Chapter 12

HYPERTENSIVE EMERGENCIES IN PREGNANCY

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Hypertensive emergencies in pregnancy are one of the leading causes of maternal and fetal morbidity and mortality. They are characterized by a significant increase in blood pressure during pregnancy, responsible for about 10% of gestational complications globally, requiring immediate medical intervention. These conditions are classified into four categories according to the American College of Obstetricians and Gynecologists Taskforce on Hypertension during Pregnancy: chronic hypertension, gestational hypertension, pre-eclampsia,

and eclampsia. In the United States (USA), it is estimated that hypertensive disorders occur in approximately 1 in 9 pregnancies, with chronic hypertension complications present in 1% to 2% of deliveries and gestational hypertension in 2% to 3% of cases. Pre-eclampsia affects between 3% and 5% of pregnancies, with progression to eclampsia in 0.6% to 2%-3% of cases, depending on the severity of the initial condition (Wilkerson; Ogunbodede, 2019).

The incidence of chronic hypertension in women of childbearing age is increasing, particularly due to rising rates of obesity, diabetes mellitus, and inadequate diets. In the USA, African-American women have a higher incidence of pre-eclampsia and a threefold higher risk of fatalities compared to white women, partly due to difficulty accessing healthcare. Thus, the development of hypertensive emergencies in pregnancy involves both physiological and socioeconomic factors, emphasizing the need for adequate knowledge of the diagnosis, treatment, and possible complications of these conditions (Wilkerson; Ogunbodede, 2019).

There are important distinctions between chronic hypertension and gestational hypertension: the former occurs before pregnancy or is diagnosed before 20 weeks, while the latter is diagnosed after 20 weeks of pregnancy, with blood pressure values exceeding 140/90 mmHg (mild gestational hypertension) or 160/110 mmHg (severe gestational hypertension). Pre-eclampsia is characterized by the presence of hypertension with or without proteinuria, with possible additional signs in previously hypertensive pregnant women, including thrombocytopenia, pulmonary congestion, pulmonary edema, elevated liver transaminases, acute renal failure, and central nervous system disorders (Vadhera; Simon, 2014).

Eclampsia, defined by the occurrence of tonic-clonic seizures in pregnant women with pre-eclampsia without other causes, can occur before, during, or after delivery, with more than 90% of cases occurring after 28 weeks of gestation (Wilkerson & Ogunbodede, 2019). Delivery is considered the ideal treatment for severe cases, provided the mother is stable and the fetus is viable, usually after 34 weeks of gestation. Before this period, the aim is to stabilize the mother until the fetus is viable (Vadhera; Simon, 2014).

Hypertensive disorders in pregnancy affect between 10% and 20% of pregnancies in the United States, significantly resulting in maternal and fetal morbidity and mortality. They are also one of the main causes of postpartum readmission. Possible complications include pulmonary edema, premature placental abruption, stroke, thromboembolic events, disseminated intravascular coagulation, and multiple organ failure. The fetus is at risk of intrauterine growth restriction or even intrauterine death (Hauspurg; Jeyabalan, 2020).

According to the Department of Medicine II, Charles University in Prague, First Faculty of Medicine, there is a reduction in blood pressure (BP) during the first trimester, especially in diastolic BP (DBP), with values decreasing between 8 and 15 mmHg at weeks 20-24, due to vasodilation induced by local mediators such as prostacyclin and nitric oxide. Subsequently, the stroke volume increases between 10% and 30%, returning to

pre-gestational values by week 36. These variations can occur in both hypertensive and normotensive women. There are three main types of hypertension in pregnancy: pre-existing hypertension (diagnosed before pregnancy or up to 20 weeks and persistent after 42 days postpartum, possibly associated with proteinuria), gestational hypertension (diagnosed after 20 weeks and disappearing after 42 days postpartum), and pre-eclampsia (systemic disorder associated with significant proteinuria, >0.3g/24h). Regular attendance at health centers for BP monitoring is crucial to avoid hypertensive emergencies (Cífková, 2023).

