

Blood Pressure Levels and Maternal Outcome in Women with Preeclampsia – a Retrospective Study from a Large **Tertiary Obstetric Centre**

Blutdruckwerte und mütterliches Outcome bei Frauen mit Präeklampsie – eine retrospektive Studie aus einem Perinatalzentrum Level I









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ABSTRACT

Introduction Patients with high blood pressure levels are at high risk for acute complications as well as serious long-term consequences. Women with preeclampsia often experience very high blood pressure levels during pregnancy and postpartum and are also known to have a higher cardiovascular risk in later life.

Material and Methods In our single-centre retrospective cohort study, we analysed 158 pregnancies complicated by preeclampsia in regard to maternal outcome. We divided the patient cohort into three subgroups according to the blood pressure levels during hospital stay.

Results Pre-existing arterial hypertension was significantly more common in patients with a hypertensive crisis (systolic blood pressure ≥ 180 mmHq and/or diastolic blood pressure ≥ 120 mmHq) during pregnancy than in patients with moderate or severe hypertension (p = 0.001). Women with a hypertensive crisis had an unfavourable outcome compared to women with lower blood pressure levels. These women developed a HELLP-syndrome significantly more often (p = 0.013). Moreover, most of the women with a hypertensive crisis during pregnancy were still hypertensive at hospital discharge (p = 0.004), even though they were administrated antihypertensive agents more often (p < 0.001) compared to women with lower blood pressure values.

Conclusion Preeclamptic women with hypertensive crises should be identified quickly and monitored closely to avoid further complications. Standardized follow-up programs are lacking, but especially these patients seem to be at high risk for persistent hypertension and increased cardiovascular morbidity and therefore should receive specialist follow-up, including hypertensiologists, cardiologists and gynaecologists. Large prospective trials are required for a better understanding of these interrelations and to develop a specific follow-up program.

ZUSAMMENFASSUNG

Einleitung Das Risiko für akute Komplikationen und schwerwiegende Langzeitfolgen ist höher bei Patientinnen mit Bluthochdruck. Frauen mit Präeklampsie haben oft sehr hohe Blutdruckwerte während der Schwangerschaft und postpartal und haben bekanntlich auch eine höheres Risiko für Herz-Gefäß-Erkrankungen im späteren Leben.

Material und Methoden Diese monozentrische retrospektive Kohortenstudie untersucht 158 Schwangerschaften mit Präeklampsie im Hinblick auf das mütterliche Outcome. Die Patientinnenkohorte wurde gemäß den Blutdruckwerten der Patientinnen während ihres Krankenhausaufenthalts in 3 Untergruppen aufgeteilt.

Ergebnisse Verglichen mit Patientinnen mit mittelschwerer oder schwerer Hypertonie hatten Patientinnen, die während der Schwangerschaft eine hypertensive Krise (systolischer Blutdruck ≥ 180 mmHg und/oder diastolischer Blutdruck ≥ 120 mmHg) erlitten, signifikant häufiger eine vorbestehen-

de arterielle Hypertonie (p = 0,001). Frauen, die eine hypertensive Krise erlebten, hatten ein ungünstigeres Outcome verglichen mit Frauen mit niedrigerem Blutdruck. Diese Frauen entwickelten auch deutlich häufiger ein HELLP-Syndrom (p = 0,013). Außerdem hatten die meisten Frauen, die eine hypertensive Krise während der Schwangerschaft erlitten, immer noch hypertensive Blutdruckwerte zum Zeitpunkt ihrer Entlassung aus dem Krankenhaus (p = 0,004), obwohl sie öfters mit antihypertensiven Mitteln behandelt wurden (p < 0,001) als Frauen mit niedrigerem Blutdruck.

Schlussfolgerung Präeklamptische Frauen mit hypertensiven Krisen sollten rasch identifiziert und intensiv überwacht werden, um weitere Komplikationen zu verhindern. Es fehlt an standardisierten Nachsorgeprogrammen. Diese Patientinnen weisen ein besonders hohes Risiko für anhaltende Hypertonie und höhere kardiovaskuläre Morbidität auf und sollten daher eine fachärztliche Nachsorge durch Hypertensiolog*innen, Kardiolog*innen und Gynäkolog*innen erhalten. Große prospektive Studien sind nötig, um die Kenntnisse dieser Zusammenhänge zu verbessern und ein gezieltes Nachsorgeprogramm zu entwickeln.

