Open Access Journal of Gynecology and Obstetrics

ISSN: 2638-5244

Volume 3, Issue 2, 2020, PP: 01-06

Hypertension, Pregnancy and Chronic Kidney Disease

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Abstract

Blood pressure is the pressure of blood on the walls of blood vessels, arteries. Arteries carry blood from the heart to other parts of the body. If the pressure in the arteries becomes too high, the person has high blood pressure called hypertension. Normal blood pressure is 110/80, and in high blood pressure the upper number is 140 or more, or the lower number is greater than 90. High blood pressure is one of the most common factors that can endanger a pregnant woman's health and occurs in 8-10% of pregnancies. The causes can be varied, from genetic predisposition to overweight. A pregnant woman can have high blood pressure without symptoms, which reason why blood pressure must be measured at every examination, regardless of the early or late stage of pregnancy.

Keywords: *Hypertension, Pregnancy, Blood Pressure, Kidney*

Introduction

Hypertension is a common pregnancy complication in healthy women and in women with essential hypertension [1]. Management of most hypertensive pregnant women should result in a healthy mother and baby.

Pregnancy in women with pre-existing renal disease can be harrowing for both the mother and the doctors, but increasingly results in healthy infants. Pregnancy is typically complicated by hypertension, worsening proteinuria, and prematurity with or without worsening renal function.

There is a decrease in systolic blood pressure of about 9 mmHg and in diastolic blood pressure of 17 mmHg during pregnancy. The lowest blood pressure is seen between 16 and 20 weeks of gestation, and the blood pressure gradually increases toward term. Hypertension is the most common medical problem occurring during pregnancy.

The diagnosis is easiest if a history of hypertension before pregnancy is available or if hypertension occurs before 20 weeks of gestation.Almost half of the women with preexisting hypertension will experience a pregnancy-related drop in blood pressure between 13 and 20 weeks of gestation, and the diagnosis of essential hypertension will not be apparent if the woman is first seen during that period.

The renal system undergoes significant adaptations in pregnancy to meet the needs of both the pregnant woman and her growing fetus [2]. These changes have important implications in the evaluation and management of gravidas with kidney disorders. Renal disease in pregnancy falls into several categories. It may be chronic and diagnosed prior to pregnancy, chronic but first recognized during pregnancy, or it may present for the first time as an acute disorder in pregnancy. While the majority of women with underlying renal disease in pregnancy will have good pregnancy outcomes, there is an increased risk for adverse maternal and fetal outcomes especially in pregnant women with moderate to severe renal disease. These risks include worsening renal function, increase of baseline proteinuria, worsening hypertension, and the development of superimposed preeclampsia. From the fetal perspective, there is an increased risk of fetal growth restriction, preterm delivery, and the complications of superimposed preeclampsia. Other common disorders during pregnancy include pyelonephritis and renal stones.

Hypertension

Hypertension and chronic kidney disease are common in disadvantaged communities, where maternal health

is also suboptimal and risk factors for poor pregnancy outcomes are common [3]. Multiple exposures during pregnancy and early childhood impact fetal and infant growth and nephrogenesis, which in turn affect the risk of hypertension and kidney disease throughout the life course. Being small for gestational age is the strongest risk predictor for renal programming, but being born preterm, of low birth weight, large for gestational age, or being exposed to gestational diabetes and preeclampsia are also risk markers. This programmed risk could be mitigated by optimization of maternal health before pregnancy, education about healthy lifestyles, and screening of individuals who may have experienced developmental programming, to permit early diagnosis and intervention. Given that millions of babies are born too small, too early, or in complicated pregnancies, increased awareness of programmed risk of hypertension and kidney disease should provide a window of opportunity to reduce the global burden of these conditions across the life course through prevention, early diagnosis and treatment, and education.

Pregnancy

Normal pregnancy is characterized by alterations in renal and cardiovascular functions that accommodate the hemodynamic and metabolic demands of the growing fetus [4]. Glomerular filtration rate (GFR) and renal blood flow increase in the first trimester, coincident with the dramatic increases in pregnancy-related hormones. Generalized vasodilation is present, and in normal gestation, maternal blood pressure (BP) decreases and cardiac output (CO) increases. These physiologic adjustments are necessary for normal fetal growth and well-being. Reduced GFR and hypertension are risk factors for poor pregnancy outcomes, including fetal growth restriction, preeclampsia, and fetal death

Although the pregnancy rate of women with chronic kidney disease (CKD) and the overall survival rate of their fetuses have improved, pregnancy in women with CKD still have a high risk of adverse maternal and fetal outcomes [5]. To achieve better outcomes for this particular population, managing pregnancy in women with CKD has become a considerable challenge shared by both nephrologists and obstetricians. Strengthened management, including prepregnancy preparation, pregnancy management, peripartum management, and postpartum care, could prevent or mitigate maternal renal damage and adverse maternal and fetal outcomes. Women with CKD require risk assessment of pregnancy before conceiving, close follow-up by both nephrologists and obstetricians to monitor disease activity and detect obstetric complications during pregnancy, evaluation of indications for termination of pregnancy and selection of delivery mode, and assessment of disease activity and emotional support to prevent depression after delivery.