EPIDEMIOLOGY

Despite a reduction in prevalence after years of interventions, hypertensive diseases in pregnancy remain one of the leading causes of maternal morbidity and mortality worldwide, especially in low- and middle-income countries. These conditions are responsible for approximately 14% of maternal deaths globally, with a prevalence of 116.4 per 100,000 women of reproductive age (Jiang *et al.*, 2022).

Among hypertensive diseases in pregnancy, hypertensive emergencies had a prevalence of 0.3%, while hypertensive urgencies had a prevalence of 0.9%. This shows that hypertensive urgencies are 2.5 times more common than hypertensive emergencies in emergency departments. Various subtypes of adverse organ damage caused by hypertension have been identified, including pulmonary edema/heart failure (32%), ischemic stroke (29%), acute coronary syndrome (18%), hemorrhagic stroke (11%), acute aortic syndrome (2%), and hypertensive encephalopathy (2%) (Vallelonga *et al.*, 2020).

Data from a study indicate that among hypertensive disorders of pregnancy, the adjusted prevalence of chronic hypertension ranged from 1.0% in Hawaii to 3.4% in Alaska. In the case of hypertensive disorders of pregnancy, adjusted rates ranged from 4.3% in Massachusetts to 9.3% in Louisiana. Eclampsia showed even greater variation, with adjusted prevalences ranging from 0.03% in Delaware to 2.8% in Hawaii, with four states (Hawaii; Alaska; Virginia and Alabama) showing prevalences above 1% (Butwick; Druzin; Shaw and Guo, 2020).

Another study showed that in the United States, between 10% and 20% of pregnancies are complicated by hypertensive disorders of pregnancy. These disorders are responsible for a considerable portion of maternal morbidity and mortality and are the main factor for postpartum readmission of puerperal women in the early postpartum period (Hauspurg; Jeyabalan, 2022).

About 7.4% of maternal deaths are attributable to hypertensive diseases during pregnancy, representing approximately one-fifth of prenatal hospitalizations and two-thirds of referrals to day assessment units (Jiang *et al.*, 2022). In 2017, the analysis of 3,855,500 live births in the USA revealed that the average probability of eclampsia was 2.4 times higher for a woman, depending on the state where the delivery occurred. State-level

variation in the prevalence of chronic hypertension and hypertensive disorders of pregnancy was smaller, suggesting the need for public health efforts to understand and reduce these variations (Butwick; Druzin; Shaw and Guo., 2020).

A study with 571 women investigated the development of chronic conditions after pregnancies complicated by hypertensive diseases, comparing them to 1,142 age- and parity-matched referents. Women with a history of hypertensive diseases of pregnancy had a higher risk of cardiovascular events and experienced accelerated accumulation of 16 chronic conditions, with no difference in all-cause mortality rates between the groups (Garovic et al., 2020). About 60% of women who develop late postpartum eclampsia have no previous history of hypertensive disorder during pregnancy, manifesting the first symptoms in the first 7 to 10 days postpartum, with headache being the most common symptom (Hauspurg; Jeyabalan, 2022). Furthermore, there are few national and international guidelines addressing late-onset postpartum hypertension, and existing guidelines do not clearly define the issue (Hauspurg; Jeyabalan, 2022).

Although maternal mortality is significantly lower in high-income countries (HICs) compared to low- and middle-income countries, hypertensive diseases of pregnancy are still one of the leading causes of maternal death worldwide. In the United Kingdom and Ireland, the proportion of maternal deaths from these diseases was 2.8% between 2011 and 2013, while maternal mortality associated with these conditions ranged between 0.08 and 0.42 per 100,000 pregnancies from 2009 to 2015 (Jiang *et al.*, 2022).

Regionally, Africa recorded the highest prevalence of hypertensive diseases of pregnancy, with an average of 334.9 cases per 100,000 women of reproductive age, followed by Southeast Asia. African-American and Filipino women, for example, have a higher risk of developing these diseases. Additionally, higher incidence rates were observed among Māori, Indigenous Australian, American Indian, and Alaska Native populations. On the other hand, the risk of hypertensive diseases of pregnancy among Pacific Islander populations is still a subject of debate (Jiang *et al.*, 2022).