Background

Preeclampsia remains one of the most dangerous complications of pregnancy for mother and child [1,2]. It is defined as hypertension in combination with proteinuria and/or onset of other organ dysfunction and/or fetal growth restriction. Preeclampsia is one of the main reasons for maternal and fetal morbidity and mortality worldwide and occurs in approximately 3–5% of all pregnancies [1]. Furthermore, it is known that women with a history of preeclampsia have a higher cardiovascular risk in later life [3].

Until now, pathogenesis of preeclampsia is not fully understood. Several factors seem to play a role in its development, including shallow trophoblast invasion, an imbalance of pro- and anti-angiogenic factors, but also pre-existing maternal conditions such as arterial hypertension, diabetes mellitus or kidney disease, rheumatological disorders and autoimmune diseases [4,5].

Although it is known that women with a history of preeclampsia have a higher risk of severe cardiovascular events, e.g. stroke or acute coronary syndrome, currently no specific preventive care concept exists for this cohort [6]. However, in current national guidelines, a regular follow-up is recommended for women with early onset or severe course of preeclampsia [7].

Moreover, factors predicting the progression of preeclampsia and onset of complications (e.g. HELLP-syndrome, eclampsia) are sparse. Especially in light of the very limited therapeutic options, with delivery as one and only causal therapy, predictors for severe complications would be very helpful for early and exact risk stratification and timing of delivery [8, 9].

Current international guidelines on hypertension grade hypertensive blood pressure levels into different degrees of severity, as it is known that patients with higher blood pressure levels are at higher risk for acute and long-term complications [10].

The aim of this study was to analyse maternal outcome in correlation with blood pressure levels in women with preeclampsia. We suspected that women with hypertensive crisis (systolic blood pressure ≥ 180 mmHg or diastolic blood pressure ≥ 120 mmHg) would have an unfavourable outcome compared to women with only moderate hypertension (systolic blood pressure up to 159 mmHg and diastolic blood up to 109 mmHg). Furthermore, blood pressure levels might guide risk stratification regarding necessity and frequency of medical follow-up after delivery and the need for further medical interventions to reduce the risk of cardiovascular morbidity in later life.

Methods

We conducted a retrospective cohort study at the University Hospital Münster, a tertiary obstetric centre. All deliveries at the University Hospital Münster from 1st January 2017 until 31st December 2020 were reviewed (5149 women) and included in the study if preeclampsia was diagnosed (158 women). A flow chart of patients screened and included in the study is shown in Fig. S1. The study was designed according to the Declaration of Helsinki and approved by the institutional review board.

The definition of preeclampsia, as described by the International Society for the Study of Hypertension in Pregnancy (ISSHP) and as defined in the current ACOG practice bulletin as well as in the current AWMF-guideline [7,11,12], was applied as followed: hypertension (repeated blood pressure measurement ≥ 140/90 mmHg) plus at least one of the following in or after the 20th week of gestation:

- significant proteinuria (double positive urine test strip and/or elevated protein/creatinine ratio ≥ 30 mg/mmol)
- thrombocytopenia < 100 000/µl



- elevated liver enzymes (alanine transaminase ≥ twice the normal concentration)
- elevated serum creatinine > 1.0 mg/dl
- pulmonary oedema
- neurological dysfunction
- fetal growth restriction < 10th percentile

If these criteria of preeclampsia were not met or if data acquisition was incomplete, the patient was excluded from this study.

During the hospital stay, demographic data, medical history, blood pressure recordings, laboratory results, clinical symptoms, and obstetric outcome were recorded. The following clinical symptoms were recorded: epigastric pain, headache, visual sensations, hyperreflexia and other neurological symptoms (e.g. vomiting, hypaesthesia). Blood pressure was recorded either with an auscultatory or oscillometric semiautomatic or automatic sphygmomanometer with fitted cuff. All sphygmomanometers used were certified for use in pregnancy. Before blood pressure measurement was performed, patients were sitting for at least 5 minutes in a quiet environment and the cuff was positioned at heart level. Blood pressure was measured at least 4–6 times a day by medical staff only.

