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Influence of Protein Intake Source During Pregnancy and Future Risk of Hypertension

Linda May[1-4]*, Siri Pederson[1-3], Filip Jevtovic[6], Ericka M Biagioni-Barton[1-3] and Samantha M Mcdonald[6]

[1]Department of Kinesiology, ECU, Greenville, NC, USA

[2]Human Performance Lab, ECU, Greenville, NC, USA

[3]East Carolina Diabetes and Obesity Institute, ECU, Greenville, NC, USA

[4]Department of Obstetrics and Gynecology, ECU, Greenville, NC, USA

[5]Department of Translational Neuroscience, Division of Molecular Medicine, Wake Forest School of Medicine, Winston Salem, NC, USA

[6]School of Kinesiology and Recreation, Illinois State University, Normal, IL, USA

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***Corresponding author:** Linda E May, Department of Kinesiology, Obstetrics and Gynecology, East Carolina University, Greenville, NC, 27858, USA, Tel: +252-737-7072; E-mail: mayl@ecu.edu

ABSTRACT

Hypertension is a leading cardiovascular health risk for women and is closely associated with pregnancy-related blood pressure complications. While hypertensive disorders of pregnancy increase long-term cardiovascular disease risk, many women develop postpartum hypertension despite normal blood pressure during pregnancy, making pregnancy a key period for identifying future risk. Postpartum hypertension often develops silently and is thought to originate from pregnancy-related vascular and inflammatory changes. While the management of hypertension during pregnancy follows standard treatment like non-gravid patients, growing evidence emphasizes lifestyle interventions, including diet, that could have a profound effect on hypertension. Emerging evidence suggests that maternal protein intake and protein source during pregnancy may influence long-term blood pressure outcomes. Higher intake of dairy and lean animal proteins, particularly fish, appears protective, whereas higher red meat intake may increase risk. These findings highlight pregnancy as an important opportunity for nutritional strategies to support long-term maternal cardiovascular health.

Purpose: The purpose of this review is to describe the pathophysiology of postpartum hypertension and the current treatments of it, primarily focusing on the nutritional interventions with an emphasis on the impact of protein intake as observed in the current literature.

Keywords: Postpartum hypertension, Pregnancy, Animal protein, Dairy protein, Vegetable protein

Abbreviations: WHO: World Health Organization; HTN: Hypertension; BP: Blood Pressure; BMI: Body Mass Index; DASH: Dietary Approaches to Stop Hypertension; FFQ: Food Frequency Questionnaire

1. Introduction

1.1. Postpartum Hypertension Worldwide

The most common risk factor for death in women worldwide is hypertension[1]. In 2019, the World Health Organization (WHO) estimated 10.8 million deaths globally were attributed to Hypertension (HTN), with nearly 50% occurring among women[2,3]. Further, the prevalence of HTN, specifically among women of reproductive age, increased (metric) globally[4]. Importantly and unique to women, developing HTN during pregnancy significantly increases the risk of future cardiovascular disease[5,6]. Studies show that in women diagnosed with hypertensive disorders of pregnancy (HDP) the risk of developing later CVD is 1.5-2 times higher than in normotensive pregnancies (REF Oliver-William, et al BMC Med 2022). The risk of cardiovascular disease is increased in a doseresponse manner-by approximately 200% to 300% among women with more severe hypertensive disorders of pregnancy, particularly preeclampsia[5,6]. Interestingly, though, 10% to 40% of women with normotensive pregnancies exhibited HTN in the postpartum period[5,7-10]; This evidence highlights pregnancy as a "window" into a woman's future cardiovascular health[11].

1.2. What are Gestational HTN and Postpartum HTN?

Blood Pressure (BP) is defined as the pressure exerted in the arterial system. Systolic and diastolic blood pressures represent the pressure the blood exerts on the walls of the arterial vasculature during cardiac ventricular contraction and relaxation, respectively. Although BP is a non-invasive measure and easy to acquire vital signs, it is an important marker of cardiovascular health[12-14]. The American Heart Association and the American College of Cardiology classify specific BP levels into the following categories: Normal, elevated or hypertensive, with Stages 1 to Severe or a hypertensive emergency[12,13]. These agencies define HTN as: Stage 1 HTN, a systolic blood pressure between 130 mmHg to 139 mmHg or a diastolic blood pressure between 80 mmHg to 89 mmHg; Stage 2 HTN, a systolic blood pressure ≥140 mmHg or a diastolic blood pressure ≥90 mmHg[12,13].

