Open Access

Journal of the Faculty of Medicine Baghdad
Print ISSN: 0041-9419, OnlineISSN: 2410-8057
DOI: https://doi.org/10.32007/jfacmedbaghdad2992

Research Article

Evaluation of Key Indicators for Assessing and Grading Severity of Preeclampsia

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Received: Oct. 2024
Revised: April, 2025
Accepted: May, 2025
Published Online: May, 2025

Abstract

Background: Preeclampsia (PE) is a condition that is specific to pregnancy and has a substantial impact on the morbidity and mortality of the mother and the fetus worldwide. Currently, various markers may serve as possible predictors or markers for illness severity.

Objectives: The present study aimed to identify and evaluate the key clinical indicators that differentiate between preeclampsia with and without severe features.

Methods: The research included 90 pregnant Iraqi women who manifested preeclampsia subsequent to 24 weeks of gestation and were selected from Al-Elwiya Teaching Hospital for Maternity between April and June 2024. The patients were categorized into two groups: 45 with preeclampsia without severe features and 45 with preeclampsia with severe features. Key indicators assessed included blood pressure and laboratory parameters. Outcomes such as birth weight and FHR and complications, such as Caesarean section, intrauterine death, and eclampsia were also determined.

Results: The levels of AST, ALT, blood urea, and serum creatinine were significantly elevated in PE with severe features, while platelet counts were substantially reduced. Additionally, there was a noticeable rise in proteinuria; in PE without severe features, proteinuria reaches +2. While in PE with severe features, proteinuria exceeds +4. Pregnant women with preeclampsia with severe features had a lower birth weight of 2.32 kg, compared to those without severe features, who birth weight of 3.14 kg. The baseline fetal heart rate (FHR) decreased from 139 bpm in PE without severe features to 119 bpm in PE with severe features. PE with severe features is linked to greater maternal and fetal complications and shows increased rates of intensive care unit (ICU) (71.11%), Caesarean section (CS) (75.56%), intrauterine death (IUD) (15.55%), and eclampsia (11.11%).

Conclusion: The previously mentioned indicators AST, ALT, blood urea, serum creatinine, and proteinuria, in addition to fetal heart rate and birth weight, are valuable for assessing preeclampsia severity, highlighting the importance of monitoring.

Keywords: ALT; AST; Platelets; Preeclampsia; Proteinuria.

Introduction:

Preeclampsia is the most frequent medical illness during pregnancy, and it can cause morbidity and even death for both the mother and the fetus (1). Worldwide, preeclampsia affects between 2% and 10% of pregnancies (2). Every year, it impacts almost eight million pairs of mothers and babies (3). Preeclampsia is defined as a new-onset hypertension (over 140 mmHg systolic or 90 mmHg diastolic) occurring after 20 weeks of gestation, accompanied by proteinuria or other maternal organ impairment. (4). The latter includes renal, hepatic, uteroplacental, haematological and neurological (5). The underlying etiology is not entirely known; however, it is thought to begin in an ischemic placenta with the release of antiangiogenic substances into the maternal circulation, resulting in maternal endothelial dysfunction and multiorgan failure. Additionally, researchers have linked numerous structural, metabolic, and genetic mechanisms to pre-eclampsia (6). It begins with gestational hypertension and progresses to more serious conditions (4). Preeclampsia may be categorized as "nonsevere" or "severe" depending on the severity of the symptoms that may be present, including blood pressure that is higher than 160/100 mmHg, headache, visual disturbances, upper abdominal pain, oliguria, elevated serum creatinine, thrombocytopenia, elevated liver enzyme levels, and other maternal and neonatal complications (7).

Severe preeclampsia requires hospitalization in the intensive care unit. However, preeclampsia management focuses on blood pressure control, seizure prevention, and optimal delivery timing. Intravenous magnesium sulfate is the preferred drug for preventing or treating seizures, alongside other intravenous antihypertensive drugs (8).

There are various fetal complications connected with PE, particularly when the condition is severe. These consist of premature birth, oligohydramniosis, intrauterine fetal death (IUFD), fetal growth retardation (FGR), and non-reassuring fetal heart rate (FHR) during labor (9). Uteroplacental dysfunction, which contributes to the development of PE, may

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result from inadequate trophoblast invasion, angiogenesis, and remodelling of uterine spiral arteries. Fetal growth retardation (FGR) can occur as a result of hypoxic conditions and nutritional deficiencies caused by uteroplacental dysfunction (10, 11). As per the 2019 guidelines published by the National Institute for Health and Care Excellence (NICE), a woman is considered to be at high risk of developing preeclampsia if there is a history of hypertensive disease during the previous pregnancy or if there is a maternal disease such as diabetes, autoimmune diseases, chronic hypertension, or chronic kidney disease (12). This study aimed to evaluate liver enzymes, renal function markers, platelet count, and proteinuria that differentiate preeclampsia with severe features cases from preeclampsia without severe features cases.

