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Potential risk factors for severe preeclampsia among women from North-Western Algeria; a case-control study

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Abstract

The incidence of preeclampsia (PE) is associated with numerous risk factors that are classified as high and moderate risk factors. In this context, we carried out this study to determine the potential risks of PE and to highlight those associated with the severity of the disease. This is a case-control study of 200 pregnant women, groups of 100 preeclamptic (PG) and 100 non-preeclamptic (NPG) admitted between March 2022 and January 2023 at the Maternity Ward of Sidi Bel Abbes (Algeria). Data were analyzed using SPSS for Windows version 20. Frequencies and percentages were calculated for categorical variables; the Chi-square test was performed to compare between the two groups; the risk factors and the odds ratio were identified using binary regression. The current study showed that the development of PE was associated with several risk factors, in particular renal disease, BMI ≥ 35 and represented potential risk factors for the development of PE with an aOR of (21.65, 95% CI; 2.56-182.75) and (18.47, 95% CI; 4.37-78.01), respectively. Furthermore, a history of PE and gestational hypertension were potential risk factors and contributed to the development of the severe form of PE with an aOR of (6.55, 95% CI; 2.78-15.43) and (7.32, 95% CI; 1.60-33.35); respectively.

Keywords: preeclampsia, severity, risk factors, potential.

Introduction

Worldwide, PE is a serious health issue for expectant mothers and fetus. About 5% of pregnant women are affected by PE. Up to 500,000 fetal and neonatal deaths and 46,000 maternal deaths are caused by this illness each year, most of which occur in developing countries (Laura et al., 2022). A pregnant woman is diagnosed with PE, when her blood pressure reaches 140/90 mm Hg or higher after 20 weeks of pregnancy, along with a number of other symptoms like intense headaches, blurred or flickering vision, pain just below the ribs, vomiting.

Complications of this disorder will damage several organs, such as kidney failure, pulmonary edema, and problems with liver function. as well as neurological conditions such cerebral oedema, epileptic seizures, and strokes Tagetti and Fava (2020).

Numerous environmental and sociodemographic factors are linked to preeclampsia, and these factors frequently hasten the disease's progression. Additionally, maternal factors can also be risk factors for the development of PE Jim and Karumanchi (2017) and may contribute to generate severe forms. While the prevalence of this pathology is in relation with the changing living conditions in each country and genetic factors, which plays a very important role in increasing woman's predisposition to PE (Wainstock et al., 2020). These risk factors can be classified as moderate or high (Wheeler et al., 2022), and include maternal age, obesity, nulliparity, multiparity, history of preeclampsia, and other maternal chronic diseases, especially diabetes, hypertension, and nephropathy Hirshberg and Srinivas (2017). This highlights the importance of identifying these risk factors in order to minimize the risk of this pathology and its complications. Therefore, we felt it necessary to carry out this study in order to assess the potential risk factors in population of pregnant with severe and mild preeclampsia and to explore the factors that may trigger the severe form.

Methods

Study population

This case-control study was conducted at the Maternity Ward of Sidi Bel Abbes (Algeria) from march 2022 to January 2023, we have recruited 200 pregnant , 100 controls who are not preeclamptic (NPG) (Non Preeclamptic Group) as normotensive pregnant and 100 preeclamptic pregnant (PG) (Preeclamptic Group) of which 61 with severe form and 39 with mild form. PE was defined according to the American College of Obstetricians and Gynecologists ACOG (2002) (systolic blood pressure: SBP ≥ 140 mmHg and/or diastolic blood pressure: DBP ≥ 90 mmHg on ≥ 2 recordings taken ≥ 4 hours apart, after 20 weeks' gestation) with proteinuria ($\geq 2+$ by dipstick, ≥ 0.3 g/day by 24-hour). Mild preeclampsia group (MPG) are recruited as patients with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and proteinuria ≥ 300 mg/24h in the absence of features of severity of the disease.