From the Rochester Epidemiology Project, it was identified that the rate of pre-eclampsia per pregnancy in women under 20 was significantly higher than in women aged 20-34, with 6.5 cases per 100 pregnancies (95% confidence interval: 4.8 to 8.6) compared to 3.0 cases per 100 pregnancies (95% confidence interval: 2.7 to 3.4). Additionally, the rate of gestational hypertension was higher in women aged 35 and older (Garovic et al., 2020).

New evidence indicates that women with postpartum eclampsia face a higher risk of severe maternal morbidity compared to those who develop the disease before delivery. This study, however, has limitations due to the use of administrative database data, but the authors highlighted an increased risk of severe complications associated with recent postpartum hypertension compared to women who presented hypertension during pregnancy (12.1% vs 6.9%; $P<0.01$) (Hauspurg; Jeyabalan, 2022).

According to data from recent studies, most women who present late-onset postpartum pre-eclampsia manifest symptoms in the first 7 to 10 days postpartum. The

most frequent symptoms are neurological, with headache being the most prevalent and the main reason for seeking medical assistance (Hauspurg; Jeyabalan, 2022).

In recent decades, there has been a substantial increase in the prevalence of hypertension, resulting in a greater number of cases of hypertensive emergencies and urgencies recorded in emergency departments (Vallelonga *et al.*, 2020). Recently, there has been a growing trend in recognizing hypertensive urgencies, which have a higher prevalence compared to hypertensive emergencies, possibly due to better patient education on the importance of blood pressure control and greater access to healthcare (Vallelonga *et al.*, 2020). In the last 10 years, the definition of pre-eclampsia has been expanded to include cases without proteinuria but with dysfunction in maternal or uteroplacental organs. This change, adopted by the International Society for the Study of Hypertension in Pregnancy and the American College of Obstetricians and Gynecologists, is influencing clinical management, increasing hospitalizations and inducing labor (Jiang *et al.*, 2022).

The risks of renal and cardiac diseases in women with a history of hypertensive diseases in pregnancy have been underestimated. The percentage of women at risk due to these histories (15.3%) is comparable to the proportions of cardiovascular risk from smoking (13.7%), hyperlipidemia (14.8%), and diabetes (12%) (Garovic *et al.*, 2020). The increase in mortality rates from coronary heart disease among women aged 35 to 54 and in patients with severe pre-eclampsia, who face the risk of cardiovascular death shortly after pregnancies, along with recent evidence of increased rates of hypertensive diseases of pregnancy over the last three decades, indicates the growing relevance of this specific risk factor for cardiovascular diseases (Garovic *et al.*, 2020).

Risk factors for hypertension in pregnancy include a history of previous gestational hypertension, family history of hypertension during pregnancy, and pre-existing medical conditions such as chronic hypertension, pre-gestational diabetes mellitus, thrombophilia, systemic lupus erythematosus, antiphospholipid antibody syndrome, kidney disease, and obstructive sleep apnea. Additionally, hypertensive and cardiometabolic diseases in pregnancy share risk factors such as advanced maternal age, overweight or obesity, inadequate nutrition, and dietary habits before and/or during pregnancy. A study revealed that women exposed to indoor air pollution, especially those using biomass and solid fuels, have twice the chance of reporting symptoms of pre-eclampsia compared to those using clean fuels (Jiang *et al.*, 2022).

Advanced maternal age, black race, and maternal obesity are associated with a higher risk of postpartum eclampsia. Women over 35 years of age have twice the risk of postpartum eclampsia, while pre-gestational obesity increases this risk in a dose-dependent manner, reaching 7.7 times for a BMI >40 kg/m². Black women have a 2 to 4 times higher risk of postpartum eclampsia compared to other races (Hauspurg; Jeyabalan, 2022). Younger patients tend to develop hypertensive urgencies more frequently than hypertensive emergencies, with an average age difference of 5.4 years (Vallelonga *et al.*, 2020). Women

with gestational hypertension have an increased risk of future cardiovascular events and other conditions such as arrhythmias, coronary artery disease, heart failure, stroke, chronic kidney disease, dementia, hyperlipidemia, hypertension, and diabetes, regardless of factors such as education, smoking, and obesity (Garovic *et al.*, 2020).

