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Hypertensive complications of pregnancy: A clinical overview

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ABSTRACT

Hypertensive disorders in pregnancy are a worldwide health problem for women and their infants complicating up to 10% of pregnancies and associated with increased maternal and neonatal morbidity and mortality. In Europe, 2.3–3% of pregnancies are complicated by preeclampsia. Gestational diabetes, obesity, no previous or multiple births, maternal age less than 20 or greater than 35 years old and thrombophilia can be some of the possible factors related to increased risk for hypertension in pregnancy. Complications of hypertension during pregnancy affect both mothers and their infants. Ambulatory blood pressure monitoring helps to distinguish true hypertension from the white coat as pregnant women with office abnormal values may have normal out of office blood pressure. Imbalance between proangiogenic and antiangiogenic factors in placenta may lead to endothelial dysfunction, vasoconstriction, activation of the coagulation system, and hemolysis. Carotid intima-media thickness, pulse wave velocity, augmentation index, and arterial wall tension were found to be significantly increased in women with preeclampsia compared to normotensive pregnant women. Uterine artery Doppler and serum biomarkers can be used to evaluate the probability of hypertension and complications during pregnancy, but further research in the field is needed. Lately, micro ribonucleic acids have also been the focus of research as potential biomarkers.

1. Introduction

Hippocrates first recognized pregnancy-induced hypertension (PIH) around 400 BCE and stated that headache accompanied by heaviness and convulsions is considered an unhealthy pregnancy. Bossier de Sauvages (1739) differentiated the seizures of eclampsia (E) from epilepsy, Demanet (1797) recognized the extreme swelling in eclamptic women and Pierre Rayer described proteinuria in eclamptic women in his classic text “Diseases of the Kidney” (1840). The introduc-

Abbreviations: PIH, pregnancy-induced hypertension; GH, gestational hypertension; PE, preeclampsia; BMI, body mass index; BP, blood pressure; E, eclampsia; SGA, small-for-gestational age; SBP, systolic blood pressure; DBP, diastolic blood pressure; *HELLP syndrome*, hemolysis, elevated liver enzyme levels, and low platelet levels; DIC, disseminated intravascular coagulation; OR, odds ratio; RR, relative risk; ABPM, ambulatory blood pressure measurement; WCH, white coat hypertension; ADAM-12, disintegrin and metalloprotease 12; PAPP-A, pregnancy associated plasma protein A; PlGF, placental growth factor; PP-13, placental protein 13; IGFBPs, insulin-like growth factor binding proteins; microRNA or miRNA, micro ribonucleic acid; VEGF, vascular endothelial growth factor; SERPINA3, Serpin Family A Member 3; cIMT, carotid intima media thickness; PWV, pulse wave velocity; RCTs, randomized control trials; ESH/ESC, European Society of Hypertension/European Society of Cardiology; WHO, World Health Organization.

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tion of Riva-Rocci's mercury manometer (1896) to measure blood pressure recognized preeclampsia (PE) as a pregnancy induced hypertensive disorder. In the 21st century PIH is still a worldwide health problem for women and their infants and affects an estimated 240,000 women in the United States every year [1]. During 1995–2004 in the USA, gestational hypertension (GH) and PE seem to be the most commonly diagnosed hypertensive disorders in pregnancy, while pre-existing hypertension was infrequent [2]. In Europe, the German Perinatal Quality Registry 2006 that contains the complete national birth cohort of newborn infants and mothers from German obstetric clinics reported a 2.3–3% prevalence of PE [3,4].

Hypertensive disorders can complicate up to 10% of pregnancies and are associated with increased maternal, neonatal, and fetal morbidity and mortality. Pre-existing hypertension is a strong risk factor for developing PE. Other possible risk factors associated with PE are gestational diabetes, no previous or multiple births, pre-pregnancy obesity and above-average weight gain during pregnancy [3,4]. Obesity is an important risk factor since 46% of women who developed PE were obese [5]. A case-control study using a population dataset of twin pregnancies reported that pre-pregnancy body mass index (BMI) in the obesity range increased the risk of PE almost 5 times and gestational diabetes doubles the risk of PE [6].

