ANALYZING THE RELATIONSHIP BETWEEN NON-PHARMACOLOGIC INTERVENTIONS AND PREGNANCY-INDUCED HYPERTENSION: AN INTEGRATIVE REVIEW

A Scholarly Project

Submitted to the

Faculty of Liberty University

In partial fulfillment of

The requirements for the degree

Of Doctor of Nursing Practice

By

Karen Ann Ellis

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Lynchburg, VA

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Scholarly Project Chair Approval:

Vickie Moore, RN, DNP, FNP-C Date

ABSTRACT

Maternal and fetal health outcomes are threatened due to pregnancy-induced hypertension, which complicates nearly 6%–10% of pregnancies worldwide. This disease carries a high risk of maternal and fetal morbidity and mortality. Medications are commonly used to reduce blood pressure and physical consequences related to high blood pressure. However, the use of medications does not resolve the disease as there is no pharmacological cure. Current evidence demonstrates the detrimental long-term effects of pregnancy-induced hypertension and the increased risk of future cardiac disease. Close surveillance and effective treatment during pregnancy is needed to prevent serious complications. The aim of this integrative review is to analyze the relationship between non-pharmacologic interventions and the evidence that supports their use in the treatment of pregnancy-induced hypertension. Recommendations for patient education and monitoring during pregnancy were devised as a result of this review. An analysis of the literature found an inverse relationship between non-pharmacologic interventions and pregnancy-induced hypertension. The review lays the foundation for the acknowledgment and integration of the identified common themes to better inform research, support a comprehensive understanding, and produce suggestions for practice to decrease the prevalence of pregnancy-induced hypertension.

Keywords: pregnancy-induced hypertension, non-pharmacologic, hypertension in pregnancy, complementary therapies, alternative therapies, treatment or intervention or therapy or management

Dedication

I would like to dedicate this integrative review to my former Women's Health colleagues and all of the mothers that I cared for during their pregnancy and postpartum period. My treasured time with this population of patients as a nurse practitioner inspired the topic for my scholarly project. It is my desire that this project provide meaningful evidence for my colleagues to incorporate into practice as well as stimulate further research to continually improve upon maternal and fetal outcomes as well as the postpartum recovery period.

Acknowledgments

First, I would like to acknowledge my sincerest gratitude to my scholarly project chair, Dr. Vickie Moore. She provided continuous support during my DNP journey with her endless encouragement, patience, understanding, guidance, and support. I will forever be grateful for her mentorship and wisdom throughout the development of this integrative review. I am also grateful for Dr. Tonia Kennedy, who provided practicum support and most importantly continued to check in on my physical and mental well-being by providing me with ongoing encouragement, support, and prayers. What an inspiration both of these ladies have been to me professionally, but also as sisters in Christ, exemplifying such a selfless, servant attitude.

My sincere appreciation also goes to my family and my husband, Shay, for the countless hours that he cleaned, grocery shopped, did laundry, and kept the house in order when I didn't have the time. My children, Madison and Austin, also endured this time of tedious paper-writing, late nights, and weekends doing homework all while providing me so much joy, laughter, and continued support. Thanks also to my Mom and Dad, who truly are my biggest fans and who were always available for emotional support and encouragement, often at a moment's notice.

This journey was never walked alone. Christ was and is my continued provider and strength. With Him all things are possible.

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List of Abbreviations

Chronic hypertension (CHTN)

Diastolic blood pressure (DBP)

Dietary approaches to stop hypertension (DASH)

Gestational hypertension (GHTN)

Hypertension (HTN)

Institutional Review Board (IRB)

Pregnancy-induced hypertension (PIH)

Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA)

Systolic blood pressure (SBP)

SECTION ONE: INTRODUCTION

Hypertensive disorders of pregnancy complicate nearly 10% of pregnancies worldwide and are one of the leading causes of increased maternal and perinatal morbidity and mortality (Antza et al., 2018). These hypertensive disorders include preexisting or chronic hypertension (CHTN), gestational hypertension (GHTN), and preeclampsia. Although different variations of hypertensive disorders exist in pregnancy, preeclampsia affects approximately 4% of pregnancies within the United States and is the second-leading cause of maternal mortality worldwide (Bibbins-Domingo et al., 2017).

