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Research Article

Puerperal Preeclampsia among Women with No History of Perinatal Preeclampsia

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ABSTRACT

Objective: To study the characteristics of delayed puerperal preeclampsia/eclampsia in women after delivery and its clinical management.

Study design: This multicenter retrospective study involved analysis of cases diagnosed with delayed-onset puerperal preeclampsia/eclampsia upon readmission, from 48 hours-6 weeks after delivery. Total of 170 women were included in the study, out of which 50 were included in case group, and 120 in control group. The identification of cases was made by using the International Classification of Diseases (ICD-9). Data were collected by chart review and the current version of the SPSS software package was used for data analysis.

Results: Case group had mostly non-white racial origin women, 16% of whom were found to be smokers with an elevated maternal pre-pregnancy BMI. There was an increased risk factor for readmission in association with gestational diabetes, and 50% in the case group had a C-section for delivery. Greater birth weight is observed in women with delayed puerperal preeclampsia than those in the control group. Multiple gestations were correlated with a higher risk for readmission. About 34% of patients had a prior history of eclamptic fit at home and were admitted with headaches as a typical symptom observed. HELLP syndrome was observed in 10% of patients. Intracranial hemorrhage was secondarily responsible for 4% of maternal deaths and 8 women were admitted to the ICU.

Conclusion: Postpartum women should be monitored for early detection of symptoms of preeclampsia. Especially women with this risk factor need appropriate treatment to reduce maternal mortality.

Keywords: Humans; Pregnancy; Pre-eclampsia; Maternal mortality; Eclampsia

INTRODUCTION

Preeclampsia is a condition defined by hypertension, proteinuria, and symptoms relating to organ damage. Although the pathophysiology is not fully understood, preeclampsia is correlated with abnormal maternal trophoblast function and microvascular disease. There is no particular treatment for preeclampsia other than the delivery of the fetus and placenta. There have been studies on developing hypertension in the antepartum duration or immediately postpartum phase. Addressing the condition of *de novo* diagnosis of delayed-onset preeclampsia needs attention. Preeclampsia itself is a complication responsible for maternal morbidity and mortality [1]. But delayed-onset postpartum preeclampsia is now considered an important contributor to maternal morbidity and mortality. Delayed-onset postpartum preeclampsia is also known as puerperal preeclampsia. This condition has been previously defined as new onset preeclampsia 48 hours to 6 weeks after birth. Puerperal preeclampsia reports have been limited to smaller case series. Delayed-onset preeclampsia or puerperal preeclampsia is typically diagnosed when it recurs within 48 hours of delivery but less than 6 weeks post-delivery.

Previous studies report that one-two thirds of women admit due to recurrence of delayed-onset preeclampsia with no prior diagnosis of hypertension during pregnancy. But these have been mostly single-institution studies where risk factors have been

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reported for readmissions due to late puerperal preeclampsia [2]. Hence a broad, population-based examination of the risk may guide us in scrutinizing women who are predicted to be at lower risk. The diagnosis is made for the first time in the postpartum period when Systolic Blood Pressure (SBP) is ≥ 140 mm Hg or Diastolic Blood Pressure (DBP) is ≥ 90 mm Hg along with the protein uria condition (≥ 0.3 g in a 24-hour urine specimen) or when the protein/creatinine ratio ≥ 0.3 and/or there is end-organ damage in an earlier normotensive woman.

After delivery, if these patients present to the emergency department, they should be provided optimal care as this condition is critical to maternal health. There are contradictory reports on delayed-onset preeclampsia, with the most severe cases. Many data reveal similar risk factors for puerperal preeclampsia and antepartum preeclampsia [3]. Past studies have always focused on puerperal preeclampsia risk factors, but enhanced studies on delayed-onset preeclampsia are a matter of concern. The identified risk factors present with demographic and clinical features, including older maternal age, maternal obesity, non-Hispanic black race gestational diabetes, delivery *via* C-section, and elevated intrapartum hypertension. Presentation of delayed-onset puerperal preeclampsia is usually within the first 7-10 days post-delivery, with headache as its typical symptom. Hence, the critical period is identified as the first 7 days post-delivery after discharge for the occurrence of eclampsia.