Currently, various approaches are used in clinical practice for the treatment and prevention of hypertensive diseases during pregnancy, including calcium, vitamin D, and folic acid supplementation, as well as the use of aspirin or antiplatelet agents (Jiang et al., 2022). Lifestyle interventions, such as education, diet, exercise, and personal monitoring of blood glucose levels, are also implemented. However, there is no conclusive evidence on the effectiveness of these interventions in preventing hypertensive diseases in pregnancy. A Cochrane review showed an average risk reduction of 0.70 (95% CI 0.40-1.22; four trials, 2,796 women; I2=79%; low-quality evidence) with these interventions (Jiang *et al.*, 2022).

To improve screening and treatment of gestational hypertensive diseases, it is essential that public health accurately assess how these disorders are coded in US birth records. Due to the low number of births in some locations or lack of reporting, it was not feasible to estimate the variation in the prevalence of each hypertensive disorder at the county level. Collecting accurate data from all counties can help public health authorities identify areas that need increased surveillance and treatment, especially in states with high prevalence of these disorders (Butwick; Druzin; Shaw and Guo, 2020).

It is recommended to consider the diagnosis of postpartum eclampsia in women who develop eclampsia between 48 hours and 6 weeks postpartum. For pre-delivery onset eclampsia, it is suggested that confirmation of elevated blood pressure be performed on two occasions separated by at least 4 hours, except in cases of severe hypertension, where confirmation should be immediate to allow for urgent treatment. Since there are no specific definitions for the postpartum period by the American College of Obstetricians and Gynecologists, it is proposed that the presence of any severe features (such as severely elevated blood pressure in women without a previous history of hypertension) be classified as postpartum eclampsia after excluding other possible causes (Hauspurg; Jeyabalan, 2022).

Including the history of hypertensive diseases in pregnancy can substantially reduce misclassification using current cardiovascular disease risk scores, which are particularly inaccurate in women. The proportion of women who may be at risk based on their history of hypertensive diseases in pregnancy is similar to the proportions of women at risk for cardiovascular diseases based on the presence of traditional risk factors (Garovic et al., 2020).

DIAGNOSIS

Early identification of the signs and symptoms of gestational hypertension and pre-eclampsia improves prognosis and prevents emergencies such as eclampsia or HELLP syndrome. It is essential to monitor pregnant women with hypertension associated with headache, visual disturbances, severe abdominal pain (especially in the upper right quadrant or epigastric), lower limb edema, and laboratory changes such as proteinuria, elevated transaminases, and thrombocytopenia. Any suspected pre-eclampsia or hypertensive emergency should be referred for hospital evaluation (Arbe; Pastor and Franco, 2018; Cífková, 2023).

In the assessment of hypertension in pregnancy, a systematic approach is essential, involving blood pressure measurement, laboratory tests, and umbilical artery Doppler ultrasound. Hypertension is diagnosed with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, confirmed on two separate occasions or at intervals of at least 15 minutes for severe hypertension (≥ 160/110 mmHg). Laboratory tests are crucial to identify complications such as proteinuria (> 0.3 g/24h or > 30 mg/mmol in the protein/creatinine ratio), elevated serum creatinine (> 90 µmol/L) for acute kidney injury, and liver enzymes (alanine aminotransferase > 40 IU) to assess liver involvement. Platelet count and hemolysis detection help diagnose HELLP syndrome (thrombocytopenia < 150 × 10^9/L and hemolysis). Doppler ultrasound is used to assess uteroplacental insufficiency, associated with fetal growth restriction, depending on the operator's experience (Cífková, 2023; Sinkey *et al.*, 2020; Wiles; Damodaram and Frise, 2021).