CHTN antecedes pregnancy or is documented on two occasions prior to the 20th week of gestation. Pregnancy-induced hypertension (PIH) is defined as hypertension (HTN) that begins after the 20th week of pregnancy and is measured in intervals with systolic blood pressure (SBP) > 140 mmHg and diastolic blood pressure (DBP) > 90 mmHg without any evidence of proteinuria or other systemic findings. PIH can be classified as either mild (SBP 140–149 and DBP 90–99 mmHg), moderate (SBP 150–159 and DBP 100–109 mmHg), or severe (SBP > 160 and DBP > 110 mmHg; Kintiraki et al., 2015; Song et al., 2018). Approximately 10%–25% of individuals with GHTN proceed to develop signs and symptoms of preeclampsia (August & Sibai, 2022). Preeclampsia, which has serious and even fatal outcomes, can be defined as new-onset or worsening (in those with pre-existing HTN) HTN that occurs after the 20th week of pregnancy. It is accompanied by proteinuria or other signs and symptoms of multiple organ system involvement (U.S. Preventative Services Task Force, 2018).

Maternal complications pose a serious threat and can include eclampsia, stroke, organ failure, and increased risk for long-term cardiovascular disease. Other adverse outcomes affecting both mothers and their infants include placental abruption, preterm delivery,

intrauterine growth restriction, small for gestational age, and stillbirth (U.S. Preventative Services Task Force, 2018).

Research shows that treatment of hypertensive disorders of pregnancy can reduce maternal and perinatal morbidity and mortality, as 60% of preeclampsia deaths are preventable (Preeclampsia Foundation, 2020). Best practices for managing these hypertensive disorders and the causes of preeclampsia remain unclear. Due to preeclampsia's ability to evolve quickly, severity of disease, and potential for fatal maternal and fetal outcomes, early identification and treatment is imperative in this population.

The purpose of this review is to examine the effectiveness of non-pharmacologic interventions on hypertensive disorders of pregnancy with the aim of determining which interventions improve maternal and perinatal health outcomes.

Defining Concepts and Variables

The central concept of this integrative review is the relationship between the utilization of non-pharmacologic interventions for PIH and maternal and fetal health outcomes. For this review, non-pharmacologic interventions include exercise/physical activity, nutrition/dietary patterns, mind-body interventions, calcium supplementation, vitamin D supplementation, and folic acid supplementation. To understand the relationship between maternal and fetal health outcomes and non-pharmacologic interventions of PIH, a variety of variables for non-pharmacologic interventions were examined.

Rationale for Conducting the Review

During employment within a women's health practice, this writer identified a trend of increasing numbers of pregnant women with PIH, with the incidence of preeclampsia development significantly increasing as well. Complications from PIH are a major health

concern among the obstetrics population and are one of the leading causes of maternal and perinatal morbidity and mortality. It is estimated that every seven seconds, at least one woman dies due to complications arising from PIH (Gudeta & Regassa, 2019). Women not only face immediate pregnancy risks with PIH but also long-term associated risks. Following recovery, women are at a higher risk of developing HTN, stroke, renal disease, heart failure, and Alzheimer's. Maternal offspring are at an increased risk of cardiovascular diseases, and female offspring more likely to develop preeclampsia, complicating their own pregnancies (Tsigas, 2021). Both mother and fetus are at an increased risk of adverse outcomes. These increased adverse outcomes lead to increased health care costs and economic burdens associated with low birth weight, prematurity, and longer hospital stays (Tsigas, 2021).

After witnessing the increasing prevalence of hypertensive disorders of pregnancy and the complications occurring as a result, this writer was motivated to perform further research on the topic. The initial diagnosis of CHTN or GHTN does not always indicate the need for medication initiation. However, these diagnoses are considered high-level risk factors for developing preeclampsia and place the mother at an increased risk for adverse maternal or fetal outcomes, warranting closer monitoring throughout pregnancy (Bello et al., 2021). With appropriate identification of these women and initiation of non-pharmacologic interventions (with or without antihypertensive therapy), further adverse events may be prevented, pregnancies prolonged, and outcomes improved for both mother and infant.

Identify Purpose and/or Review Question(s)

The purpose of this review is to focus on the topic of PIH and evaluate the effects of non-pharmacologic interventions as the primary treatment, or as a complementary therapy. This research supports optimal maternal and fetal outcomes of pregnancy and fewer adverse effects

from PIH. This integrative review addresses the following question: What is the impact of non-pharmacologic interventions during pregnancy on pregnancy-induced hypertension? Is there evidence to support use of these interventions in practice?

Formulate Inclusion and Exclusion Criteria

The following inclusion criteria were used for articles in this integrative review: full articles, published within the last five years, written in English, published in peer-reviewed journals, and addressed hypertensive disorders of pregnancy and non-pharmacologic interventions. The following exclusion criteria were used: doctoral theses and studies published more than five years ago. There was no restriction on study design. However, articles with a higher level of evidence were prioritized over studies with lower-level evidence.