Based on the presenting signs and symptoms, a thorough history and physical examination should be included in the diagnostic evaluation of new-onset postpartum hypertension. The measurement of electrolytes, renal function, platelet count, liver enzymes and urine protein levels should all be included in the serum laboratory analysis. Previous research has shown that 20% to 40% of women had increased urine protein-to-creatinine ratios (>0.3) and that 25% of women have abnormal serum laboratory findings [4]. A previously published report has also suggested detailing the differential diagnosis and methods for the workup of alternate etiologies of hypertension in this time period.

There are data regarding the treatment and the outcome of delayed-onset preeclampsia. Acute treatment is required to manage severe hypertension for puerperal preeclampsia, acute treatment is required. American College of Obstetricians and Gynecologists (ACOG) suggests treating women with fast-acting antihypertensive agents within 30-60 minutes. These antihypertensivedrugs are similar to those used during pregnancy and include oral nifedipine, IV labetalol and IV hydralazine as fine-line treatments [5]. Available data do not well support the effectiveness of particular antihypertensive medications during the postpartum period. More research is required to establish the ideal BP targets and ranges for commencement and maintenance in the context of postpartum preeclampsia. In the absence of standardized treatment guidelines for specific antihypertensive drugs or parameters for postnatal drug titration in the postpartum period, physician preference, experience, drug cost, safety during breast feeding and dosing frequency are the factors that need to be considered for a suitable choice of therapy.

Magnesium sulfate for seizure prevention is an important component in managing prenatal preeclampsia with severe symptoms. Still, there are few evidence-based recommendations for magnesium sulfate use in women with postpartum preeclampsia. ACOG advises using magnesium sulfate when there is a severe condition of headaches or hazy vision. Also, this recommendation is constituted with low-quality evidence. Hence, we aimed to analyze the features of delayed puerperal preeclampsia/eclampsia in women after delivery and its clinical management [6].

MATERIALS AND METHODS

The research was a multicenter retrospective study conducted from May 2016 to May 2021 at Duhok's obstetrics and gynecology teaching hospital, Azadi teaching hospital, emergency teaching hospital and Kurdistan hospital in Kurdistan region's Dohuk city, Iraq. The ethics and scientific committee of Kurdistan's higher council of medical specialties approved conducting the research. A total of 170 women were included in the study [7].

The study involved analysis of cases with no history of preeclampsia/eclampsia/pregnancy-induced hypertension and chronic high BP in the antepartum, intrapartum or early postpartum period (within 48 hours after delivery) right before the discharge process in the current pregnancy and again readmitted with a diagnosis of delayed-onset puerperal preeclampsia/eclampsia within the duration of 48 hours up to 6 weeks after delivery. Women with prior history of hypertension were excluded [8].

International Classification of Diseases (ICD-9) was used to identify the cases. Data were collected by chart review, and records were reviewed for the following information: Patient information, obstetric and medical history, presenting clinical features, the occurrence of seizures, physical examination, complications, laboratory findings, radiology tests, emergency management, and discharge details. These data were compared with the data from women in the control group. The control group had no complicated pregnancies and no readmissions for puerperal complications and matched the delivery dates to the women in the case group [9].

Statistical analysis

Data were collected and analyzed statistically using an SPSS statistical software package. Normal variables were considered as numbers and percentages (%) in descriptive statistics, while quantitative variables were interpreted as mean ± standard deviation. The mean difference of the quantitative variables was done by using the Student's t-test. The difference in frequency was studied by performing the *Chi-square* test, and a p-value<0.05 was taken to be statistically significant [10].

RESULTS

A total of 170 women were included in the study, where high BP was not found in the 50 women in the case group with the present pregnancy condition. Although, the patients got

diagnosed with delayed puerperal preeclampsia/eclampsia and readmitted within the first 6 weeks after delivery. The control group involved 120 women with no complications in pregnancies admitted at the same time for delivery as that of the case group; hence, the control group was compared with the case group (Table 1) [11].