Subjects and Methods:

This cross-sectional, descriptive investigation was conducted at the Al-Elwiya Teaching Hospital for Maternity in Baghdad from April to June 2024.

The study included 90 patients diagnosed with preeclampsia after 24 weeks.The cohort was divided into two groups: 45 women had PE without severe features and 45 women had PE with severe features. In this study, severe preeclampsia was defined as a systolic blood pressure of 160 mmHg or higher and a diastolic blood pressure of 110 mmHg or higher, associated with severe hypertension unresponsive to treatment. It may also present with severe headaches, visual disturbances, or epigastric pain. Additionally, there was a progressive deterioration in laboratory blood tests, characterized by elevated creatinine levels or liver transaminases, declining platelet counts, impaired fetal growth, or abnormal Doppler findings. Conversely, preeclampsia without severe features is defined by a systolic pressure exceeding 140 mmHg and a diastolic pressure exceeding 90 mmHg, in the absence of any of the severe features. Pregnant with Diabetes, chronic renal disease, and chronic hypertension were excluded from the study.

Blood sample collection and laboratory analysis

Blood samples were collected from all participants to isolate serum. Following serum isolation, a fully automated chemistry analyzer (BioREX Mannheim, Malaysia) was employed to measure creatinine, urea, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) using an enzymatic colorimetric method. Platelet counts were measured using automated complete blood count machines, while proteinuria in urine samples was assessed using a dipstick test.

Statistical analysis

The Statistical Analysis System (SAS) software (version 9.6; 2018) was utilized for data analysis. The *t*-tests were conducted for mean comparisons, and Chi-squared tests were used for percentage comparisons.

Results:

The reported mean ages were (27.56±3.08 years) for PE without severe features and (29.80±4.22 years) for PE with severe features, with corresponding BMIs of (28.75±1.37 and 29.17±1.42 kg/m²), respectively. The mean values of the two groups showed no statistically significant differences. In contrast, the PE with severe features group had higher mean systolic and diastolic blood pressures (168.78±13.07 and 110.71±8.06 mmHg), respectively than the PE without severe features group (143.22±10.95 and 90.33±7.41 mmHg), respectively. The study found that 20% of women with PE without severe features had a previous history of gestational hypertension (GHT) or preeclampsia, compared to 28.88% of those with PE with severe features. However, this difference was not statistically significant. Also, there was no significant difference between PE without severe features (38.21 ±5.85 week) and PE with severe features (34.71 ±5.02 week) when GA was considered at delivery. But the GA at admission for PE without severe features (36.71 ±2.69 week) and PE with severe features (33.71 ±2.94 week) differed significantly ($P < 0.01$), as shown in Table 1.

Table 1: Demographic characteristics of the two study groups

Variable	PE without severe features	PE with Severe features	*t*-test	P-value
Age (year)	27.56 ±3.08	29.80 ±4.22	2.778 NS	0.112
BMI (kg/m^2)	28.75 ±1.37	29.17 ±1.42	0.813 NS	0.313
SBP (mm Hg)	143.22±10.95	168.78±13.07	16.538 *	0.03665
DBP (mm Hg)	90.33 ±7.41	110.71 ±8.06	12.863 *	0.03091
GA on admission (week)	36.71 ±2.69	33.71 ±2.94	1.557 **	0.0002
GA on delivery (week)	38.21 ±5.85	34.71 ±5.02	7.216 NS	0.0947
History of GHT\PE	9 (20.00%)	13 (28.88%)		0.393 NS

BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure. **: $P \leq 0.01$; *: $P \leq 0.05$; NS: non-significant; SD: standard deviation.

Blood tests revealed that patients with PE with severe features had higher levels of AST (36.42 ± 3.76 IU/L), ALT (24.28 ± 5.13 IU/L), urea (4.08 ± 0.71 nmol/L), and creatinine (0.778 ± 0.12 mg/dl), along with lower platelet counts (181.87±33.05x10³/ml) compared to those with PE without Severe features, whose levels were AST (22.39±2.92 IU/L), ALT (13.11±1.57 IU/L), urea (2.79±0.86 nmol/L), creatinine (0.576±0.13 mg/dl), and platelet counts (218.24±29.71x10³/ml). Severe PE was associated with a significant increase in proteinuria compared to PE without severe features, Table 2.