With advances in medicine, the pregnancy rate of female patients with chronic kidney disease has improved, along with an apparent increase in the overall survival rate of fetuses. However, women with CKD remain a major part of the patient population that carries the highest risk of adverse maternal and fetal outcomes. Adverse maternal outcomes include aggravated renal damage, acute kidney injury, pregnancy- associated kidney disease, increased proteinuria, hypertension, and preeclampsia (PE). Furthermore, adverse fetal outcomes include stillbirth, fetal growth restriction (FGR), and preterm delivery. Therefore, managing pregnancy in patients with CKD has become a considerable challenge shared by both nephrologists and obstetricians. To mitigate maternal renal damage and adverse maternal and fetal outcomes, both nephrologists and obstetricians need to assess the risk of pregnancy in patients with CKD in a standardized manner, determine the optimal timing of pregnancy, stabilize the condition of patients, and closely monitor any changes during pregnancy for the early detection of maternal and fetal complications.

The incidence of hypertension is higher in patients with CKD than in ordinary individuals, which further increases after pregnancy. The rate of new hypertension in pregnant women with stage 1 CKD and stage 4–5 CKD is 7.9% and 50%, respectively. Poorly controlled hypertension significantly adds to the risk of pregnancy, including the risk of early pregnancy loss, superimposed placental ischemia and PE, and premature delivery and FGR. The recently published Control of Hypertension in Pregnancy Study confirmed that treating hypertension in pregnancy to a lower diastolic blood pressure target is not associated with adverse neonatal events or pregnancy outcomes. A blood pressure target <140/90 mmHg has been recommended for women with CKD during pregnancy.

Kidney size increases by approximately 1 cm during pregnancy [6]. The urinary collecting system (renal calyces, pelvis, and ureters) dilates. Hormonal and

mechanical forces are thought to account for ureteral dilation as early as 6 weeks gestation. In the later stages of pregnancy, mechanical compression of the ureter against the pelvic brim may lead to hydroureter and hydronephrosis. Hydronephrosis occurs on the right in 90% of cases due to dextrorotation of the uterus by the sigmoid colon.

In rare instances this becomes a clinically significant cause of obstructive uropathy. The dilated collecting systems can hold up to 300 mL of urine and hence serve as a reservoir for bacteria. The dilated urinary tract also allows for urinary stasis and increases the risk of pyelonephritis in pregnant women with asymptomatic bacteriuria.

Blood

Such a result may occur when there is a genuine increase in red blood cells in the urine or may be a consequence of the presence of an abnormal amount of the pigment haemoglobin in the urine [7]. Haemoglobin is the pigment which gives blood its red colour and which is responsible for the carriage of oxygen within red blood cells. Haemoglobinuria occurs when there is rapid destruction of red cells within the circulation (haemolysis) in, for example, malaria, after trauma or snake bite. A positive result on stix testing should prompt examination of a fresh urine sample under the microscope. The absence of an excess of red blood cells suggests the presence of haemoglobinuria. Error may be introduced if the urine is examined many hours after it has been passed, as red cells break down with time and may no longer be discernible.

Blood in urine does not invariably indicate that it has issued from the urinary tract. A major trap for the unwary is to find a positive stix test result in a woman who is menstruating. The institution of detailed investigations, some of which carry risk, under such circumstances would be negligent. The finding of blood in urine which is not discernible to the naked eye is termed 'microscopic haematuria'. Further investigation is mandatory. The causes are many and include bladder and kidney tumours, urinary tract stones and immunologically mediated disease of the filtering units of the kidney (glomeruli), the general term for which is 'glomerulonephritis'. Investigation will include in many cases a search for malignant cells in urine under the microscope, assessment of renal function, imaging of the urinary tract and perhaps direct inspection of the bladder via a cystoscope introduced through the urethra, the passage leading from the bladder to the exterior. Cystoscopy is usually the province of the urologist rather than the nephrologist.

