Cardiovascular and Metabolic Science www.ancam.org.mx

Chapter 10

Vol. 35 Supplement 1
January-March 2024

doi: 10.35366/115060

Chronic kidney disease in women with a history of hypertensive disorders of pregnancy

Enfermedad renal crónica en la mujer con antecedente de enfermedad hipertensiva del embarazo

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Keywords:
hypertensive disorders, pregnancy, chronic kidney disease, arterial hypertension, preeclampsia.

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INTRODUCTION

Chronic kidney disease (CKD) is a significant health problem, increasing exponentially in Mexico and Latin America (LATAM). The biological characteristics that regulate the life cycle of women are characterized by the interrelationship of various traditional and sex-specific cardiovascular (CV) risk factors, which combine to favor hypertensive disorders of pregnancy (HDP), where the transient and long-term kidney disease, complicate the CV health of women in later years. A history of HDP increases the risk of CKD, especially in women with comorbidities such as diabetes and high blood pressure (HBP), recognized as the main causes of chronic renal failure (CKD) worldwide.

EPIDEMIOLOGICAL ASPECTS OF CKD AND HDP IN MEXICO AND LATAM

In Mexico, it is estimated that approximately 11% of the population has CKD, equivalent to 13 million people, while in South America, the prevalence is between 7-13%. The incidence is approximately 1,142 cases/million inhabitants, and CKD mortality is about 9.14% and ranks 6th among the causes of death in Latin America.[1] In Mexico, the *Instituto Mexicano del Seguro Social* is the public institution that cares for most kidney patients. Caring for patients in substitution therapy costs approximately 25,700 million pesos (1,427.77 million USD) annually.[2]

HDP is the general term to describe various diseases characterized by hypertension and kidney damage. Includes preeclampsia, gestational hypertension, superimposed preeclampsia, and chronic HBP.[3] The clinical definition is summarized in *Table 1*. HDP continues to cause maternal and fetal mortality in low-income countries and the first world. They generate approximately 50,000 maternal deaths and 900,000 perinatal deaths and represent a predisposition for the development of CV complications in the future.[4] Worldwide, its incidence is 5-10%, the most prevalent being gestational hypertension and preeclampsia. This incidence depends on whether the event is analyzed by pregnancy or by the affected woman. In the first case, the incidence is around 7.3%; in the second, it rises to 15.3%.[5] The sub-analysis of the may measurement month (MMM) 2019 campaign in the States of Mexico and Michoacán, included 5,901 adults, of whom 77.5% were women. 14.5% of the women reported having had HDP, 16.4% continued to be hypertensive with antihypertensive treatment, and 8.3% were unaware that they were hypertensive and were detected in the campaign.[6]

LONG-TERM CARDIOVASCULAR INVOLVEMENT ASSOCIATED WITH HDP

HDP is considered a CV risk factor for the development of stroke and CV disease, particularly gestational hypertension, and preeclampsia, since they double the risk

How to cite: Palomo-Piñón S. Chronic kidney disease in women with a history of hypertensive disorders of pregnancy. Cardiovasc Metab Sci. 2024; 35 (s1): s40-s42. https://dx.doi.org/10.35366/115060

of developing cardiovascular disease in a woman, especially in those who achieve pregnancy despite living with hypertension, CKD, dyslipidemia, diabetes, and subclinical atherosclerosis. Recent studies have reported that coronary heart disease risk ratio (HR) is 1.89 (95% CI, 1.26-2.82), for stroke 2.27 (95% CI, 1.37-3.76), arrhythmias 1.62 (95% CI, 1.28-2.05), CKD 2.41(95% CI, 1.54-3.78) and for combined morbidities of 1.25 (95% CI, 1.15-1.35. The Relative Risk (RR) for a peripheral arterial disease is 1.87, and it increases considerably the more early the HDP is presented.[5] The most relevant mechanisms involved are: 1) pregnancy induces CV risk; 2) genetic predisposition before pregnancy; 3) combination of both factors. The delay in the first pregnancy is the common denominator, especially in developed countries. Maternal comorbidities such as obesity, a family history of hypertension, gestational diabetes, multiple pregnancies, and rheumatic, autoimmune, renal, or hematological diseases are other associated factors. Likewise, it has been described that African-American women with a previous history of preeclampsia or hydatidiform mole and a low socioeconomic level are particularly susceptible to presenting preeclampsia.[7,8]

The problem is of such magnitude that recently, International Societies included HDP as part of the CV risk factors for women, encouraging physicians to stratify CV risk in the immediate postpartum period and to implement the best strategy to care for the CV health of women with a history of HDP. At least during the first five years of BP, lipids, and glucose, annual monitoring is part of primary care.