Conceptual Framework (Whittemore and Knafl)

Integrative reviews are considered research of research and should be conducted with the same standards of methodological rigor. A detailed framework must be in place when performing an integrative review, as the use of a methodological strategy enhances the rigor of the process (Whittemore & Knafl, 2005). The framework for this project was initially defined by Harris M. Cooper in 1998 and was further modified to address issues specific to an integrative review and documented by Whittemore and Knafl (2005). This integrative review provides a synthesis of empirical and theoretical literature to support the topic of interest. Specifically, this scholarly project identifies non-pharmacologic interventions used in patients with PIH. A five-stage research synthesis process was used to help support this review and raise awareness of the topic at hand. These five stages outlined by Whittemore and Knafl (2005) are as follows: (a) problem identification, (b) literature search, (c) data evaluation, (d) data analysis, and (e) presentation of results.

SECTION TWO: COMPREHENSIVE AND SYSTEMATIC SEARCH

Search Strategy

Search strategies must be clearly defined and are imperative to the review process to generate enhanced rigor and the greatest number of unbiased results (Whittemore & Knafl, 2005). Obtaining all the relevant literature pertaining to the topic of interest for inclusion in the review is ideal but often challenging (Whittemore & Knafl, 2005). Using two to three strategies at minimum is the goal to conduct a comprehensive search of the literature and produce the greatest number of qualified sources.

Librarian support from the Jerry Falwell Library was utilized in the search process and to provide guidance as research-related questions arose. Toronto and Remington (2020) suggested that librarians play a valuable role in the integrative review process due to their experience building searches, identifying documentation tools, and organizing results to help support a more comprehensive, thorough, and unbiased search process. Rigor is supported with utilization of a librarian, especially when a reviewer would otherwise be performing the review alone (Toronto & Remington, 2020).

Establishing systematic process for the collection of data that is reliable and valid is foundational to conducting a quality integrative review (Murphy et al., 2018). A systematic review of the literature utilizing a computer-assisted search of various databases to include MEDLINE Plus with Full Text, Health Source: Nursing/Academic Edition, Cumulative Index of Nursing and Allied Health Literature Plus with Full Text, and Cochrane Library was initiated. Articles published between 2016 and 2022 were included in this review. With substantial amounts of data returned, results were narrowed further to focus on relevant key words, most recent publications, and studies of higher quality/levels of evidence according to Melnyk's levels

of evidence. Articles were saved in an organized manner and then screened by the title, abstract, purpose, and conclusion to further narrow the review's focus and determine inclusion for final review.

Keywords and natural language search terms were used and combined with the Boolean operators *AND* and *OR* to expand the search. The largest number of results are usually obtained through keyword searches; however, these results may not be the highest in relevance (Toronto & Remington, 2020). Keywords and phrases were utilized in different combinations in the search and included: pregnancy-induced hypertension, non-pharmacologic, hypertension in pregnancy, complementary therapies, alternative therapies, treatment or intervention or therapy or management. Alternate terms used were as follows: preeclampsia or toxemia and gestational hypertension. The parameters included full-text articles, peer-reviewed studies, articles published in English, and studies published within the past five years. The initial search yielded over 4,500 articles.

Quality Appraisal

Analysis of the quality of selected research is a critical component of an integrative review (Toronto & Remington, 2020). The literature selected should be relevant to the review question to continually guide each decision along the way and determine inclusion or exclusion based on quality (Toronto & Remington, 2020). Relevance of the literature helps to avoid digression during the review process. The Melnyk levels of evidence rating system was utilized as the quality appraisal tool for the integrative review. Sources were designated as Level 1 through Level 7 as appropriate based on the rating system for the hierarchy of evidence (Melnyk & Fineout-Overholt, 2019).

PRISMA

The aim of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) is to provide authors support with the reporting of data from systematic reviews, other research, and evaluations of interventions in an effort toward further assessment and appraisal. The 27-item checklist and four-phase flow diagram were used to facilitate the reporting of information. The flowchart visually summarizes the number of identified records in the review: included articles and excluded studies and their reasons for exclusion. This tool assures rigor and proper reporting of the findings. It also serves to reduce bias that might exist from too narrow of a focus during the literature search. The 27-item checklist further supported the documentation of essential reportable items in the review (Liberati et al., 2009).

Synthesis of the Literature

Toronto and Remington (2020) note that synthesizing the literature can be a challenging process during the integrative review. The primary goal of this review was to better understand the impact of non-pharmacologic interventions during pregnancy on PIH through synthesis of diverse sources.