Preeclamptic women presenting the severe form are recruited according to ACOG (2002) guidelines and are characterized by the presence of one of the following criteria:

SBP ≥ 160 mmHg and/or a DBP ≥ 110 mmHg. Measured on 2 occasions (at least 6 hours apart); proteinuria ≥ 5 g/24 hours; creatinine $> 135 \mu\text{mol/L}$ (>14 mg/L); oliguria (<500 ml/24 hours); eclampsia; pulmonary edema; cortical blindness; hepatocellular dysfunction; thrombocytopenia (platelet count $< 100,000$); HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count); Placental abruption and FGR (fetal growth restriction).

The data was collected from patient files, and Face-to-face interviews concerning all clinical information relating to the pregnant women; obstetrical data, clinical, biological and therapeutic, data relating to hospitalization, history of diseases during previous pregnancies, employment status, number of pregnancies, chronic disease, anthropometric data of each patient. The inclusion criteria for pregnant women in this study were as follows agree to take part in the study, have a pregnancy between the 20th and 40th week of gestation, living in urban and rural area.

For preeclamptic group inclusion criteria were to comply, in the first instance, with ACOG criteria, being diagnosed with gestational diabetes mellitus (GDM), chronic hypertension, renal disease. Pregnant women who have mental problems and those who did not consent to participate in this study were excluded.

The study protocol is adapted to the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent (approved by our Institutional Ethics Committee) was obtained from each patient in the study.

Variables description

Body Mass Index (BMI) was calculated as the ratio of weight (kg) to height square (m)² base on maternal height and pregnancy weight report. based on the obtained BMI, patients will be classified based on their BMI into one of the following categories according to the WHO global classification (2000): 18,5 to 24,9 kg/m² is considered as normal weight, 25.0 to 29.9 kg/m² considered as overweight, ≥ 30 kg/m² the pregnant is obese. Advanced maternal age was defined as ≥ 35 years old.

Biochemical analysis

Venous blood samples were collected to measure the patient's biochemical parameters (glycaemia, urea, creatinine, uric acid, ASAT, ALAT, albumin). These parameters were measured using the enzymatic colorimetric method (ERBA Reagent) except ASAT and ALAT, which were determined using cinetic UV method on an automatic analyzer (ERBA XL-300).

Statistical Analysis

Data were analyzed using SPSS 20.0. Chi-square test, ANOVA and student's t-test were used to determine the mean standard deviation, frequency and percentage, Categorical data was described in terms of frequencies and percentages, numerical data was described in terms of mean and standard deviations, $p \leq 0.05$ was considered as statistically significant and $p^{***} \leq 10^{-3}$ as highly significant. Binary regression was used to calculate the odds ratios (ORs) to define the risk factors of preeclampsia and highlight the potential risk factors in severe form. .

Results

The study involved 200 pregnant, 100 normotensives and 100 preeclamptic. Who presents many differences on age, parity, obesity, residence area, occupation, presence or not of gestational diabetes mellitus, chronic hypertension, chronic renal disease, parity, highly significant differences were reported on history of gestational hypertension and history of preeclampsia, in contrast, both groups were diagnosed with urinary and vaginal infection (**Table 1**).

Table 1: Socio-demographic, anthropometric and medical characteristics of the study population according to the presence or absence of PE.