In conformity with current international guidelines for arterial hypertension, we divided the patients into three subgroups depending on their maximum blood pressure [10, 13]:

- patients with moderate hypertension: a systolic blood pressure up to 159 mmHq and a diastolic blood up to 109 mmHq
- patients with severe hypertension: a systolic blood pressure between 160–179 mmHg and/or a diastolic blood pressure between 110–119 mmHg
- patients with a hypertensive crisis: a systolic blood pressure
 ≥ 180 mmHq or a diastolic blood pressure ≥ 120 mmHq

According to the ESC/ESH guidelines on arterial hypertension and following the results of the SPRINT study, the blood pressure measurement at the day of hospital discharge was also divided into three groups [10, 14]:

- optimal blood pressure level: systolic blood pressure ≤ 120 and diastolic blood pressure ≤ 80 mmHq
- tolerable blood pressure level: systolic blood pressure 121–139 and/or diastolic blood pressure 81–89 mmHg
- hypertension: systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mmHq.

According to current national guidelines, antihypertensive treatment pre- as well as postnatal was initiated if repeated (\geq 3) blood pressure levels \geq 150/100 mmHq were recorded [7].

Statistical analysis

All statistical calculations were performed using SPSS Statistics, version 27 (IBM, Armonk, NY, USA). For descriptive data analysis of continuous variables we provided mean values and standard deviation, categorical data were expressed as frequencies/percentages. For comparison of two ordinally scaled variables, we used the chi-squared test after constructing contingency tables; we also used the chi-squared test for expressing odd's ratio, if indicated. To test for correlation between groups, one-way ANOVA

was used (after having proven variance homogeneity with the Levene-test). Student's t-test was used to compare the mean values between groups of normally-distributed metric variables.

A p-value < 0.05 was considered statistically significant, and significance levels were presented as follows: p-values < 0.05 are summarized with one asterisk (*), p-values < 0.01 with two asterisks (**) and p-values < 0.001 with three asterisks (***).

Results

Patient characteristics

158 patients were included in this study. The mean maternal age was 31.9 ± 5.1 years. The majority of these women were primiparous (69.0%). Most patients were from Germany, 18.3% were from another country. Of these patients 15.8% had a history of preconceptual hypertension, 11.4% of coagulation disorders with 3.8% of thrombosis. 3.2% of women continued smoking during their pregnancy. 5.1% of included women had pre-existing diabetes. During pregnancy, about one fifth of patients developed a gestational diabetes: 13.9% of all patients developed gestational diabetes with dietary treatment and 5.7% of all patients developed insulin-depending gestational diabetes.

Only 30.4% of all patients did not take any form of medication during their pregnancy. 11.4% of pregnancies in our cohort were the result of fertility treatment. 45.6% of all patients had a positive family history for cardiovascular diseases.

We differentiated between women with moderate hypertension (n = 48, 30.4%), women with severe hypertension (n = 69, 43.7%) and women with hypertensive crises (n = 41, 25.9%) in accordance with the maximal prepartum blood pressure values during the hospital stay. Demographic data of the study population and study subgroups are displayed in ► **Table 1**.

Pre-existing hypertension was significantly associated with prepartum maternal blood pressure levels (p < 0.001), details are displayed in \triangleright Fig. 1.

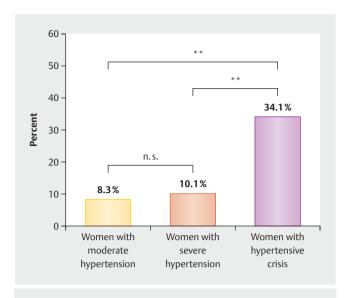
Moreover, we found that patients in the moderate hypertension group more often had a positive history for thrombosis than either of the other groups (p < 0.001).

Symptoms

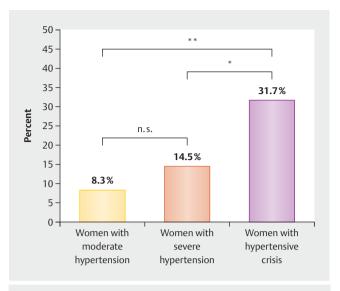
Of all the symptoms assessed, only the occurrence of headaches correlated positively to the level of arterial hypertension (p = 0.025). None of the other symptoms showed a significant relationship to blood pressure levels. The sum of all symptoms reported did not show a significant correlation to blood pressure levels either.

Complications and severity of preeclampsia

We investigated the correlation between blood pressure levels and laboratory parameters. There was no significant relationship between blood pressure levels and serum creatinine, potassium levels, lactate dehydrogenase levels or thrombocytopenia. Furthermore, blood pressure levels did not correlate with the protein/creatinine-ratio. But we could show a significant positive association of the blood pressure level and uric acid and alanine transaminase levels (p = 0.049 and p = 0.003, respectively).