Due to the physiological changes during pregnancy, especially of the cardiovascular system, the staging of blood pressure is slightly different. During the three trimesters of pregnancy, as well as the "fourth trimester" or 1-12 weeks postpartum, HTN is classified as systolic blood pressure ≥140 mmHg or a diastolic blood pressure of ≥90 mmHg[12,13,15,16]. Additionally, obstetric providers will stage the HTN diagnosis based on when it occurred during gestation. Therefore, HTN <20 weeks of gestation is considered chronic HTN, whereas HTN ≥20 weeks of gestation is classified as gestational HTN or preeclampsia, depending on other symptoms[17,18]. After the fourth trimester, the standard cutoffs for adult HTN apply for HTN diagnosis[12,13,15,16]. Studies note that 12% to 40% of women develop new HTN within the first 12 months after delivery, even if they had normal blood pressure during pregnancy[8-10]. However, based on the standard HTN guidelines, many women develop HTN within 1 to 15 years postpartum[5,17-21].

1.3. Connection between Postpartum Hypertension and Maternal Environment

Women endure significant cardiovascular, metabolic, hormonal and structural challenges throughout nine months, all of which are stressful. It is suggested that the nature of her pregnancy predicts her future health trajectory. Since pregnancy provides a window into a woman's future cardiovascular health, it is important to understand how the maternal environment can influence her future health[5,6,11,22]. There are many risk factors during pregnancy associated with future maternal CVD. For example, risk factors for new-onset postpartum high blood pressure include non-modifiable traits, such as genetics, race, age ≥35 years and delivery via cesarean, as well as modifiable traits such as high Body Mass Index (BMI), high lipids, current or previous cigarette smoking, physical activity levels and diet[8,23-25]. Women with at least three risk factors had an even greater risk of developing new-onset postpartum high blood pressure[8]. Importantly, governing bodies such as the American College of Obstetrics and Gynecology, the American College of Sports Medicine and the Academy of Nutrition and Dietetics support lifestyle interventions, such as exercise and diet, to improve outcomes before, during and after pregnancy[14,26-29].

Most interventions during pregnancy that focus on improving current and future maternal and child health aim at exercise and/or dietary lifestyle changes[30-40]. Although exercise during pregnancy is important, the majority of these studies demonstrate that maternal nutrition should be the primary focus and exercise secondary[30-40]. As such, many studies have focused on the influence of maternal diet and the risk of HDP[41-45]. In addition, studies have focused on how maternal diet can influence future maternal cardiovascular health[22,30-40,46]. Besides the focus on decreased sodium intake, such as the Dietary Approaches to Stop Hypertension (DASH) and Mediterranean diets, studies also focus on the influence of protein sources (i.e., animal, dairy, vegetable) during pregnancy and maternal blood pressure outcomes[25,47-50].

Therefore, research supports the connection between maternal environment and future risk of CVD. Although there are numerous non-modifiable risk factors, there are also modifiable ones that can be adjusted during pregnancy to improve maternal future health. Typically, interventions focus on either or both exercise and diet during pregnancy as an opportunity to improve maternal health during and after the pregnancy. With this in mind, the purpose of this review is to provide an overview of the pathophysiology and clinical presentation of postpartum HTN, current treatments and nutritional interventions, as well as a review of current literature on the topic of maternal protein sources during pregnancy and postpartum HTN.