Maternal age was associated with the risk of E. Young mothers less than 20 years of age or old mothers greater than 35 years of age had increased E risk. Gestational diabetes, obesity before pregnancy, excess weight gain during pregnancy, longer interval time between births and lower socio-economic status were other possible risk factors for the development of E [7].

Impaired thrombophilia was found in 3% of the patients developing PE [5]. About one-third of untreated women with antiphospholipid syndrome, an autoimmune syndrome characterized by recurrent thrombosis, may develop PE during pregnancy and more than 10% of these women will deliver small-for-gestational age infants (SGA) [8].

The prevalence of PE was reported to be increased in Māori women and lower in Chinese women [9]. Moreover, black women and those of Hispanic origin seem to be at increased risk for developing hypertension in pregnancy compared to white women suggesting that different ethnicities have different relative risk for developing PE [2].

Gestational hypertension and PE have many common risk factors such as BMI >25 kg/m^2, nulliparity, PE history, diabetes mellitus and twin birth, but the effect sizes of PE history and twin birth were substantially different between GH and PE [10].

In this review, definition, classification and possible complications of hypertension in pregnancy will be analyzed. We will also emphasize how the diagnosis should be confirmed and the risk assessment of PE in pregnancy as well as possible treatment options.

2. Definition and Classification of Hypertension in Pregnancy

Hypertension in pregnancy is defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg. According to the levels of BP, hypertension is mild if SBP is measured between 140–149 mmHg and DBP 90–99 mmHg, moderate if SBP is 150–159 and DBP 100–109 mmHg and severe if SBP is equal or greater than 160 mmHg and DBP than 110 mmHg [11].

Hypertensive disorders in pregnancy are not a single entity, but include: 1) Pre-existing hypertension which is essential in most of the cases but could also be secondary due to various causes and may be associated with proteinuria. Pre-existing hypertension is present before the 20th gestational week and usually persists after 42 days postpartum. 2) Gestational hypertension that develops after the 20th week of pregnancy in women who have had no high BP values before. Blood pressure usually returns to normal during the first 42 days postpartum. PE is GH associated with significant proteinuria (>0.3 g/24 h or ≥30 mg/mmol urinary protein: creatinine ratio in a spot urine random sample). 3) Pre-existing hypertension associated with further worsening of BP and protein excretion ≥3 g/d in 24-h urine collection after the 20th week of gestation is defined as pre-existing hypertension plus superimposed GH with proteinuria. 4) Finally, in unclassified gestational hypertension BP was first recorded after the 20th week of gestation and we do not know if hypertension existed before pregnancy and should wait until the 42nd day after delivery to correctly classify the hypertensive disorder [12]. Data are summarized in Table 1.

PE is associated with maternal, fetal, and neonatal morbidity and mortality. In Europe, PE is one of the most common reasons for maternal mortality [13]. In Latin America, 25% of maternal deaths may be attributed to PE complications, while this proportion is smaller in Africa. In other regions such as China and India, PE is the second and third cause of maternal death, respectively [14,15]. In India, hypertension or E-related deaths accounted for 10% of

Table 1 – Classification of hypertension in pregnancy.

	Gestational week	Postpartum days	Proteinuria
Pre-existing hypertension	<20	≥42	+/–
Gestational hypertension and preeclampsia	>20	<42	GH: <0.3 g/d PE ≥0.3 g/d or ≥30 mg/mmol urinary protein:creatinine ratio in a spot urine random sample
Pre-existing hypertension plus superimposed gestational hypertension with proteinuria	<20	-	>3.0 g/d
Unclassified hypertension	>20	GH <42 pre-existing ≥42	+/–

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