Table 1: Baseline characteristics of patients readmitted with a diagnosis of late-onset postpartum preeclampsia/eclampsia (case) versus uncomplicated pregnancies without readmissions for postpartum complications (control).

Baseline characteristics	Case group N=(50)	Control group N=(120)	P value
Maternal age (years)	28.96 ± 7.188	25.30 ± 4.190	0.001
Parity			
Primigravida	25 (50%)	55 (45.8%)	0.62
Multigravida	25 (50%)	65 (54.2%)	
Race			
White race	18 (36%)	79 (65.8%)	0
Non-white	32 (64%)	41 (34.2%)	
Smoking status			
Smoker	8 (16%)	2 (1.7%)	0.001
Non-smoker	42 (84%)	118 (98.3%)	
Pre-pregnancy BMI (kg/m^2)	24.16 ± 3.733	22.84 ± 2.436	0.003
Gestational diabetes			
Yes	7 (14%)	2 (1.7%)	0.003
No	43 (86%)	118 (98.3%)	
Mode of delivery			
NVD	25 (50%)	99 (82.5%)	0
CD	25 (50%)	21 (17.5%)	
Gestational age (wk)	38.74 ± 1.562	37.72 ± 1.101	0.007
Birth weight (kg)	3.409 ± 0.588	3.132 ± 0.371	0.01
Multiple gestations			
Yes	5 (10%)	1 (0.8%)	0.009
No	45 (90%)	119 (99.2%)	
Intravenous fluid infusion			
Yes	48 (96%)	120 (100.0%)	0.085
No	2 (4%)	0 (0.0%)	
Ergot after delivery			
Yes	15 (30%)	37 (30.8%)	0.914
No	35 (70%)	83 (69.2%)	

Note: Quantitative variables presented as mean ± SD, nominal variables as number (percent), P<0.05=significant, P<0.001=highly significant, P>0.05=not significant

Table 1 lists the patients basic features related to demography or past medical history or any pregnancy-related issues. The average age of women in the case group was 28.96 ± 7.188, while for the control group, it was 25.30 ± 4.19 years. A significant difference was observed regarding the age factor between both groups [12]. The case group with delayed puerperal preeclampsia had patients in a higher age group than the control group. Also, there was no correlation observed between the groups regarding parity.

The case group had more non-caucasians as compared to the control group. A significant difference was observed in both the groups concerning smoking status, where 16% of the case group (8 women) was found to be smoking. The mean difference for maternal pre-pregnancy Body Mass Index (BMI) for the case group and control group were (24.16 ± 3.733) and (22.84 ± 2.436) respectively.

Women diagnosed with any medical disease, such as gestational diabetes, were significantly correlated with a risk for readmission. A statistically significant correlation between both groups was noted concerning the mode of delivery as 50% (25 women) with delayed puerperal preeclampsia were delivered by C-section.

The average fetal age at the time of delivery for the control and case groups were (38.74 ± 1.562) and (37.72 ± 1.101) respectively and a higher fetal age was observed in the control group than case group [13]. Women with delayed puerperal preeclampsia have a higher birth weight than those in the control group. Hence, a difference in birth weight could be observed between both groups, which were statistically significant.

There was a higher risk for readmission due to multiple gestations. No significant correlation was found between the groups regarding intrapartum intravenous fluid administration and postpartum ergot injections (Table 2).

Table 2: Clinical presentation and complications of patients readmitted with a diagnosis of late-onset postpartum preeclampsia/eclampsia (n=50).