2. Clinical Manifestation and Pathophysiology

2.1. Clinical Manifestation

Although HTN affects one in three adults, of which at least half are women, it usually presents with no symptoms and thus, is called the "silent killer"[12,13,51]. Almost half of the people, most of whom are women, with HTN are unaware of their condition[12,13,51]. For women in whom the symptoms are not silent, they will present with cardiovascular, cerebrovascular, renal or other system clinical manifestations. For cardiovascular manifestations, women may thus have clinically developed coronary artery disease, dilated right ventricular dysfunction, left ventricular hypertrophy and chronic heart failure, resulting in a low ejection fraction or even a myocardial infarction (heart attack)[52,53]. Other women will develop cerebrovascular conditions, but present with severe and/or frequent headaches with unknown origin or a cerebrovascular event (stroke). For those women who have renal manifestations associated with postpartum, HTN might present with decreased renal function (i.e., creatinine, BUN), which can ultimately lead to chronic kidney disease[52,53]. Other clinical manifestations of postpartum HTN are peripheral artery disease and vision changes due to retinopathy[52,53]. It is important to realize that some women will not present with symptoms associated with coronary artery disease, heart function, headaches, renal changes or visual changes, even with these changes, until years later, when it culminates in a change in their resting blood pressure[52,53].

2.2. Pathophysiology

Although underlying changes are occurring postpartum and initial postpartum hypertension may not be measured until 1 to 15 years after delivery, the initial pathophysiological changes are initiated during pregnancy. For example, women who experience HDP, such as gestational HTN, preeclampsia (HTN with proteinuria), have an increased risk of future CVD[5,7]. Furthermore, if HDP presents with other APOs, a woman's risk of future CVD increases 2-3 fold[5,7,54]. However, some women who experience postpartum HTN had normal blood pressure during pregnancy[9-11]. This is thought to be related to underlying systemic inflammation during the pregnancy that might not present with specific symptoms, such as blood pressure changes in gestation[55-57]. Sometimes, the underlying systemic inflammation will present with placental ischemia or other placental abnormalities.

Whether symptoms occur in pregnancy or not, the etiology is thought to be elevated levels of circulating inflammatory markers, such as sFlt-1[55-57]. Since sFlt-1 is anti-angiogenic, for instance, elevated levels could lead to placental ischemia. Thus, even after the baby and placenta are delivered, there is still underlying systemic inflammation (i.e., cytokines), which leads to endothelial damage of smaller vessels of the eye, brain, cardiac muscle and kidneys, which will then continue to worsen across the years until another physiological insult occurs. Often, a woman will have another hormone shift from another pregnancy or perimenopause, which further exacerbates the system and presents as her first high blood pressure.

3. Current Treatments and Nutrition Interventions

3.1. Current Treatments

Standard treatments for postpartum HTN will be the same for any HTN and include regular blood pressure monitoring[16,17,56]. Pharmacological treatments are usually ACE Inhibitors (i.e., enalapril), beta-blockers (i.e., labetalol), calcium channel blockers (i.e., nifedipine, amlodipine) and potentially diuretics (i.e., furosemide)[14,51-53]. If these first-line medications do not work, then a central alpha-2 adrenergic agonist (i.e., methyldopa, clonidine) with diuretics (i.e., hydrochlorothiazide) may be initiated. In addition, medical nutrition therapy provided by a dietitian is often recommended for long-term management of HTN[12,13,51].

3.2. Nutritional interventions

For nutrition interventions, the Academy of Nutrition and Dietetics recommends adopting the DASH diet, Mediterranean diet or something similar[58]. The standard recommendations of the DASH diet always begin with decreasing sodium intake to <1500 mg each day[58-60]. There is a plethora of evidence-based nutrition practice guidelines for MNT in individuals with HTN. The overall nutritional recommendations for those with postpartum HTN will focus on a balanced diet. For example, women should be educated on the appropriate quantity and quality of protein sources from animal, vegetable and dairy sources for each day and each meal. Next, she will also be counseled on how many vegetables and fruits to consume each day and with each meal. They will also be taught about sources and amounts of carbohydrates throughout the day. Lastly, they need to know about unsaturated *vs.* saturated fats to consume each day and focus on mono- and polyunsaturated fats.

4. Review of Literature

Knowing that pregnancy is associated with increased systemic inflammation, we know that pregnancy is a physiological stress test and is considered a window into a woman's future cardiovascular health. Thus, it is important to focus on pregnancy as a critical time to positively influence a woman's current and future cardiovascular health. Importantly, modifiable factors such as diet during pregnancy are influential on cardiovascular health as well. In addition to limiting sodium intake, protein intake and specifically protein sources are important for her cardiovascular health as well.