Characteristics	Preeclamptic Group n (%)	Non preeclamptic Group n (%)	P value
N	100	100	
Age (M±SD)	34,08(6.97)	31.01(5,82)	0.001
< 35	55(55.6)	24(24.0)	
≥ 35	44(44.4)	76(76.0)	0.003
Body Mass Index			
Mean (SD)	31.50(5.6)	28.51(3.55)	≤ 10 ⁻³ ***
Normal weight	22(22.0)	49(49.0)	
Overweight	23(23.0)	13(13.0)	≤ 10 ⁻³ ***
Obesity	55(55.0)	38(38.0)	
Region of residence			
Urbain	46(46.0)	64(64.0)	0.015
Rural	54(54.0)	36(36.0)	
Occupation			
Housewife	23(23.0)	98(98.0)	≤0.001
Worker	77(77.0)	2(2.0)	
Gestational Diabetes Mellitus			
Yes	10(10.0)	2(2.0)	0.033
No	90(90.0)	98(98.0)	
Chronic hypertension			
Yes	13(13.0)	2(2.0)	
No	87(87.0)	98(98.0)	0.005
Chronic Renal disease			
Yes	15(15.0)	01(1.0)	
No	85(85.0)	99(99.0)	≤ 10 ⁻³ ***
Nulliparity			
Yes	24(24.0)	27(27.0)	
No	76(76.0)	73(73.0)	0.746
Multiple gestation			
Yes	70(70.0)	47(47.0)	
No	30(30.0)	53(53.0)	0.002
History of gestational hypertension			
Yes	52(52.0)	05(5.0)	
No	48(48.0)	95(95.0)	≤ 10 ⁻³ ***
History of preeclampsia			
Yes	34(34.0)	09(9.0)	
No	66(66.0)	91(91.0)	≤ 10 ⁻³ ***
Urinary tract infection			

Yes	34(34.0)	34(34.0)	
No	66(66.0)	66(66.0)	1.00
Vaginal infection			
Yes	36(36.0)	35(35.0)	
No	64(64.0)	65(65.0)	1.00

Our study focused on the several risk factors associated with preeclampsia cited by many authors. Our studies showed that renal disease is associated with 15% of chronic PE, 15% of

Parameters	Preeclamptic Group (Mean ±SD)	Non preeclamptic Group (Mean ± SD)	P value*
Glycemia (g/l)	1.05± 0.38	0.99± 0.30	0.034
ASAT (UI/L)	37.27± 36.44	22.16± 3.96	≤10 ^{-3***}
ALAT (UI/L)	25.48 ± 29.71	11.91± 6.18	≤10 ^{-3***}
Urea (g/L)	0.28± 0.16	0.25 ± 0.15	0.119
Creatinine(mg/L)	9.19± 3.51	8.39± 1.73	0.044
Uric acid (mg/L)	68.24± 19.24	55.78± 8.15	≤10 ^{-3***}
Albumin (g/L)	31.77± 2.75	36.92± 4.07	≤10 ^{-3***}

preeclamptic pregnant suffered from renal disease, compared with 1% of non-preeclamptic. 13% present chronic hypertension via 2% and 10% have gestational diabetes via 3%. Both groups are nulliparous (24% for PG and 27% for NPG). However, PG have a higher percentage of multiparty than the NPG (70% via 47%). A highly significant differences (>0,001) was reported between the two groups in history of gestational hypertension (52% for PG via 5% for NPG), and history of preeclampsia (34% for PG via 9% for NPG) .

Regarding the clinical aspects of our population, the two groups are different in most levels of biomarkers, including uric acid, albumin and transaminases (p≤ 10-3), glucose and creatinine; an insignificant difference was found for urea (p:0,11) (**Table 2**).

Table 2: Clinical characteristics of study population.

Table 3 showed that most of the factors analyzed were confirmed as significant risk factors for preeclampsia, with the exception of nulliparity (p = 0.622, OR = 0.85, 95% CI: 0.45–1.61). The results also indicated that

working status acts as a protective factor against preeclampsia. The Chi-square test revealed that the majority of nulliparous women (98%) were housewives, compared to only 2% who were employed, while 23% of pregnant women (PG) were workers, with 77% being non-workers ($p \leq 0.001$). The odds ratio (OR) for this association was 0.06 (95% CI: 0.01–0.29), indicating a reduced risk among workers.