Each diagnostic method has its specificities, sensitivities, and limitations. Blood pressure measurement is simple and accessible but susceptible to technical and environmental variations. Proteinuria assessment is specific but can be influenced by inadequate samples or urinary infections. Creatinine and liver enzyme tests are sensitive to renal and hepatic lesions but do not adequately distinguish pre-eclampsia from other conditions. Doppler ultrasound, effective in detecting uteroplacental insufficiency, requires operational skill. Combining these methods allows for accurate diagnosis of hypertensive conditions in pregnancy, guiding clinical management and appropriate interventions (Cífková, 2023; Wiles; Damodaram and Frise, 2021; Sinkey *et al.*, 2020).

In the differential diagnosis of hypertension in pregnancy, it is crucial to distinguish pre-eclampsia from other conditions with similar symptoms, such as gestational hypertension, renal diseases, and metabolic disorders. Pre-eclampsia manifests with hypertension and significant proteinuria, differing from gestational hypertension which occurs without proteinuria, and chronic hypertension which persists before and after pregnancy. Symptoms such as headache, visual disturbances, abdominal pain, and laboratory changes (low platelet count and abnormal liver enzymes) help distinguish pre-eclampsia. Associated conditions such as multiple pregnancy, hydatidiform mole, antiphospholipid syndrome, and

comorbidities like renal disease or diabetes influence clinical presentation. Differentiating these conditions is crucial for immediate interventions in pre-eclampsia and monitoring gestational hypertension to prevent complications (Arbe; Pastor and Franco, 2018; Wiles; Damodaram and Frise, 2021).

Recent advances include studies on serum total bile acid (TBA) as a biomarker associated with pre-eclampsia. The increased incidence of pre-eclampsia in patients with intrahepatic cholestasis suggests a significant relationship. Elevated TBA levels are correlated with the severity of pre-eclampsia, indicating its potential as a prognostic indicator and monitoring for recent-onset hypertension in pregnancy. It is recommended to include TBA tests in routine exams for pregnant women as a risk assessment for hypertensive disorders (Deng *et al.*, 2022).

TREATMENT

Treatment aims to reduce maternal and fetal morbidity and mortality, preventing complications such as prematurity, oligohydramnios, and fetal growth restriction (Vadhera; Simon, 2014). Despite challenges in developing new drugs, current treatments provide effective clinical management, reducing the risk of serious complications such as acute pulmonary edema, stroke, renal dysfunction, and mortality. The goal is to stabilize the patient, minimize damage to target organs, and ensure fetal viability (Cífková, 2023).

Initial treatment of gestational hypertension involves the use of antihypertensives, initiated when diastolic blood pressure (DBP) reaches values above 100-110 mmHg. Laboratory tests and ultrasound are complementary tools in patient management. Therapeutic adjustments are necessary based on response to treatment and blood pressure control. Clinical and laboratory manifestations should be monitored carefully, guiding adjustments and hospital interventions (Vadhera; Simon, 2014).

Pregnant women with hypertensive emergencies are at higher risk of developing acute pulmonary edema and stroke due to changes in hydrostatic pressure and uteroplacental flow. For severe hypertension (BP > 160/110 mmHg), with or without target organ involvement, intravenous medications such as labetalol, hydralazine, and nifedipine are indicated, with maternal intra-hospital monitoring. During stabilization, it is crucial to periodically monitor fetal heart rate to assess its viability, considering delivery as the definitive treatment after maternal stabilization in pregnancies beyond 34 weeks (Vadhera; Simon, 2014).

European guidelines recommend initiating medication in pregnant women with persistent elevation of blood pressure ≥ 150/95 mmHg, or values > 140/90 mmHg in cases of gestational hypertension (with or without proteinuria), chronic hypertension superimposed on gestational, or subclinical or symptomatic target organ damage, at any stage of pregnancy. Preferred drugs include methyldopa, labetalol, and calcium antagonists, with the most evidence of safety available for nifedipine (Cífková, 2023).