► Fig. 1 Frequency distribution of pre-existing hypertension between hypertension subgroups.



▶ Fig. 2 Incidence of HELLP-syndrome in the three blood pressure groups.

There was no significant correlation between blood pressure levels and occurrence of pre- or postnatal anaemia. However, we did see a tendency for severe postpartum anaemia in women with higher blood pressure levels (p = 0.068).

Laboratory findings within hypertension subgroups are displayed in Table **S1**.

High blood pressure levels were a predictor for the development of HELLP-syndrome (p = 0.013). The higher the maternal blood pressure levels, the more often a HELLP-syndrome developed, as shown in \triangleright **Fig. 2**.

High blood pressure levels also correlated positively with the administration of intravenous magnesium as prophylaxis for eclampsia (p = 0.001).

Severe complications of preeclampsia such as intracerebral haemorrhage and eclampsia were scarce. Of 158 patients, one developed pituitary haemorrhage and two patients abruptio placentae. All women were part of the severe hypertension group. No cases of posterior reversible encephalopathy syndrome or eclampsia were recorded.

Blood pressure at hospital discharge

A significant relationship between the highest blood pressure measured during the hospital stay and the blood pressure measured at hospital discharge was seen (p = 0.004). While patients with moderate hypertension were discharged with an optimal or acceptable blood pressure in 72.9% of the cases, this was the case

	Moderate hypertension (n = 48; group 1)	Severe hypertension (n = 69; group 2)	Hypertensive crisis (n = 41; group 3)	Significance levels
Mean Age ± SD (years)	31.9 ± 4.5	31.1 ± 5.3	32.8 ± 5.4	n.s. (p = 0.07)
BMI ± SD (kg/m²)	31.1 ± 7.3	30.7 ± 7.4	32.4 ± 7.7	n.s. (p = 0.07)
Nulliparous women	36 (75.0%)	49 (71.0%)	24 (58.5%)	n.s. (p = 0.09)
Pre-existing diabetes	5 (10.4%)	1 (1.4%)	2 (4.9%)	n.s. (p = 0.43)
Family history of hypertension	23 (47.9%)	33 (47.8%)	20 (48.8%)	n. s. (p = 0.86)
Gestational diabetes	16 (33.3%)	16 (23.2%)	5 (12.2%)	1 vs. 3: p = 0.007 1 vs. 2: p = 0.12 2 vs. 3: p = 0.07
Chronic kidney disease	1 (2.1%)	0 (0%)	4 (9.8%)	2 vs. 3: p = 0.018 1 vs. 2: p = 0.16 1 vs. 3: p = 0.07
ASS for preeclampsia prevention	4 (8.3%)	5 (7.2%)	8 (19.5%)	n.s. (p = 0.11)
In-vitro fertilization	6 (12.5%)	7 (10.1%)	5 (12.2%)	n.s. (p = 0.95)
Active smoking	2 (4.9%)	1 (1.4%)	2 (4.2%)	n.s. (p = 0.89)



▶ Table 2 Blood pressure levels at hospital discharge in the three blood pressure groups.

	Moderate hyper- tension (group 1)	Severe hyper- tension (group 2)	Hypertensive crisis (group 3)	Significant pairs among groups	Significance levels
BP at discharge:					
Optimal	6 (12.5%)	3 (4.3%)	1 (2.4%)	1 vs. 3(*)	1 vs. 2: p = 0.06 1 vs. 3: p = 0.03 2 vs. 3: p = 0.29
Tolerable	29 (60.4%)	40 (58%)	14 (34.1%)	1 vs. 3 (**) 2 vs. 3 (**)	1 vs. 2: p = 0.39 1 vs. 3: p = 0.005 2 vs. 3: p = 0.006
Hypertensive	13 (27.1%)	26 (37.7%)	26 (63.5%)	1 vs. 3 (***) 2 vs. 3 (**)	1 vs. 2: p = 0.11 1 vs. 3: p < 0.001 2 vs. 3: p = 0.003
Systolic BP (mmHg)	131.8 ± 10.2	136.1 ± 10.5	140.5 ± 12.2	All pairs	1 vs. 2: p = 0.03 1 vs. 3: p < 0.001 2 vs. 3: p = 0.048
Diastolic BP (mmHg)	80.5 ± 11.8	86.4 ± 8.6	89.8 ± 11.8	1 vs. 2, 1 vs. 3	1 vs. 2: p = 0.002 1 vs. 3: p < 0.001 2 vs. 3: p = 0.08
MAD BP (mmHg)	97.7 ± 0.8	103.0 ± 8.2	106.7 ± 11.0	All pairs	1 vs. 2: p < 0.001 1 vs. 3: p < 0.001 2 vs. 3: p = 0.047

► Table 3 Association of prepartum blood pressure levels in patients with preeclampsia and antihypertensive treatment at hospital discharge.