In general, the Academy of Nutrition and Dietetics categorizes proteins as either animal, vegetable/plant or dairy sources[61-63]. Within each of these categories, there are different food components. For instance, dairy proteins can come from sources such as yogurt, milk, cheese and cottage cheese[61-63]. Vegetable/plant proteins can be sub-categorized as either legume (i.e., beans, split peas, lentils, soy) or nuts and seeds (i.e., walnuts, almonds, chia seeds, pumpkin seeds, pistachios, cashews and peanuts)[61-63]. Lastly, animal protein is subcategorized as either from seafood/fish components (i.e., salmon, tuna, cod, shrimp, mackerel, lobster, catfish) or meat/poultry/eggs (i.e., lean cuts of beef, lamb, goat, pork loin, skinless chicken and turkey, quail and duck) [61-63]. Importantly, there are differences in protein digestibility and amino acid profiles between these protein sources.

To date, there are only four studies that have examined the potential influence of the source of proteins during pregnancy on the occurrence of future postpartum hypertension. The Norwegian MoBa study assessed pregnant women's diet around 22 weeks of gestation via a Food Frequency Questionnaire

(FFQ)[47]. The FFQ assessed proteins as either from plants, dairy, eggs, seafood or other animal meats. They then assessed their recorded blood pressures about 10 years postpartum, as well as whether they were taking hypertensive medications and for how long. They assessed a total of 59,967 pregnant women; of these women, 1,480 had developed HTN requiring medications by 10 years postpartum, finding that animal protein, specifically red meat, during pregnancy had a positive association with developing HTN by 10 years postpartum. They also found that consumption of protein from fatty fish, such as salmon, during pregnancy had a negative association with developing HTN by 10 years postpartum. Similarly, maternal consumption of dairy protein, specifically milk and yogurt, during pregnancy had a negative association with developing HTN by 10 years postpartum. Interestingly, they found no association between plant protein intake during pregnancy and the occurrence of postpartum HTN[47]. However, the leanness of the protein was not considered in the analysis.

Secondly, another analysis within the MoBa study by Egeland et al. assessed women *via* a FFQ at about 22 weeks of gestation[48]. The FFQ assessed proteins as either from plants, dairy (and supplements of calcium and magnesium), eggs, seafood and other animal meats, as well as the low and high-sodium/potassium foods. They then assessed women's EHRs for their blood pressure at 10 years postpartum, as well as whether they were taking hypertensive medications and for how long. They assessed a total of 56,646 pregnant women; of these women, 1,039 had developed HTN requiring medications by 10 years postpartum. Egeland et al. found that postpartum HTN is associated with low calcium intake and foods with high sodium/potassium foods[48].

The third related study was conducted in Denmark using a large cohort study methodology again. Women were assessed via a FFQ at about 25 weeks of gestation[49]. The FFQ assessed proteins as either from fish-poultry vegetarians (vegetarians who consume dairy products and eggs), Lacto/Ovo-veg, Vegans or Omnivores. They also assessed women's EHRs for their blood pressure about 10 years postpartum, as well as whether they were taking hypertensive medications and for how long. They assessed a total of 65,872 pregnant women, finding outcomes like those of Oyen et al. They noted omnivores were less likely to have developed postpartum HTN than vegans[49]. This study suggests that the amount of protein matters, especially when combined with micronutrient deficiencies.

Lastly, a smaller study by May et al.[50], which is a randomized controlled trial focused on supervised exercise during pregnancy, assessed women via the ASA24 online 24-hr dietary recall at about 16 weeks of gestation. The dietary recall assessed dietary protein intake from plants, dairy, eggs, seafood and meats, as well as micronutrient intake levels. They also assessed the subject's recorded blood pressure postpartum. They assessed a total of 65 pregnant women. May et al. also found outcomes like Oyen et al. They noted protein source, as well as sodium and saturated fat levels, predicted maternal blood pressure[64].

5. Conclusion

Overall, these studies demonstrate that the protein source during pregnancy is related to the pregnant woman's future cardiovascular health. Thus, pregnant women may need to focus on dairy and lean animal protein. Importantly, women should ensure they have appropriate levels of sodium and saturated fat according to recommended levels. As other studies demonstrate, improving maternal health will improve future cardiovascular health. Research suggests that appropriate levels of dairy and lean animal proteins during pregnancy can be helpful for her future cardiovascular health.

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