) of the pre-eclamptic and normotensive were 28.20 ± 5.66 and 27.52 ± 4.70, respectively. Most of the study participants in the cases (97.6%) and controls (99.4%) were married and also 76.2% of the cases and 82.7% of the controls were urban dwellers. Most of the study participants in cases and controls were house-wives in their occupation with 50.6% and 57.1, respectively. In the current study, 46.4% of the cases and 58.3% of the controls were attended secondary education and above (Table 1).

TABLE 1 Sociodemographic characteristics of pregnant women attending ANC and delivery services in public hospitals of Bahir Dar city, northwest Ethiopia, 2021.

Variables	Pre-eclamptic group, *n* (%)	Control group, *n* (%)	*p* value
Age (in years)			
<35	136 (81)	149 (88.7)	0.050
≥35	32 (19)	19 (11.3)	
Mean ± *SD*	28.20 ± 5.66	27.52 ± 4.70	
Residence			
Urban	128 (76.2)	139 (82.7)	0.139
Rural	40 (23.8)	29 (17.3)	
Marital status			
Married	164 (97.6)	167 (99.4)	0.211
Single	4 (2.4)	1 (0.6)	
Educational status			
Illiterate	48 (28.6)	27 (16.1)	0.001
Primary education (grades 1–8)	42 (25)	43 (25.6)	0.080
Secondary education (grades 9–12)	44 (26.2)	40 (23.8)	0.049
Certificate and above	34 (20.2)	58 (34.5)	–
Occupation			
House wife	85 (50.6)	96 (57.1)	0.132
Employed	29 (17.3)	37 (22)	0.104
Merchant	17 (10.1)	22 (13.1)	0.123
Farmer	18 (10.7)	1 (0.6)	0.044
Student	6 (3.6)	5 (3)	0.568
Other	13 (7.7)	7 (4.2)	–
Monthly income			
<2000 ETB	32 (19.1)	20 (11.9)	0.332
2000–5000 ETB	98 (58.3)	114 (67.9)	0.337
>5000 ETB	38 (22.6)	34 (20.2)	–

Abbreviations: ANC, antenatal care; ETB, Ethiopian Birr; SD, standard deviation.

3.2 | Behavioral and obstetric characters of study participants

In the current study, 96 (57.1%) of the cases and 109 (64.9%) of the controls were multigravida, and 84 (50) cases and 102 (60.7%) controls were multiparous. A total of 39 (23.2%) of the cases and 24 (14.3%) controls had a family history of twin pregnancy. A total of 21 (12.5%) of the cases and 5 (2.9%) controls had previous history of PE

while 14 (8.3%) of the cases and 2 (1.2%) controls had family history of PE.

In our study, 148 (88.1%) of the cases and 159 (94.6%) of the controls wanted their current pregnancy whereas 10 (5.9%) of the pre-eclamptic women and 3 (1.8%) of the controls had been changing their partners in the past 6 months. Likewise, 104 (61.9%) of the pre-eclamptic women and 128 (76.2%) of the controls received nutritional counseling during ANC follow up while 132 (78.6%) of the cases and 162 (96.4%) of the controls took iron and folic acid as supplements. The sex of the fetus was determined by obstetric ultrasound (Table 2).

3.3 | Medical and dietary characters of study participants

In this study, 34 (20.2%) pre-eclamptic and 13 (7.7%) normotensive pregnant women had family history of HTN. Whereas 13 (7.7%) pre-eclamptic and 10 (5.9%) normotensive pregnant women had family history of DM. A total of 16 (9.5%) pre-eclamptic and 4 (2.4%) normotensive pregnant women had history of UTI. A total of 77 (45.8%) cases and 112 (66.7%) controls ate fruits; while 104 (61.9%) cases and 131 (77.9%) controls ate vegetables. A total of 105 (62.5%) cases and 113 (67.7%) controls had a habit of drinking alcohol, but 121 (72.1%) cases and 126 (75%) controls drank coffee (Table 3).

3.4 | Multivariable logistic regression analysis of study participants

Seventeen independent variables were analyzed in the logistic regression model to know their association with PE. Those variables with the $p \leq 0.145$ in bivariate analysis were selected and entered into multivariable logistic regression model. In the multivariable logistic regression model, eight variables were found to be significantly associated with PE in the women attending ANC and delivery services at Bahir Dar city public hospitals.