Table 2: Comparison of laboratory parameters in PE with and without severe features

Parameter		PE without Severe features	PE with Severe features	*t*-test	P-value
AST (IU/L)		22.39 ±2.92	36.42 ±3.76	4.062 **	0.0001
ALT (IU/L)		13.11 ±1.57	24.28 ±5.13	4.301 **	0.0001
Blood urea (nmol/L)		2.79 ±0.86	4.08 ±0.71	0.581 **	0.0001
Creatinine (mg/dl)		0.576 ±0.13	0.778 ±0.12	0.0699 **	0.0001
PLT (x10^3/ml)		218.24±29.71	181.87±33.05	23.354 **	0.0026
Proteinuria	++++	0(0.00%)	8(17.77%)		0.0087**
	+++	0(0.00%)	15(33.33%)		0.0001**
	++	10(22.22%)	17(37.77%)		0.177NS
	Trace/+1	35(77.77%)	5(11.11%)		0.0001**

ALT: alanine aminotransferase; AST: aspartate aminotransferase; PLT: platelets; **: P ≤ 0.01; NS: non-significant.

As shown in Table 3, there was no significant difference in the amniotic fluid index (AFI) between the two groups. However, significant differences were observed in FHR and birth weight. PE without severe features group had values of (139.87±2.61 bpm) for FHR and (3.14±0.39 kg) for birth weight, while PE with severe features group had values of (119.07±16.94 bpm) for FHR and (2.32±0.76 kg) for birth weight.

Table 3: Comparison of fetal assessment and outcomes between PE with and without severe features.

Parameter	PE without severe features	PE with severe features	*t*-test	P-value
AFI (cm)	7.09 ±0.87	7.68 ±1.49	1.283 NS	0.361
FHR (bpm)	139.87 ±2.61	119.07±16.94	14.374 **	0.0051
Birth weight (kg)	3.14 ±0.39	2.32 ±0.76	0.332 **	0.0001

AFI: amniotic fluid index; FHR: fetal heart rate; **: P≤0.01; NS: non-significant

The results demonstrated a statistically significant difference (P < 0.01) in the intensive care unit (ICU) and Caesarean section (CS) between the two groups; there were 7 cases (15.55%) of intrauterine death (IUD), one case of intrauterine growth retardation (IUGR), and placental abruption in PE with severe features group, alongside 5 cases (11.11%) of eclampsia, (Table 4). Conversely, PE without severe features group reported no cases of IUD, IUGR, placental abruption, or eclampsia.

Table 4: Comparison of complications between PE with and without severe features.

Complication	without severe features No (%)	With severe features No (%)	P-value
ICU	5(12.50%)	32(71.11%)	0.0006 **
CS	17(37.78%)	34(75.56%)	0.0089 **
IUD	0(0.00%)	7(15.55%)	0.028 *
IUGR	0(0.00%)	1(2.22%)	0.841 NS
Placental abruption	0(0.00%)	1(2.22%)	0.841 NS
Eclampsia	0(0.00%)	5(11.11%)	0.0485 *

ICU: intensive care unit; CS: Caesarean section, IUD: intrauterine death; IUGR: intrauterine growth restriction; **: P ≤ 0.01; *: P ≤ 0.05; NS: non-significant; SD: standard deviation.

Discussion:

This research finding demonstrates no correlation between maternal age and the severity of preeclampsia. This outcome was consistent with an earlier study indicating no statistically significant difference in maternal age between mild and severe preeclampsia (13). Furthermore, another study found that advanced maternal age did not appear to correlate with hypertensive conditions such as preeclampsia and gestational hypertension (14). Concerning BMI, the result indicated no significant difference between the two groups of PE. Durst *et al*., (2016) reported no correlation between maternal BMI and severe symptoms of preeclampsia (15). The same finding was reported by Weiner *et al.,* (2018) who revealed no significant differences in maternal age and BMI between preeclampsia with and without severe features (16). Significant increases in arterial blood pressure were observed in pregnant women with severe preeclampsia, a finding supported by other studies. Nirupama *et al.,* (2021) found that high blood pressure during pregnancy raises the risk of PE, preterm birth, placental abruption, and Caesarean section delivery (17). The arterial blood pressure of pregnant women who had severe PE rises dramatically. Preeclampsia with severe features is officially diagnosed in patients with blood pressure readings of 160/110 mmHg or higher, based on two readings taken at least 4 hours apart, or continuous severe-range blood pressures that necessitate hospitalization (18). In cases of severe PE, there is a reduction in the gestational age at both admission and delivery. According to a study by Moldenhauer *et al.,* (2003) women with preeclampsia are more likely to have lower gestational ages at birth, which may minimize perinatal morbidity and mortality (19). However, regarding the maternal history of preeclampsia or gestational hypertension, the investigation is consistent with a previous study (20), which found that women who have experienced preeclampsia may be at an increased risk of