Blood Pressure

Mean BP starts to decrease early in gestation, with diastolic levels in midpregnancy averaging 10 mmHg less than measurements postpartum [8]. In later pregnancy, BP increases, gradually approaching nonpregnancy values near term. Because cardiac output rises quickly in the first trimester and remains relatively constant thereafter, the decrease in pressure is due to a marked decrement in systemic vascular resistance. The slow rise toward nonpregnant levels after a midtrimester nadir is interesting, because it demonstrates that increasing vasoconstrictor tone is a feature of late gestation in healthy women as well as in women in whom preeclampsia is developing. The cause of the decrease in systemic vascular resistance during pregnancy is obscure. Studies of arterial compliance in pregnancy demonstrate early rises, perhaps due to alterations in vessel ground substance. Elevations of plasma estrogen and progesterone to concentrations that may relax smooth muscle occur, and increments in vasodilating prostaglandins and relaxin are also present during gestation. Hormonally mediated increases in endothelial NO production may also contribute to the vasodilation in pregnancy. With the lower BP, the levels of all components of the renin–angiotensin system are increased during pregnancy. Exaggerated hypotensive responses to converting enzyme inhibition in normal gravidas suggest that the increased renin–angiotensin system in pregnancy is a normal physiologic response to decreased BP and increased sodium excretion.

Lack of awareness of the fluctuation in BP during normal gestation may lead to diagnostic errors. For example, women with mild essential hypertension often experience a decrease in BP during early pregnancy, and BP may even approach normal levels. They may then be erroneously labeled preeclamptic in the last trimester, when frankly elevated pressures occur.

Renal Function

Normal kidneys can be thought of as providing four main functions—glomerular function, tubular reabsorption, tubular secretion and urine excretion—

which maintain homeostasis of fluids and electrolytes in the blood within a very narrow range despite wildly varying intake and production, by excreting or reabsorbing excessive fluid or solutes [9]. Acid–base balance is maintained by several buffering systems with the kidney excreting excess bicarbonate or hydrogen ions to maintain stability. Thus, when the kidney sustains injury or insult, a wide array of biochemical and fluid derangements can result. The kidney has a role in maintaining blood pressure and AKI (acute kidney injury) can result in hypertension which could be hormonally driven or resulting from salt and water retention. The kidney in addition has a significant role in regulating bone biochemistry, and producing erythropoietin; these have increasing importance if the renal impairment persists over a prolonged period. Even in an acute intensive care situation once renal failure has persisted for more than a week or two, the monitoring and management of chronic renal disease needs to be undertaken, closely with the nephrology team.

The kidney undergoes monumental physiologic and anatomic changes during a normal pregnancy [10]. Renal plasma flow increases by 50-70%. Plasma volume increases by 50% and there is hemodilutional anemia. Cardiac output increases by 40%.Glomerular Filtration Rate (GFR) is maximum around the 13th week of pregnancy and can reach levels up to 150% of normal. Despite increased GFR the intraglomerular pressure remains normal. Serum creatinine falls by an average of 0.4 mg/dl to a pregnancy range of 0.4 to 0.8 mg/dl. Hence, a serum creatinine of 1.0 mg/dl, although normal in a non pregnant individual, reflects renal impairment in a pregnant woman. Serum creatinine rises near term and value of 1 mg/dl is considered normal. In the initial part of pregnancy there is decreased peripheral vascular resistance with a blood pressure fall of approximately 10 mm Hg in the first 24 weeks. The blood pressure gradually returns to prepregnancy level by term. Glycosuria occurs due to decrease in transport maximum for glucose(TMG) and high GFR. Aminoaciduria (2 g/d) may be seen. Increased uric acid clearance results in low uric acid level (2.5-5.5 mg/dl) but levels increase later and reach prepregnancy values at term. A value of >6 mg/dl reflects pregnancy induced hypertension (PIH). Potassium and almost 900 meq of sodium are retained. Calcium excretion increases but stone formation is not increased as there is increased excretion of inhibitors of stone formation. A reset in the osmostat occurs, resulting in increased thirst and decreased serum sodium levels (by 5 mEq/L) and low plasma osmolality (10 m0sm/kg less). Clearance of ADH is increased by placental vasopressinase and may result in transient Diabetes insipidus of pregnancy which may respond to DDAVP. On the other hand there are some reports of transient SIADH in pregnancy. Urine concentration and dilution are adequate. There is mild respiratory alkalosis and blood gas of 7.42-7.44/30 pCO2/HCO318-22 is representative.

Function Testing

Practically assessing GFR during pregnancy has all the flaws as in the non-obstetric realm but has the added nuisances of increased GFR and urinary stasis [11]. The best test was discerned by comparing inulin versus 24 h creatinine clearance as well as using the modification of diet in renal disease (MDRD) formula in healthy pregnant women and women with preeclampsia or chronic kidney disease (CKD). In healthy pregnant women the 24 h creatinine clearance was better than the MDRD by 40 cc/min. In women with preeclampsia or prior CKD the MDRD underestimated the GFR in both by 25 cc/min. Because the GFRs were >60 the MDRD formula loses its' integrity in this population. Following serum creatinines is certainly useful, but the absence of changes in creatinine may not be indicative of true GFR changes and so 24 h urine collections may be instructive.