The multivariable logistic regression model showed that the odds of developing PE in primiparous pregnant women were 3.19 times higher compared to multiparous pregnant women (AOR: 3.19 at 95% CI: 1.71, 5.97). Likewise, the odds of developing PE in those pregnant women having family history of HTN were 4.14 times higher as compared with the women who had no family history of HTN (AOR: 4.14 at 95% CI: 1.71, 10.05). Similarly, the odds of developing PE in pregnant women having previous history of PE were 7.97 times higher as compared to the women who had no previous history of PE (AOR: 7.97 at 95% CI: 2.42, 26.26).

The odds of developing PE in pregnant women who could not complete their ANC visits were 5.43 times more likely as compared with the pregnant women who could complete their ANC visits (AOR: 5.43 at 95% CI: 2.86, 10.33). Those pregnant women who could not take iron and folic acid supplements were 4.46 times more likely of

TABLE 2 Behavioral and obstetric determinants of pregnant women attending ANC and delivery services in public hospitals of Bahir Dar city, northwest Ethiopia, 2021.

Variables	Cases, *n* (%)	Controls, *n* (%)	*p* value
Gravidity			
Primigravida	72 (42.9)	59 (35.1)	0.146
Multigravida	96 (57.1)	109 (64.9)	
Parity			
Primiparous	84 (50)	66 (39.3)	0.049*
Multiparous	84 (50)	102 (60.7)	
Family history of twin pregnancy			
Yes	39 (23.2%)	24 (14.3%)	0.038*
No	129 (76.8)	144 (85.7)	
Previous history of PE			
Yes	21 (12.5)	5 (2.9)	0.003*
No	147 (87.5)	163 (97.1)	
Family history of PE			
Yes	14 (8.3)	2 (1.2)	0.008*
No	154 (91.7)	166 (98.8)	
History of still birth or congenital anomaly			
Yes	17 (10.1)	15 (8.9)	0.710
No	151 (89.9)	153 (91.1)	
History of abortion			
Yes	27 (16.1)	28 (16.7)	0.883
No	141 (83.9)	140 (83.3)	
Desire of the current pregnancy			
Wanted	148 (88.1)	159 (94.6)	0.037*
Unwanted	20 (11.9)	9 (5.4)	
New partner in the past 6 months			
Yes	10 (5.9)	3 (1.8)	0.062
No	158 (94.1)	165 (98.2)	
ANC visit			
Completed (≥4 ANC)	61 (36.3)	113 (67.3)	<0.001*
Not completed (1–3 ANC)	107 (63.7)	55 (32.7)	
Nutritional counseling			
Yes	104 (61.9)	128 (76.2)	0.005*
No	64 (38.1)	40 (23.8)	
Iron and folic acid intake			
Yes	132 (78.6)	162 (96.4)	<0.001*
No	36 (21.4)	6 (3.6)	

(Continues)

TABLE 2 (Continued)

Variables	Cases, *n* (%)	Controls, *n* (%)	*p* value
BMI			
<25 kg/m^2	103 (61.3)	121 (72)	0.038*
≥25 kg/m^2	65 (38.7)	47 (28)	
Sex of the fetus			
Male	90 (53.6)	77 (45.8)	0.156
Female	78 (46.4)	91 (54.2)	

Abbreviations: ANC, antenatal care; BMI, body mass index; kg/m^2, kilogram per meter square; PE, pre-eclampsia.

TABLE 3 Medical and dietary determinants of pregnant women attending ANC and delivery services in public hospitals of Bahir Dar city, northwest Ethiopia, 2021.

Variables	Cases, *n* (%)	Controls, *n* (%)	*p* value
Family history of HTN			
Yes	34 (20.2)	13 (7.7)	0.001*
No	134 (79.8)	155 (92.3)	
Family history of DM			
Yes	13 (7.7)	10 (5.9)	0.518
No	155 (92.3)	158 (94.1)	
History of UTI			
Yes	16 (9.5)	4 (2.4)	0.010*
No	152 (90.5)	164 (97.6)	
Fruits intake			
Yes	77 (45.8)	112 (66.7)	<0.001*
No	91 (54.2)	56 (33.3)	
Vegetables intake			
Yes	104 (61.9)	131 (77.9)	0.001*
No	64 (38.1)	37 (22.1)	
Meat intake			
Yes	58 (34.5)	98 (58.3)	<0.001*
No	110 (65.5)	70 (41.7)	
Milk, milk product, and egg intake			
Yes	40 (23.8)	83 (49.4)	<0.001*
No	128 (76.2)	85 (50.6)	
Alcohol consumption			
Yes	105 (62.5)	113 (67.3)	0.361
No	63 (37.5)	55 (32.7)	
Coffee drinking			
Yes	121 (72.1)	126 (75)	0.537
No	47 (27.9)	42 (25)	

Abbreviations: DM, diabetes mellitus; HTN, hypertension; UTI, urinary tract infection.

developing PE as compared with pregnant women who took iron and folic acid as supplements (AOR: 4.46 at 95% CI: 1.59, 12.48). The odds of developing PE were 3.47 times higher in overweight or obese pregnant women compared to those pregnant women having normal BMI (AOR: 3.47 at 95% CI: 1.78, 6.77).