	Moderate hyper- tension (group 1)	Severe hyper- tension (group 2)	Hypertensive crisis (group 3)	Significant pairs among groups	Significance levels
Antihypertensive medication:					
No medication	40 (83.3%)	23 (33.3%)	1 (2.4%)	All pairs	1 vs. 2: p < 0.001 1 vs. 3: p < 0.001 2 vs. 3: p < 0.001
1 drug	7 (4.6%)	36 (52.2%)	24 (58.6%)	1 vs. 2 1 vs. 3	1 vs. 2: p < 0.001 1 vs. 3: p < 0.001 2 vs. 3: p = 0.25
≥2 drugs	1 (2.1%)	10 (14.5%)	16 (39%)	All pairs	1 vs. 2: p = 0.004 1 vs. 3: p < 0.001 2 vs. 3: p = 0.002

for only 62.3% of the patients with severe hypertension and 36.5% of the patients with a hypertensive crisis during their hospital stay. The Odd's Ratio of being discharged with an insufficient blood pressure control was 4.7-fold higher in patients in the hypertensive crisis group than in patients with only moderate hypertension (> Table 2).

Patients with pre-existing arterial hypertension before pregnancy were discharged with optimal or acceptable blood pressure values in 46.2%, this was the case in 57.1% of patients without pre-existing hypertension (p = 0.15). Subgroup analysis regarding the three different blood pressure groups, pre-existing arterial hypertension and blood pressure levels at hospital discharge could not show a significant difference either.

Antihypertensive medication at discharge

We found that 83.3% of patients in the group with moderate hypertension were discharged without any blood pressure medication, while patients with a hypertensive crisis during pregnancy were discharged with at least one antihypertensive drug in 97.6% of the cases. In this group, 58.5% of patients were discharged with an antihypertensive monotherapy and 39.2% with a combination of antihypertensive agents underlining a highly significant association of highest blood pressure and medication at discharge (p < 0.001), see also > Table 3.

Discussion

In our study, we could show that far beyond being a diagnostic criterion for preeclampsia, the level of hypertension in preeclamptic women can improve risk stratification in case of maternal deterioration and is an independent marker for poor maternal outcome. Succinctly, preeclamptic patients with a hypertensive crisis during pregnancy experience more complications and a more severe course of disease compared to women with blood pressure levels below 180/120 mmHg. Additionally, these patients are at higher risk of persistent hypertension at hospital discharge.

So far, little attention has been devoted to the severity of hypertension in preeclamptic patients and its significance for their clinical management. In most cases, a distinction is only made between preeclampsia with or without severe features, assigning all women with blood pressure levels ≥ 160/110 mmHg to the group of preeclampsia with severe features, without further differentiation [12]. In their study, Buchbinder and colleagues demonstrated that women with severe gestational hypertension had higher rates of adverse perinatal outcomes compared to women with mild preeclampsia. No significant differences were found between the normotensive/mild gestational hypertension and the mild preeclampsia group, underlining the importance of a differentiated blood pressure analysis in hypertensive diseases of pregnancy [15].

Our study underlines the importance of a differentiated analysis of blood pressure levels in patients with preeclampsia as this particular parameter is paramount for clinical surveillance and antenatal monitoring. According to the severity of hypertension, patients can be stratified into different risk groups and managed accordingly. Antihypertensive medication should be initiated promptly in women with very high blood pressure levels to reduce the risk of severe complications, especially in the postpartum period.