Clinical presentation	Value
Mean readmission postpartum (days)	3.02 ± 0.94
Mean duration of hospital stay	3.09 ± 2.243
Headache	41 (82%)
Visual changes	35 (70%)
Shortness of breath	34 (68%)
Nausea/vomiting	29 (58%)
Edema	29 (58%)
Epigastric pain	27 (54%)
Eclampsia	17 (34%)
Mean highest systolic BP (mmHg)	170.40 ± 23.296
Mean highest diastolic BP (mmHg)	100.50 ± 13.749
HELLP syndrome	5 (10%)
Pulmonary edema	3 (6%)
Cerebrovascular accident	2 (4%)

Cardiomyopathy	2 (4%)
Venous thromboembolism	2 (4%)
Admitted to intensive care unit	8 (4%)
Maternal mortality	2 (4%)

Note: Quantitative variables presented as mean ± SD, nominal variables as number (percent)

Table 2 enlists the clinical presentation and complications of women readmitted due to delayed-onset puerperal preeclampsia/eclampsia [14]. The mean postpartum day of presentation was (3.02 ± 0.94) and the duration of hospital stay was (3.09 ± 2.243).

The most typical indicator was headache found in 82% of patients (41 women) followed by visual changes in 70% of patients (35 women) and 34% of patients were admitted due to eclamptic fit at home. All the symptoms were observed three days after delivery.

The mean highest systolic and diastolic blood pressure was (170.40 ± 23.296) mmHg and (100.50 ± 13.749) mmHg, respectively, during the readmission period. HELLP syndrome could be observed in 10% of cases (5 women). Serious complications like pulmonary edema were seen in 6% of cases (3 women), while cerebrovascular accident, cardiomyopathy and venous thromboembolism were indicated for about 4% of cases (2 women). Intensive Care Unit (ICU) admission was required for eight patients. Two (4%) maternal deaths were recorded as secondary to intracranial hemorrhage (Table 3).

Table 3: Management of patients readmitted with a diagnosis of late-onset postpartum preeclampsia/eclampsia (n=50).

Clinical management	Value
Low platelets (<150)	39 (78%)
Proteinuria >2+	49 (98%)
Elevatedserum creatinine	2 (4%)
Abnormal serum transaminase	17 (34%)
Chest X-ray	5 (10%)
Head CT	4 (8%)
Echocardiogram	5 (10%)
Parenteral antihypertensive agents	50 (100%)
Magnesium sulfate prophylaxis	50 (100%)
Diuretic treatment	5 (10%)

Table 3 summarizes the clinical management of patients who were readmitted due to delayed-onset puerperal preeclampsia/eclampsia. Thirty-nine women (78%) had low platelet count, 49 (98%) women had proteinuria with greater than 2+ protein levels, elevated serum creatinine levels were found in 2 women (4%), and abnormal serum transaminase levels could be observed in 17 women (34%) [15].

Five women underwent chest X-rays, 4 (8%) underwent head CT, and 5 (10%) underwent echocardiography. All 50 women in the case group (100%) received magnesium sulfate. For blood pressure management, 50 (100%) of all women readmitted for preeclampsia/eclampsia used parenteral antihypertensives and diuretics were indicated only for 5 (10%).

DISCUSSION

Placental delivery resolves the condition of preeclampsia, but developing preeclampsia days after the delivery period is demanding. It is still unclear whether late postpartum preeclampsia or eclampsia has the same pathophysiology as antepartum preeclampsia or eclampsia. Past review literature listed some risk factors associated with postpartum preeclampsia. These factors were older maternal age, maternal

obesity and the black race. There was a two-fold risk of postpartum preeclampsia occurring in women ≥ 35 years of age. A dose-dependent manner of increased risk of having postpartum preeclampsia was also observed, where a 7.7 times increase in risk was linked to a BMI of >40 kg/m^2. Finally, racial differentiation could also be noticed as a risk factor. A two-fourfold increased risk of having postpartum preeclampsia was seen in women of black ethnicity compared to women of other races. In the present study, we observed various risk factors that led to delayed postpartum preeclampsia or eclampsia, such as older maternal age, non-caucasian race, obesity, cesarean delivery, postdate and complication of gestational diabetes mellitus during pregnancy [16].

In a case-control study of women with newly diagnosed late postpartum preeclampsia and those without the condition, pregnancies complicated by older age, black race, latinos, obesity and gestational diabetes mellitus were all reported to be related to this. One study reported that women with late-onset puerperal preeclampsia were significantly belonged to the non-hispanic black race, obese and were delivered by C-section than the women in the control group.