recurrence. This study revealed that severe PE exhibited significantly elevated levels of biochemical markers compared to PE without severe features. These findings aligned with those of Hussein *et al*., (2012), who indicated that liver and kidney functions are important markers for the early identification of complications in preeclamptic pregnancies (21). Alese *et al*., (2021) identified the hepatic enzymes AST and ALT as valuable indicators for the development of preeclampsia (22). Tests for liver transaminases offer accurate predictions of both maternal and fetal complications. However, Charles *et al.,* (2020) found that changes in renal parameters during preeclampsia were linked to higher glomerular filtration resistance because of the mechanical effects of cytoplasmic swelling (23). Additionally, metabolic alterations resulted in decreased renal perfusion and glomerular filtration rate. Furthermore, Kasraeian *et al.,* (2018) discovered that women with severe type preeclampsia had much higher levels of ALT and serum creatinine than those with mild type (24). The significant decrease in platelet counts observed in cases of severe preeclampsia aligned with findings from a study by Nayyef *et al*., (2024), which revealed that platelet parameters have a significant linear correlation with mean arterial pressure, making them practical, cost-effective, and easy to measure (25). They can serve as biomarkers to predict the severity of preeclampsia (26). The placenta of preeclamptic women has severe degenerative changes in both trophoblastic and endothelial cells. The increased number of platelets in the capillary lumen reflected these changes (27). Additionally, a correlation was observed between disease severity and increases in proteinuria outcomes. Another study indicated that the degree of proteinuria is associated with increased severity of preeclampsia. This association may be attributed to the greater extent of kidney damage that occurs in severe preeclampsia (28). Albumin has the potential to act as a valuable disease marker for the early management of existing instances that can lead to preeclampsia and eclampsia (29). Nonetheless, the severity of preeclampsia cannot be determined by measuring the degree of proteinuria, as Özkara *et al.,* (2018) concluded. In the current investigation, the AFI was not related to the severity of preeclampsia (30). A retrospective study found that mildly abnormal sonographically estimated amniotic fluid does not significantly impact the risk of adverse pregnancy outcomes. Research by Magann *et al*., (2003) also indicated that the volume of amniotic fluid did not predict adverse outcomes at birth (31, 32). While birth weight was lower in severe cases, this finding is consistent with another study that found the severe preeclampsia group with complications is more likely to experience low birth weight and fetal complications (33). A similar finding was observed regarding FHR, which was lower in the severe group. According to Yum *et al*., (2004) the instability and reduced variability in FHRs are exacerbated by severe preeclampsia and growth restriction (34). In the present study, 71.11% of severe cases required admission to the ICU. This finding is consistent with published reports indicating that ICU admission is often necessary for severe preeclampsia to minimize maternal morbidity and mortality (35). In contrast to PE without severe features, severe preeclampsia more frequently necessitates a Caesarean section. The rate of Caesarean sections remains elevated in cases of severe preeclampsia, particularly those with complications (36). Among the severe group, 17.77% experienced complications such as IUD and IUGR. Sirenden *et al*., (2020) reported that severe preeclampsia with complications is associated with a higher incidence of preterm birth, low birth weight, and fetal complications, including IUGR and IUFD (37). This study reported only one case of placental abruption in the severe group. An abruption is considered an obstetric emergency. Another study found that severe adverse maternal and perinatal outcomes were more common in preeclampsia with severe characteristics, necessitating individualized and intensive monitoring and care to improve maternal and perinatal outcomes (38). Additionally, five cases (11.11%) of eclampsia were noted in the severe group. Eclamptic seizures occurred in 2% of women with severe signs of preeclampsia who were not receiving magnesium sulfate treatment, compared to less than 0.6% of those who were treated with magnesium sulfate. While the exact pathophysiology of eclamptic seizures remains unclear, the predominant theory suggests that the rupture of the blood-brain barrier allows fluid, ions, and plasma proteins to enter the brain parenchyma (39). Finally, a study conducted by Majeed *et al.,* (2020) found that preterm birth, low birth weight, Caesarean section (CS), and other maternal and neonatal problems were major concerns for pregnant women with PE (40).

Conclusion:

The previously mentioned indicators AST, ALT, blood urea, serum creatinine, and proteinuria, in addition to fetal heart rate and birth weight, are valuable for assessing preeclampsia severity, highlighting the importance of monitoring. Severe preeclampsia is associated with a higher likelihood of complications such as ICU admission, Caesarean section, IUD, and eclampsia.