The odds of developing PE in pregnant women who did not consume vegetables were 1.99 times higher compared to those women who consumed vegetables (AOR: 1.99 at 95% CI: 1.07, 3.69). Likewise, pregnant women who did not consume egg, milk and milk products were 3.00 times more likely of developing PE as compared to those women who consumed egg, milk and milk products once per day, three times per day and on weekly basis (AOR: 3.00 at 95% CI: 1.47, 6.11). In the bivariate analysis, women having a habit of consuming fruits, meats and obtaining nutritional counseling during pregnancy were found to be protective to PE but not significant in the multivariable analysis (Table 4).

4 | DISCUSSION

The current study showed detailed evidence about the determinants of PE and found that the parity of the women, family history of HTN, previous history of PE, frequency of ANC visits, those unable to take iron and folic acid supplements, being obese or overweight, with limited dietary intake of vegetables, egg, milk, and milk products during pregnancy were identified as the determinants of PE in pregnant women attending ANC and delivery services.

Primiparous pregnant women were found to be 3.19 times more likely to develop PE as compared to multiparous pregnant women. Similar reports were communicated by the researchers from East Africa,[15,26,27] Middle-East[28] and Latin America.[29] Furthermore, a review on controlled studies demonstrated that primiparity is the commonest determinant of PE.[30] PE has been recognized as the disease of the 'first pregnancy' markedly due to immune maladaptation,[31,32] genetic predispositions,[12] insulin resistance and increased circulating angiogenic factors, which, in turn, aggravate the risks of PE in primiparous women.[33] It is believed that higher placental secretion of circulating antiangiogenic protein and soluble fms-like tyrosine kinase 1 (sFlt1) plays major function in the development of PE.[33]

Our result corroborated those pregnant women who had family history of HTN were 4.14 times more likely of developing PE compared to those having no family history of HTN. Similar evidences were reported in the studies conducted in Ethiopia,[16,19,23,34,35] India,[36] and Brazil.[37] Likewise; the odds of developing PE were 7.97 times higher in pregnant women who had previous history of PE as compared to those who having no previous history of PE. Supporting evidences were reported from Ethiopia,[6] Yemen,[38] India,[36] and China.[39] Although different candidate gene discovery approaches and genome wide association studies were performed to elucidate the single responsible gene for PE, but it was not easy to identify the sole contributing gene to PE.[40–42] PE is a multifactorial and polygenic disease although several epidemiological studies have

TABLE 4 Multivariable analysis of determinants in pregnant women attending ANC and delivery services in public hospitals of Bahir Dar city, northwest Ethiopia, 2021.