Estimating proteinuria during pregnancy also has its limitations as in the non-obstetric world. If one assumes the urine protein to creatinine ratio (PCR) is expected to hold in pregnancy, it is useful for quantification for diagnosis of preeclampsia and monitor preexisting kidney disease. Urine dipsticks routinely have high rates of false positives and negatives compared to 24 h urines and do not take into consideration the specific gravity in the guidelines when assessing proteinuria such as in preeclampsia. Most nephrologists do not speak in terms of urine protein dipsticks. However, urinary stasis complicates the utility of the urine PCR. There is sufficient data in the literature that demonstrates that the spot urine PCR has been shown to correlate well with 24 h urine collections. Certainly, if the cutoff value is questionable, a 24 h urine collection for creatinine and protein should be done.

Preeclampsia

Preeclampsia, a leading cause of morbidity and mortality in pregnancy, complicates up to 5% of pregnancies worldwide [12]. The spectrum of hypertensive disorders during pregnancy comes in four varieties: gestational hypertension, preeclampsia and eclampsia syndrome, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Gestational hypertension is the development of elevated blood pressure of greater than 140/90 mmHg in previously normotensive women after 20 weeks of gestation. Proteinuria does not develop, and the elevated blood pressures resolve by 12 weeks postpartum. Preeclampsia is gestational hypertension with the presence of proteinuria and/or signs of end organ damage. The progression of the preeclampsia syndrome to eclampsia is signified by the onset of worsening hypertension and generalized tonic-clonic seizures. Preeclampsia and eclampsia are both definitively treated by delivery of the placenta, resulting in resolution of the acute syndrome. However, it has been shown that women who suffer from preeclampsia have a higher lifetime risk of cardiovascular disease (CVD), chronic kidney disease (CKD), cerebrovascular disease, and metabolic derangements including insulin resistance, overt diabetes mellitus, hyperlipidemia, and the metabolic syndrome.

While the clinical presentation is highly variable, risk of adverse outcomes increases significantly when preeclampsia develops early before 34 weeks of gestation [13]. Severe preeclampsia is characterized by severe hypertension (BP > 160/110 mmHg), evidence of end-organ damage, or intrauterine growth restriction. The most common presentation of preeclampsia is hypertension that is routinely detected at an antenatal visit in an asymptomatic woman. Most of the signs and symptoms will be present only in severe disease. The common symptoms in severe preeclampsia include vomiting, visual disturbances, headache, worsening of hand or leg edema, or severe persistent right upper quadrant or epigastric pain. On examination, in addition to higher blood pressures, patients can have papilledema, right upper quadrant tenderness, hyperreflexia with marked clonus, pulmonary edema, and altered mental status. Rapidly progressing signs and symptoms indicates impending severe disease that needs close monitoring. The major adverse outcomes include neurological complications such as seizures (eclampsia) and strokes, HELLP syndrome (defined by hemolysis, elevated liver enzymes, and low platelets), and renal dysfunction (ranging from mild reduction in glomerular filtration rate and minimal proteinuria to reversible or irreversible acute renal failure due to acute tubular necrosis or acute cortical necrosis). HELLP syndrome occurs in about 10–20% of women with severe preeclampsia and is associated with significant maternal and perinatal morbidity. Preeclampsia is a risk factor for cardiovascular disease, and preeclamptic women have 3.7 times higher risk of developing hypertension, 2.2 times increased risk of coronary heart disease, and 1.8 times higher risk of stroke. Although the absolute risk of end stage renal disease (ESRD) in women with history of preeclampsia is low, preeclampsia is associated with cumulative risk of subsequent ESRD.

Conclusion

Blood pressure and body weight are measured every two weeks; BUN and creatinine levels in addition to creatinine clearance are measured frequently, at intervals dictated by the severity and progression of the disease. Women can be hospitalized after 28 weeks to rest in bed, monitor blood pressure and fetus. Which antenatal tests are performed depends on the stage of the pregnancy. If the results remain normal and they are not worrying, the pregnancy continues. Premature birth is usually required due to the detection of preeclampsia, fetal growth retardation or uteroplacental insufficiency. Cesarean section is very common, although vaginal delivery may be possible if the cervix is mature and there are no obvious obstacles to vaginal delivery.

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Citation: **Siniša Franjić.** *Hypertension, Pregnancy and Chronic Kidney Disease. Open Access Journal of Gynecology and Obstetrics. 2020; 3(2): 01-06.*