Authors' declaration:

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to the current study, have been given permission for re-publication attached to the manuscript. Authors sign on ethical considerations' approval- Ethical Clearance: The research was approved by the College of Science Ethical Committee at the University of Baghdad under the license code CSEC/0424/0040, issued on April 22, 2024.

Conflicts of Interest: None
Funding: None

Authors' contributions:
Study conception and design: (Radhia A. Alshihabi and Dr. Yasmin L. Alsaadi). Literature search: (Radhia A. Alshihab). data acquisition: (Radhia A. Alshihabi). Data analysis and interpretation: (Radhia A. Alshihabi). Manuscript preparation: (Radhia A. Alshihabi). Manuscript editing and review: (Radhia A. Alshihabi).

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قييم المؤشرات الرئيسية لتقييم وتصنيف شدة تسمم الحمل

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الخلاصة: تسمم الحمل هو حالة خاصة بالحمل ولها آثار كبيرة على معدلات الإصابة بالأمراض والوفيات للأم والجنين في جميع أنحاء العالم. وقد حدد الباحثون العديد من المؤشرات الحيوية كمؤشرات محتملة لشدة المرض.
الهدف: هدفت الدراسة الحالية إلى تحديد وتقييم المؤشرات السريرية الرئيسية التي تميز بين تسمم الحمل مع و بدون الخصائص شديدة.
طرق العمل: تم تسجيل تسعين امرأة حامل تم تشخيص إصابتهن بتسمم الحمل بعد 24 أسبوعا من الحمل من أبريل إلى يونيو 2024 في مستشفى العلوية التعليمي للولادة في بغداد. تم تصنيف المرضى إلى مجموعتين: 45 حالة من تسمم الحمل دون الخصائص الشديدة و45 حالة من تسمم الحمل مع الخصائص الشديدة. شملت المؤشرات الرئيسية التي تم تقييمها ضغط الدم، ومقاييس المختبر. كما تم تحديد النتائج مثل الوزن عند الولادة وFHR والمضاعفات، مثل العملية القيصرية، وفاة الجنين داخل الرحم، ومقدمات الارتجاع. أجري التحليل الإحصائي باستخدام اختبار T ومربع كاي.
النتائج : ارتفعت مستويات AST وALT واليوريا في الدم والكرياتينين في المصل بشكل ملحوظ في حالات تسمم الحمل مع الخصائص الشديدة، بينما انخفضت أعداد الصفائح الدموية بشكل كبير. بالإضافة إلى ذلك، كان هناك ارتفاع ملحوظ في نسبة البروتين في البول؛ في حالات تسمم الحمل دون الخصائص الشديدة، يصل البروتين في البول إلى +2. بينما في حالات تسمم الحمل مع الخصائص الشديدة، يتجاوز البروتين في البول +4. كان لدى حالات تسمم الحمل مع الخصائص الشديدة وزن ولادة أقل بلغ 2.32 كجم، مقارنة بحالات تسمم الحمل دون الخصائص الشديدة، والتي كان وزنها 3.14 كجم. انخفض معدل ضربات القلب الولادية الأساسي من 139 نبضة في الدقيقة في حالات تسمم الحمل دون الخصائص الشديدة إلى 119 نبضة في الدقيقة في تسمم الحمل مع الخصائص الشديدة. يرتبط حالات تسمم الحمل مع الخصائص الشديدة بمضاعفات أكبر للأم والجنين، وقد أظهر زيادة في معدلات دخول وحدة العناية المركزة (71.11%)، والولادة القيصرية (75.56%)، وموت الجنين داخل الرحم (15.55%)، ومقدمات الارتجاع(11.11%).
الاستنتاج: المؤشرات المذكورة سابقا -AST وALT واليوريا في الدم والكرياتينين في المصل والبروتين في البول - بالإضافة إلى معدل ضربات قلب الجنين ووزن الولادة، تعد ذات قيمة لتقييم شدة تسمم الحمل، مما يسلط الضوء على أهمية المراقبة.
الكلمات المفتاحية: ALT، AST، الصفائح الدموية، تسمم الحمل، البروتين في البول.

How to Cite this Article
Alshihabi R, Al-Saadi YL. Evaluating Key Indicators for Assessing Severity in Moderate and Severe Preeclampsia. J Fac Med Baghdad [Internet]. [Available from: https://iqjmc.uobaghdad.edu.iq/index.php/19JFacMedBaghdad36/article/view/2992