Variables	Cases, *n* (%)	Controls, *n* (%)	COR at 95% CI	AOR at 95% CI	*p* value
Age					
<35	136 (80.9)	149 (88.7)	1	1	0.261
≥35	32 (19.1)	19 (11.3)	1.85 (1.00, 3.41)	1.64 (0.69, 3.91)	
Parity					
Primiparous	84 (50)	66 (39.3)	1.47 (0.96, 2.27)	3.19 (1.71, 5.97)	<0.001**
Multiparous	84 (50)	102 (60.7)	1	1	
Family history of HTN					
Yes	34 (20.2)	13 (7.7)	3.03 (1.53, 5.97)	4.14 (1.71, 10.05)	0.002**
No	134 (79.8)	155 (92.3)	1	1	
Family history of twin pregnancy					
Yes	39 (23.2)	24 (14.3)	1.81 (1.04, 3.18)	1.40 (0.68, 2.90)	0.362
No	129 (76.8)	144 (85.7)	1	1	
Previous history of PE					
Yes	21 (12.5)	5 (3)	4.66 (1.75, 12.67)	7.97 (2.42, 26.26)	0.001**
No	147 (87.5)	163 (97)	1	1	
Family history of PE					
Yes	14 (8.3)	2 (1.2)	7.55 (1.69, 33.74)	2.43 (0.47, 12.59)	0.291
No	154 (91.7)	166 (98.8)	1	1	
Desire of the current pregnancy					
Wanted	148 (88.1)	159 (94.6)	1	1	0.794
Unwanted	20 (11.9)	9 (5.4)	2.39 (1.05, 5.41)	1.15 (0.41, 3.21)	
New partner in the past 6 months					
Yes	10 (6)	3 (1.8)	3.48 (0.94, 12.88)	2.54 (0.61, 10.65)	0.203
No	158 (94)	165 (98.2)	1	1	
ANC visit					
Completed	61 (36.3)	113 (67.3)	1	1	<0.001**
Not completed	107 (63.7)	55 (32.7)	3.60 (2.30, 5.65)	5.43 (2.86, 10.33)	
Nutritional counseling					
Yes	104 (61.9)	128 (76.2)	1	1	0.485
No	64 (38.1)	40 (23.8)	1.97 (1.23, 3.16)	1.24 (0.68, 2.29)	
Iron/folate intake					
Yes	132 (78.6)	162 (96.4)	1	1	0.004**
No	36 (21.4)	6 (3.6)	7.36 (3.01, 18.01)	4.46 (1.59, 12.48)	
History of UTI					
Yes	16 (9.5)	4 (2.4)	4.32 (1.41, 13.20)	2.05 (0.56, 7.55)	0.278
No	152 (90.5)	164 (97.6)	1	1	
Fruits intake					
Yes	77 (45.8)	112 (66.7)	1	1	0.388
No	91 (54.2)	56 (33.3)	2.36 (1.52, 3.68)	1.30 (0.72, 2.37)	

(Continues)

TABLE 4 (Continued)

Variables	Cases, *n* (%)	Controls, *n* (%)	COR at 95% CI	AOR at 95% CI	*p* value
Vegetables intake					
Yes	104 (61.9)	131 (78)	1	1	0.030*
No	64 (38.1)	37 (22)	2.18 (1.35, 3.52)	1.99 (1.07, 3.69)	
Meat intake					
Yes	58 (34.5)	98 (58.3)	1	1	0.278
No	110 (65.5)	70 (41.7)	2.66 (1.71, 4.13)	1.43 (0.75, 2.71)	
Milk, milk product, and egg intake					
Yes	40 (23.8)	83 (49.4)	1	1	0.003**
No	128 (76.2)	85 (50.6)	3.13 (1.96, 4.98)	3.00 (1.47, 6.11)	
BMI					
<25 kg/m^2	103 (61.3)	121 (72)	1	1	<0.001*
≥25 kg/m^2	65 (38.7)	47 (28)	1.63 (1.03, 2.57)	3.47 (1.78, 6.77)	

Abbreviations: ANC, antenatal care; AOR, adjusted odds ratio; BMI, body mass index; COR, crude odds ratio; HTN, hypertension; kg/m^2, kilogram per meter square; PE, pre-eclampsia; UTI, urinary tract infection.

demonstrated familial and racial predisposition significantly associated with the disease development. In previous study, which was conducted involving full sisters and daughters of pre-eclamptic women, the risk of PE was shown to be higher in these daughters than in those from normotensive pregnant women.[41,43] Furthermore, the maternal and paternal gene interfaces have a role in placenta dysfunction and PE development due to placental growth restriction and immune maladaptation.[40]

A statistically significant difference was observed in the odds of developing PE among pregnant women having ≥4 ANC visits as compared to women having ≤3 ANC visits. Those pregnant women having ≤3 ANC visits were 5.43 times more likely of developing PE as compared to those pregnant women having ≥4 ANC visits. Comparable evidence was reported in the study conducted in Nekemte Referral Hospital, Ethiopia[44] and the result of this study was further supported by the systematic review on the same topic in Africa.[14] The more pregnant women visit the ANC, the more chance of discussing health issues which are more likely to reduce pregnancy-related complications including PE.