The following factors were significantly associated with an increased risk of preeclampsia: Renal disease, identified as a prevalent and high-risk factor (OR = 17.47; 95% CI: 2.26–135.01); Obesity (BMI > 35) (OR = 12.34; 95% CI: 3.52–43.26).; Chronic hypertension (OR = 7.32; 95% CI: 1.60–33.35); Gestational diabetes mellitus (OR = 5.44; 95% CI: 1.16–25.52); History of gestational hypertension (OR = 4.35; 95% CI: 2.06–9.21); History of preeclampsia (OR = 5.44; 95% CI: 1.16–25.52).

Table 3 present also crude ORs for the association of risk factors with mild and severe preeclampsia, we note that most of risk factors were significantly associated with both mild and severe preeclampsia , but it should be mentioned that history of preeclampsia and gestational hypertension remains more significant in case of severe preeclampsia than in mild preeclampsia (mild: OR, 3.48; 95% CI 1.29-9.41 , $p=0,014$ vs severe: OR, 6.55; 95% CI, 2.78-15.43 , $p<10^{-3}$; mild: OR, 3.17; 95% CI, 1.24-8.11 , $p=0,016$ vs severe OR, 5.24; 95% CI, 2.33-11.79 , $p<10^{-3}$, respectively).

Table 03: Crude « Odds Ratio » of PE risk factors associated with PE severity.

Risk Factors		Total ^a (n = 100) OR (95% CI) P value	Mild PE ^b Preeclampsia (n=39) OR (95% CI) P value	Severe Preeclampsia ^c (n=61) OR (95% CI) P value
AGE ≥ 35	No	Reference	Reference	Reference
	Yes	2.48(1.35-4.55) 0.003	3.33(1.53-7.25) 0.002	2.05(1.03-4.09) 0.041
Body Mass Index > 35	No	Reference	Reference	Reference
	Yes	12.34(3.52-43.26) <0.001	18.47(4.37-78.01) <0.001	10.25(2.77-37.89) <0.001
Residence area	Urban	Reference	Reference	Reference
	Rural	2.08(1.18-3.67) 0.011	2.30(1.08-4.88) 0.030	1.96(1.02-3.74) 0.041
Status of pregnant working	Workers	Reference	Reference	Reference
	No Workers	0.06(0.01-0.29) <0.001	0.05(0.01-0.28) 0.038	0.075(0.01-0.34) 0.014
Gestational Diabetes Mellitus	No	Reference	Reference	Reference
	Yes	5.44(1.16-25.52) 0.032	5.60 (0.98-31.92) 0.052	5.34(1.04-27.39) 0.044
Chronic hypertension	No	Reference	Reference	Reference
	Yes	7.32(1.60-33.35) 0.010	7.20(1.336-38.88) <0.001	7.39(1.51-36.09) <0.001

Renal disease	No	Reference 17.47(2.26- 135.01) 0.006	Reference 21.65(2.56-182.75) 0.005	Reference 14.94(1.82-122.69) 0.012
	Yes			
Nulliparity	No	Reference 0.85(0.45-1.61) 0.622	Reference 0.93(0.40-2.16) 0.871	Reference 0,80(0,38-1,69) 0,805
	Yes			
Multiparity	No	Reference 2.63(1.47-4.70) <0.001	Reference 2,87(1.28-6.39) 0.010	Reference 2.49(1.27-4.86) 0.007
	Yes			
Historyof gestational hypertension	No	Reference 4.35(2.06-9.21) <0.001	Reference 3.17(1.24-8.11) 0.016	Reference 5.24(2.33-11.79) <0.001
	Yes			
History of PE	No	Reference 5.20(2.34-11.59) <0.001	Reference 3.48(1,29-9.41) 0.014	Reference 6.55(2.78-15.43) <0.001
	Yes			

Discussion

Preeclampsia, a hypertensive disorder of pregnancy, affects women across various countries, races, and age groups, which accounts for its varying features due to multiple factors, including genetic, physical, environmental, and social influences (Zhang et al., 2020). As such, preeclampsia is considered a multifactorial disease (Vigil-De Gracia et al., 2023), and assessing the degree of exposure to these risk factors is crucial for preventing the disease (Syahfirda et al., 2023). In our study, women who were multiparous or over the age of 35 were categorized as being at high risk. The combination of these two factors contributes to a significantly higher risk of hypertensive disorders during pregnancy (Wei et al., 2016). Age and its associated effects on health and organ function are important, as women over 35 are more likely to experience elevated blood pressure (Yushida and Evi, 2020).