Women who develop postpartum pre-eclampsia (recent-onset hypertension, 48 hours to 6 weeks postpartum) should be treated when BP values reach 150/110 mmHg, to prevent progression to severe hypertension. Treatment includes the use of antihypertensives such as labetalol, intravenous hydralazine, and oral nifedipine. For women with severe hypertension and neurological symptoms postpartum, magnesium sulfate prophylaxis is recommended. Volume overload management is based on the use of diuretics, preferably IV or oral furosemide for 3 to 5 days, aiming to stimulate diuresis and reduce excess volume and BP (Hausurg; Jeyabalan, 2022).

Non-pharmacological interventions play a crucial role in preventing gestational complications such as hypertensive disorders and gestational diabetes mellitus. Obesity is a significant risk factor. For pregnant women with overweight (BMI 25.0-29.9 kg/m²), it is recommended to limit weight gain to 6.8-11.2 kg, while those with obesity (BMI ≥ 30 kg/m²) should restrict it to a maximum of 6.8 kg. These measures are essential to mitigate maternal-fetal risks. Regular physical activity during pregnancy is advisable to prevent the development of gestational diabetes and hypertensive disorders. Supervised aerobic exercises of light to moderate intensity, performed three to four times a week for 30 to 60 minutes, should be initiated in the first trimester, except in cases of contraindications (Cífková, 2023).

Table 1.0 - Prophylactic Medications for Pre-eclampsia and Eclampsia

Medications	Dose	Considerations
Aspirin PO	75 to 150 mg	Recommended for high-risk women between 12 and 28 weeks of gestation
Magnesium sulfate IV	Loading dose: 4g	Continuous infusion: 1g/h until delivery, for a maximum of 24h

Source: Cífková (2023).

Table 2.0 - Medications Used in Gestational Hypertensive Emergencies

Medications	Dose	Precautions	Considerations
Labetalol	100 to 800 mg	Asthma	Monitor neonatal hypoglycemia
Nifedipine	10 to 40 mg		
Methyldopa	250 mg - 1 g	Liver dysfunction	Mood disorder
Labetalol	Bolus: 10 to 50 mg infused over 1 to 2 min, every 10 min, with a maximum of 4 doses	Infusion: 20 mg/h, every 30 min, with a maximum of 160 mg/h	Asthma
Hydralaze	Bolus: 5 mg over 10 min, repeated every 20 to 30 min	Infusion: 5 mg/h	Maternal tachycardia

Source: Braunthal; Brateanu (2019); Sinkey *et al.* (2020); Tita *et al.* (2022); Vadhera; Simon (2014); Cífková (2023).

Home blood pressure monitoring (BP) is recommended for pregnant women with a history of hypertension, using antihypertensives, at high risk of pre-eclampsia, and those who develop hypertensive disorders during pregnancy. This practice is particularly useful for detecting BP elevations between the third and seventh day postpartum, facilitating early detection of severe hypertension and promoting appropriate management. However, evidence on its effectiveness in reducing outpatient visits and hospital interventions is still limited (Cífková, 2023).

Studies are being conducted to evaluate the withdrawal of hydralazine as a first-line drug in treatment due to its association with persistent arterial hypertension and complications such as maternal hypotension, cesarean section, premature placental abruption, oliguria, fetal cardiac arrhythmias, and low Apgar score in the first minute (Braunthal; Brateanu, 2019). In 2011, the World Health Organization (WHO) recommended the use of magnesium sulfate for prophylaxis, along with low-dose aspirin and calcium supplementation for areas with low intake. Interventions that have not demonstrated benefits, such as vitamin C, D, or E supplementation, bed rest, and sodium restriction, are discouraged. Diuretics and corticosteroids are contraindicated for complications. The International Federation of Gynecology and Obstetrics (FIGO) is evaluating the feasibility of additional ultrasound examinations, although the cost-benefit of this proposal needs further study (Sinkey *et al.*, 2020).

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