Pregnant women who could not take iron and folic acid as supplements were more likely to develop PE as compared to those pregnant women who could take iron and folic acid as supplements. The odds of developing PE were 4.46 times higher in pregnant women who could not take iron and folic acid as supplements as compared to their counterparts. Other studies conducted in Bahir Dar, Ethiopia,[23] and Beijing, China[45] support the results of the present study. Folic acid supplementation will decrease the chance of PE by facilitating normal placental development and placental implantation in early stages of pregnancy.[46] Besides, folic acid supplementation will decrease the blood homocysteine level and improves systemic endothelial function and decrease the risk of PE.[46] Iron is required for every cell for normal metabolic function and proper development. Iron deficiency anemia is common in pregnant women and young children. Hence, iron supplementation during pregnancy will decrease adverse outcomes like anemia and PE during pregnancy.[47]

Obesity or overweight is the commonest risk factor for PE.[48] Pregnant women having BMI ≥25 were 3.47 times more likely to develop PE compared to pregnant women having BMI <25. This is in line with the evidences reported elsewhere in Ethiopia[6,49] and China.[50] Even though, there is no clear explanation about the mechanism how obesity or overweight leads to PE, experts suggested that hyperinsulinism, insulin resistance and maternal systemic inflammation might lead to endothelial malfunction, high blood pressure, proteinuria and maternal syndrome that are being exhibited in PE.[51]

Maternal nutrition during pregnancy is vital for the normal development of new the born and also for the mother.[52] The results of our study showed that consuming vegetables during pregnancy reduced the risk of developing PE in pregnant women who consumed vegetables compared to those pregnant women who did not consume vegetables. The odds of developing PE were 1.99 times higher women who did not consume vegetables as compared to their counterparts. Supporting evidences were reported in studies conducted in Ethiopia,[17,18] Norway,[53] India,[54] and China.[55] Although the exact mechanism of vegetable consumption reducing the risk of PE is not clear, it is speculated that vegetables have antioxidant properties to scavenge free radicals and inflammatory mediators that have been produced during normal pregnancy.[9,55]

Pregnant women who self-reported consuming egg, milk and milk products were less risk of developing PE as compared to their counterparts. Similar result was also reported from India.[54] The pathophysiological association between consumption of egg, milk, and milk products and PE is not clearly elaborated, but egg, milk, and

milk products are major sources of protein and calcium. Hence, these dietary nutrients are helpful for normal pregnancy and fetal development and also for cell cycle progression. Calcium is involved in different physiological and metabolic pathways. Studies revealed that calcium administration reduces the risk of PE, gestational HTN, HTN, maternal death, pre-term birth and neonatal mortality.[56–60] Some studies showed an association between PE and low birth weight leading to adverse neonatal outcomes.[61,62] The disease mechanism between PE and intrauterine fetal growth restriction (IUGR) follows similar pathological mechanisms.[8,63]

5 | LIMITATIONS

In this study, the cases and controls were selected from the same population and also the cases and controls were comparable and representative to draw an inference. However, the results of this study should be observed in light of the following limitations: dietary assessment was made during diagnosis by asking pregnant women; hence, recall bias is inevitable and also we did not assess the effects of wide range of dietary factors on PE; therefore, causal relationship could not be inferred from this study. Besides, selection bias could not be excluded since cases were selected as they presented at diagnosis and also we could not make comparison between early onset and late onset PE. The institution-based case-control study design cannot represent the entire population of the pregnant women for exploring determinants of PE. Therefore, to identify the determinants of PE at community level, prospective cohort studies are recommended.

6 | CONCLUSION

This study identified different determinants of PE among pregnant women. Characters like; being primiparous, family history of HTN, previous history of PE, number of ANC visits, not taking iron and folic acid as supplements during pregnancy, BMI ≥25, not consuming vegetables and egg, milk and milk products were the determinants of PE in our study. For the early diagnosis and treatment of PE, special attention should be given for those primiparous women, women having previous history of PE and women having family history of HTN. Moreover, nutritional counseling should be given for pregnant women during ANC visits. Besides, higher officials should design appropriate strategies to increase the number of mothers to complete their ANC visits and to take iron and folic acid as supplements during pregnancy. Furthermore, large scale prospective cohort studies are recommended to corroborate the current identified determinants of PE.

AUTHOR CONTRIBUTIONS

Endalamaw Tesfa: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Writing—original draft; Writing—review & editing. **Abaineh Munshea**: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Writing—review & editing. **Endalkachew Nibret**: Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Writing—review & editing. **Solomon Tebeje Gizaw**: Data curation; Formal analysis; Investigation; Methodology; Supervision; Validation; Visualization; Writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

All data pertaining to this study are presented in the manuscript.

ETHICS STATEMENT

All authors agree and provided their consent for submitting and publishing this work. This study was approved by the ethical review committee of Bahir Dar University and Amhara Public Health institute.

TRANSPARENCY STATEMENT

The lead author Endalamaw Tesfa affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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