After delivery, it is known that blood pressure levels normalize within the first week postpartum in many patients with hypertension during pregnancy, but women with chronic hypertension, preterm preeclampsia and/or very high blood pressure levels during pregnancy often remain hypertensive in the postpartum period and beyond [16-19]. Studies analysing the correlation of blood pressure levels during preeclampsia and cardiovascular morbidity in later life are sparse. In his review article, Aronow points out that women with a history of preeclampsia have a higher risk of developing persistent hypertension, but also for strokes, ischemic heart disease, kidney diseases and diabetes in later life [20]. Benschop and colleagues pointed out that women with a history of severe preeclampsia have a higher cardiovascular risk profile and that no uniform follow-up care program exists for women with a former hypertensive pregnancy disorder [6]. Recommendations on frequency and extent of follow-up examinations differ extensively between existing guidelines, if recommendations are specified at all [21]. Benschop et al. proposed a schedule of cardiovascular follow-ups after a pregnancy with hypertensive disorders, starting 6-8 weeks after delivery [6]. Muijsers and colleagues also pointed out that a standardized prevention guideline for patients with a history of preeclampsia is lacking and have started a clinical trial to improve detection and prevention of hypertension in women aged 40-60 years with a history of preeclampsia to reduce cardiovascular morbidity [22]. The current national guideline for Germany, Austria and Switzerland recommends an extensive assessment of the patients' cardiovascular status and specific risk factors in the first 3–6 months after delivery and screening for cardiovascular risk factors every 5 years from then on [7].

In our study, 41% of all patients were still hypertensive at hospital discharge, even though they were treated with antihypertensive agents. Although the patient cohort is young and most of the patients have few comorbidities, physicians should not restrain from prescribing antihypertensive medication and adjust the dosage, if necessary. In case a persistent hypertension remains untreated, there is a higher cumulative risk for complications due to the longer duration of hypertension and secondary damage to target organs [23]. Moreover, physicians should also determine the patients' lipid status and recommend lifestyle changes and/ or statin therapy, if indicated [6]. Polypills may increase acceptance and adherence to the antihypertensive therapy in young women, as these advantages have been shown extensively in other patient cohorts [24-26]. We conclude that especially in women with elevated blood pressure levels at discharge, a closer follow-up involving general practitioners and outpatient gynaecologists seems mandatory for monitoring and treatment of persistent arterial hypertension and should be organized with fixed appointments to achieve a higher therapy adherence. Particular attention should be given to women with pre-existent hypertension as it is obvious that these patients need a reliable permanent antihypertensive treatment. Women with former preeclampsia should receive a regular long-term follow-up, for example every five years [7].

A limitation of this study is its retrospective approach and the risk for bias inherent in this study design. Since the University Hospital Münster is a tertiary obstetric centre, our patient cohort includes a high number of patients with pre-existing hypertension, which may influence outcome parameters. However, most women were young and healthy without any pre-existing medical conditions. Since management of patients at risk for preeclampsia is recommended to take place in obstetric centres, our results can be considered valid in this particular setting. Another point worth mentioning is that there were no measures to prevent bias such as white coat hypertension. However, as there were repeated daily blood pressure measurements, this risk can be deemed small.

One strength of this study is the differentiation between subgroups according to maternal blood pressure levels, and separate analysis of maternal outcome. We were able to show that in preeclampsia the nuanced quantification of hypertension enables patient stratification and can help identify patients at risk for an unfavourable outcome. To our knowledge, our study is the first to highlight the importance of a differentiated approach to the degree of arterial hypertension in pregnancy.

Current guidelines do not differentiate between different blood pressures levels, which may be a relevant shortcoming in the management of women with preeclampsia. Large prospective studies with a long-term follow-up including patients with a history of preeclampsia are needed in order to identify cardiovascular complications connected to preeclampsia and to develop a specific medical follow-up program.



Conclusion

This study could show that blood pressure levels correlate with maternal outcome in preeclampsia. Since preeclamptic women with hypertensive crisis have an unfavourable outcome, quantification of hypertension enables patient stratification in preeclampsia. This can help improve the clinical management and therefore potentially reduce maternal complications. Moreover, especially this patient cohort needs to be followed up closely to reduce future cardiovascular morbidity. Therefore, an interdisciplinary team of hypertensiologists, cardiologists and gynaecologists seems to be the most suitable option.

Supplements

Fig. S1: Flow chart of patients screened and included in the study. **Table S1:** Laboratory findings within hypertension subgroups. Potassium, creatinine, uric acid, alanine transaminase (GPT) and lactate dehydrogenase (LDH) levels are shown as maximum levels, whereas haemoglobin levels and platelet counts are displayed as minimum levels. Presented are mean values ± standard deviation.

Conflict of Interest

The authors declare that they have no conflict of interest.

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