LONG-TERM RENAL INVOLVEMENT IN WOMEN WITH A HISTORY OF HDP

Several studies have established that HDP impacts long-term renal function, regardless of whether the woman was already living with chronic SAH. Malek et al., in the United States of America,[9] evaluated the incidence of CKD in 391,838 women 14 years postpartum. 0.4% lived with chronic SAH, 16.3% had HDP, and 2.5% had chronic SAH and superimposed HDP, particularly preeclampsia. Fourteen years after delivery, both non-Hispanic black and white women with chronic SAH or HDP during pregnancy had a higher incidence of CKD five years after delivery (black HR 2.30 (95% CI, 1.94-2.73); whites HR 1.97 (95% CI, 1.64-2.37).

Table 1: Clinical definition of hypertensive disease of pregnancy (HDP).

	Definition
Preeclampsia (1)/ eclampsia (2)	1. SBP elevation ≥ 140 mmHg or DBP ≥ 90 mmHg after 20 weeks of gestation, accompanied by any of the following clinical data: a) proteinuria ≥ 300 mg/day or ≥ 1 g/L per test strip; b) organic dysfunction of any of the maternal organs: kidney, liver, brain and hematological system; c) fetal growth restriction 2. Presence of unexplained generalized seizures in patients with preeclampsia
Gestational hypertension	Elevated SBP ≥ 140 mmHg or DBP ≥ 90 mmHg after 20 weeks of gestation without any systemic complications
Chronic hypertension added to preeclampsia	It is the development of preeclampsia or eclampsia in a woman with pre-existing chronic SAH
Chronic hypertension	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg before pregnancy or before the 20th week of pregnancy, or when blood pressure does not return to normal within 12 weeks postpartum, associated or not with proteinuria

SAH = systemic arterial hypertension. SBP = systolic blood pressure. DBP = diastolic blood pressure. mmHg = millimeters of mercury.
Adapted from Brown MA et al.[3]

In hypertensives with superimposed HDP, black women had the highest risk: HR 3.88 (95% CI, 3.05-4.93) vs. white women HR 1.86 (95% CI, 1.20-2.87, $p < 0.003$). Clinical criteria for CKD diagnosis in these studies could be met five years after delivery.[10,11] Ishaku et al.[12] prospectively measured changes in estimated glomerular filtration rate (eGFR) at nine weeks, six months, and one year after delivery in 488 women in Nigeria, of whom 418 developed HDP. Considering an eGFR < 60 mL/min/1.73 m^2, women with HDP had a CKD prevalence of 7.6%. The older age of the woman was a statistically significant factor for the deterioration of the eGFR. Sandvik et al.'s meta-analysis of Norwegian[13] women with preeclampsia did not show any 10-year markers of renal damage (albuminuria and changes in eGFR). The eGFR remained within ranges considered normal according to the definitions of the time (average of 107 mL/min/1.73 m^2). The authors consider that the surprise of these results is due to the characteristics of the sample studied, which are unique in that region of the world.

In Mexico, the risk factors for CKD in women with a history of HDP are highly prevalent: pregnancy at extreme ages, poverty that hinders access to medical services, traditional CV risk factors that are increasing, and the non-modifiable influence of genetic factors are a call to attention.

CONCLUSIONS

HDP increases cardiovascular risk and the risk of presenting CKD in the future, particularly in women with comorbidities such as chronic hypertension. The other traditional CV risk factors, such as overweight, obesity, and diabetes, increase the probability of presenting HDP and future CV complications and CKD. This vicious circle requires specific actions ranging from identifying and monitoring renal function and metabolic profile at least during the first five years after delivery and raising awareness of the importance of modifying traditional CV risk factors throughout life.

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