The condition of late-onset puerperal pneumonia patients does not show a previous diagnosis of hypertensive pregnancy disorder in approximately 60% of the cases. Most women with this condition present within their first 7-10 days after giving birth. However, this presentation varies where the condition's onset can also occur within three months after delivery. Women most commonly suffer from neurological symptoms such as headaches which are consistently reported in some studies as the typical symptom in approximately 60% to 70% of women. Postpartum headaches are very common. However, some features lead to an additional investigation by imaging or consultation with a neurologist or neurosurgeon. Headaches with altered mental status, seizures, visual problems or focal neurologic defects may require further examination for other cerebrovascular symptoms.

The present study showed the typical symptoms of headache and visual changes. A retrospective study was conducted where the common symptoms of edema, headache, hypertension and visual changes were observed in the postpartum period [17]. In response to magnesium sulfate, our patients showed a history of eclamptic fit and were admitted on the third postpartum day. One case was reported with convulsions on the 9th postpartum day. In another case, puerperal eclampsia occurred after 8 weeks of delivery. Our study demonstrated a mean value of (3.02 ± 0.94) for patients who were readmitted due to puerperal preeclampsia or eclampsia. A study has also reported that patients are readmission within a week of discharge after delivery.

In our study, nearly all patients had high BP on admission; one study report mentioned that postpartum eclamptic seizures were least likely to end up with severe diastolic hypertension. The following complications were observed; pulmonary edema in 3 cases of cerebrovascular accident (4%), cardiomyopathy in 2 cases (4%) and venous thromboembolism in 24% of cases and 2 (4%) maternal death was also recorded. In a multicenter retrospective study of women diagnosed with postpartum hypertension/preeclampsia, complications were seen with eclampsia in 24 (15.9%), pulmonary edema in 9 (5.9%), endomyometritis in 6 (3.9%), 2 (1.3%) thromboembolism and 1 maternal death.

Our study also conducted laboratory tests like urinalysis, where most of them had proteinuria. In one study, 29% to 79% of postpartum eclamptic had proteinuria. In our study, neuroimaging was done to exclude intracranial hemorrhage. Still, one also study reported that women with eclampsia do not need cerebral imaging always to diagnose or manage the condition. In our study, all women received magnesium sulfate. There are 4 large randomized trials that compared patients who had undergone treatment with magnesium sulfate and patients who had no treatment with severe preeclampsia. The incidence of eclampsia was significantly lower in patients receiving magnesium sulfate. There were two significant limitations in the current study that must be taken into consideration. The first was insufficient sample size. The second limitation was that the study was retrospective, and the information was limited to viewing the hospital records.

CONCLUSION

Delivery of the placenta does not completely end the development of preeclampsia. Although postpartum readmission due to hypertension or preeclampsia is rare in low-risk women, risk factors for prepartum readmission can be identified. Prospective studies among women with large sample sizes with uncomplicated pregnancies should be documented and recorded to examine the inherent history of BP trajectory delivery which may lead to checking the true occurrence of the disease. The postpartum woman need seducation and monitoring for early detection of symptoms of preeclampsia and recognizing warning signs for eclampsia, especially women who pose this risk factor. Precise diagnosis of high-risk puerperal preeclampsia in women for hypertension makes an opportunity to target and triage post-delivery care. These patients need appropriate treatment to decrease serious complications and maternal mortality. A predictive model is needed to design steps to identify risk factors and manage the condition. Patients, obstetricians and clinicians need attention to timely recognition of symptoms and indications. The condition of puerperal preeclampsia is less studied and studies related to late-onset postpartum preeclampsia are very limited to small case series or case reports. The research priorities for studying delayed-onset puerperal preeclampsia are: Determining the incidences and further risk factors of the disease, gaining in-depth knowledge of the etiology and pathophysiology, developing evidence-based models for examining outcomes, analyzing the risk of having future pregnancies and optimal management and finally an assessment of future risks to maternal health.

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