The initial literature search identified over 4,500 references. Duplicates were removed from the review. Following the removal of duplicates, the titles and abstracts of the remaining articles were reviewed. Common themes were identified and included exercise/physical activity, vitamin D/calcium/iron/folic acid supplementation, DASH diet, mind-body therapies, and guided imagery. Additional articles were then excluded that did not meet the established criteria. Further eligibility assessment resulted in additional studies being eliminated based on the exclusion criteria. This left 24 studies for critical review. According to Melnyk's levels of evidence, there

were eight Level 1 articles, four Level 2 articles, one article as a Level 3, 10 Level 4 articles, and one Level 5 article in this review. The critical review of studies is available in Appendix A.

Summary

This literature review's purpose was to confirm the need for an integrative review to determine the impact of non-pharmacologic interventions on PIH. Through a synthesis of published articles that identify interventions having an effect on PIH, the project leader was able to ascertain evidence-based recommendations for non-pharmacologic interventions as well as determine indicators for further research on this topic. A literature matrix was utilized to systematically review the articles included in this scholarly project and outlines methods, study results, level of evidence, limitations, and implications for practice.

The literature review revealed a significant amount of evidence showing a positive relationship between physical activity, vitamin D/calcium/folic acid supplementation, and mind-body interventions on PIH and pregnancy outcomes. Although the evidence surrounding these various themes provides some good foundational information and beneficial evidence, there are gaps remaining that indicate the need for further research.

SECTION THREE: RESULTS

This integrative review included 24 research articles. The characteristics of the studies were homogenous regarding type of research but varied by design. The designs of the studies were as follows: eight systematic reviews and meta-analyses of randomized controlled trials (Bulloch et al., 2018; Du et al., 2018; Haruna et al., 2019; He et al., 2016; Hofmeyr et al., 2018; Hua et al., 2016; Magro-Malosso et al., 2017; Smith et al., 2020), four randomized controlled trials (Ali et al., 2019; Behjat Sasan et al., 2017; da Silva et al., 2017; Sun & Niu, 2020); one controlled trial (Puspitasari et al., 2022); 10 case-control or cohort studies (Benachi et al., 2020;

Cao et al., 2020; Chen et al., 2020; Fulay et al., 2018; Gebreyohannes et al., 2021; Jirakittidul et al., 2018; Kyozuka et al., 2020; Raguema et al., 2020; Spracklen et al., 2016; Yue et al., 2021); and one systematic review of descriptive and qualitative studies (Pourheidari et al., 2019). Three of these studies were published in 2016, 11 between 2017 and 2019, and 10 in the last three years, = 2020–2022. Results are discussed further in a descriptive manner.

Thematic Data Analysis

The relationship between non-pharmacologic interventions and PIH was analyzed in this integrative review. The review of the literature identified seven common recurring themes: physical activity and exercise, vitamin D supplementation, calcium supplementation, folic acid supplementation, iron supplementation, dietary changes, and guided imagery/mind-body interventions. The following subsections address the evidence-based findings and further discuss each theme with the support of the 24 research articles included in the review.

Physical Activity and Exercise

Five of the 24 articles studied looked at increased physical activity or exercise and its effect during pregnancy on the risk of gestational hypertensive disorders and maternal and fetal outcomes (da Silva et al., 2017; Du et al., 2018; Magro-Malosso et al., 2017; Raguema et al., 2020; Spracklen et al., 2016). Three of the five articles focused on the association of physical activity in pregnancy with gestational hypertensive disorders as a primary outcome. The studies of Raguema et al. (2020), Magro-Malosso et al. (2017), and Spracklen et al. (2016) all showed a very positive correlation between physical activity during pregnancy and reduced risk of gestational hypertensive disorders as well as overall healthier pregnancies, while sedentary lifestyles were found to be associated with an increased risk of hypertensive disorders and preeclampsia in pregnancy.

The last two articles that related to this theme focused more specifically on the effects of physical exercise during pregnancy on maternal and fetal outcomes (da Silva et al., 2017; Du et al., 2018). The findings of Du et al. (2018) showed that physical exercise interventions during pregnancy reduced gestational weight gain and the risk of gestational diabetes in pregnant women who were obese or overweight, therefore reinforcing the benefits of maternal exercise during pregnancy. On the contrary, the findings from a randomized controlled trial by da Silva et al. (2017) lacked evidence to support the benefits of exercise performed during pregnancy on preeclampsia, infant birth weight, gestational diabetes, and weight gain. Of note , this study also lacked statistical power and displayed very low compliance.

Vitamin D Supplementation

Vitamin D is thought to be involved in the pathogenesis of preeclampsia. There are known associated anti-inflammatory properties of vitamin D as well as evidence of an inverse relationship between dietary calcium intake and the incidence of preeclampsia.