Our findings also indicate that pregnant women living in rural areas are more likely to develop preeclampsia compared to those living in urban areas. This increased risk may stem from lifestyle differences, dietary habits, socio-economic status, and limited access to healthcare, all of which make it more difficult for rural women to monitor their pregnancies (Kershaw et al., 2021). Moreover, rural women tend to follow sedentary lifestyles, with lower participation in physical activity, sports, or the workforce. The challenging living conditions they face may lead to heightened stress, fatigue, and anxiety, all of which can increase their risk of hypertension (Fitri et al., 2022).

Regarding parity as a risk factor of preeclampsia, our results show that multiparous women are 4 times more likely to develop preeclampsia whereas nulliparous are not at risk at all. This is coherent with the results found in the study by (Imad R.Musa et al.2023), which showed that parity of 5 or more is associated with hypertension; (Nur Cahyani Ari et al.2024) explain this risk by the fact that Over-stretching of the uterus leads to excessive ischaemia and therefore to PE.

Our results showed a multiplicity of risk factors reported in several studies, four being cited as the most significant such as renal disease, BMI >35, chronic hypertension and GDM, these factors multiply the risk of PE by a coefficient of 17.47; 12.34; 7.32 and 5.44 respectively. In the study by (Piya Chaemsaitong et al .2022), who performed a comparison between some of the most important prediction models and deduced the widely elevated risks of preeclampsia such as a history of preeclampsia in previous pregnancies, chronic hypertension, autoimmune disease, renal disease, diabetes mellitus, and multifetal gestation. Obesity also represents an increased risk associated with insulin resistance related to placental ischemia (Lopez-Jaramillo, et al.), many studies also have revealed that obesity increases the risk of mild PE Baker and Haeri (2012) and severe PE (Paré et al. 2014).

We have also noted in this investigation that 15% of preeclamptic cases versus 1% of non-preeclamptic have kidney disease and 13% versus 2% have chronic hypertension, these clinical risks combined with maternal risk factors such as advanced maternal age, obesity and multiparity can contribute to increase the risk of preeclampsia (Yushida and Evi. 2020). Our results indicate a relationship between previous preeclampsia, gestational hypertension and severity of the disease. Pregnant women who have preexisting hypertension are at risk for serious problems related to end-organ malfunction, such as liver or kidney dysfunction (HELLP syndrome), central nervous system disorders (eclampsia), etc. (Lisonkova et al.2021). In concordance with our results, several studies have demonstrated that pregnant women with chronic hypertension are at increased risk for developing preeclampsia , we noted the study of Jantasing and Tanawattanacharoen (2011) about 99 patients with early severe preeclampsia, he mentioned that 14% among them had previous preeclampsia and 16.2% chronic hypertension , and another study of Guerrier et al (2013) in which 26% of the population of the study with severe preeclampsia had chronic hypertension, also (Aracil Moreno et al. 2021), identified a group of variables involved in the development of severe preeclampsia, including history of preeclampsia and chronic hypertension .

Conclusion

Given the high prevalence of risk factors for PE, our study identified potential risk factors that are supported by the majority of studies. Indeed, renal disease and BMI > 35 are the factors most potentially linked to the incidence of PE. However, history of PE and gestational hypertension contribute to the development of the severe form.

Disclosure of Interest

The authors have no conflict of interest.

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