Benachi et al. (2020) measured serum vitamin D levels, 25(OH)D, in pregnancy to evaluate the relationship of vitamin D insufficiency with preeclampsia. Women with vitamin D sufficiency in the first trimester of pregnancy had a decreased risk of preeclampsia, although statistical significance was not achieved. Conversely, the 25(OH)D levels of women who developed preeclampsia were found to be lower in the first trimester of pregnancy. Within the study, a cohort of women in France received a bolus vitamin D dose of 100,000 IU of cholecalciferol administered at 28 weeks of pregnancy (Benachi et al., 2020). The percentage of women who received vitamin D supplementation did not differ between cases and controls. Regardless of supplementation and treatment groups, women with 25(OH)D greater than or equal to 30ng/mL in both early and late pregnancy developed preeclampsia less frequently

(Benachi et al., 2020). This association of maternal 25(OH)D levels and preeclampsia reveals that patients with vitamin D sufficiency (greater than or equal to 30ng/mL) in the first and third trimesters have a significantly lower risk of developing preeclampsia (Benachi et al., 2020). Vitamin D deficiency overall appears to be a risk factor for preeclampsia. However, the available studies do not support supplementation as an effective treatment for prevention of this risk (Benachi et al., 2020).

A further study included by Yue et al. (2021) confirmed the findings of Benachi et al. (2020) that vitamin D deficiency before 20 weeks' gestation is a risk factor for preeclampsia. The study of Yue et al. (2021) outlines preventative and maintenance measures to avoid deficiency for pregnant or lactating women. They recommended supplementation of 1,000–2,000 IU of vitamin D3 per day, 50,000 IU of vitamin D2 every two weeks. Up to 4,000 IU of vitamin D3 per day is safe for five months with a maintenance dose of 50,000 IU of vitamin D2 every two to four weeks. However, the evidence remains insufficient to support definite clinical recommendations. This study primarily compared serum vitamin D levels rather than supplementation with vitamin D. Findings concluded that serum vitamin D is a protective factor against preeclampsia and that vitamin D deficiency before 20 weeks' gestation is a risk factor for preeclampsia (Yue et al., 2021).

Calcium Supplementation

Kyozuka et al. (2020) suggested that dietary factors play a role in the development of hypertensive disorders of pregnancy. Evidence has shown that calcium supplementation reduces the risk of PIH and therefore has the potential to prevent preeclampsia (Kyozuka et al., 2020). The World Health Organization used this evidence as the basis for its recommendation of 1,500-2,000 mg daily for routine prenatal calcium supplementation beginning at the 20th week of

pregnancy, especially for those living in low calcium intake areas (Kyozuka et al., 2020). Despite these calcium intake recommendations, the findings of Kyozuka et al. (2020) showed that pre-pregnancy calcium intake was not associated with an increased risk of the development of hypertensive disorders in pregnancy.

Gebreyohannes et al. (2021) also studied the association of dietary calcium intake and total serum calcium levels with preeclampsia. Contrary to the findings of Kyozuka et al. (2020), the case control study of Gebreyohannes et al. (2021) found that pregnant women with a low serum-ionized calcium level had an almost eight times greater risk of developing preeclampsia and those with a low total serum calcium were at three times higher risk. Overall, this study found a significant association between low serum calcium levels and low dietary calcium intake with preeclampsia (Gebreyohannes et al., 2021).

One meta-analysis included in the review also looked at the relationship of PIH with serum calcium levels but in conjunction with serum zinc and magnesium (He et al., 2016). Although the findings were not as statistically significant as the findings of Gebreyohannes et al. (2021), this study also suggested that decreased serum calcium, zinc, and magnesium levels were associated with PIH.

Folic Acid Supplementation

Researchers Bulloch et al. (2018) and Hua et al. (2016) studied the relationship between folic acid supplementation and PIH/preeclampsia. Due to the lack of study control and primarily observational design, it was unclear in Hua et al.'s (2016) study whether the supplementation of folic acid during pregnancy can prevent the occurrence of PIH and preeclampsia. Low levels of evidence were present in the Bulloch et al. (2018) study; however, a modest association was found between folic acid supplementation during pregnancy and a reduced risk of preeclampsia.

Iron Supplementation

A retrospective cohort study was performed including 400 non-anemic pregnant women who were divided into two iron supplementation groups (Jirakittidul et al., 2018). The study group started iron supplementation prior to 16 weeks' gestation, while the control group initiated supplementation at 16 weeks or later. Jirakittidul et al. (2018) found that participants had a significantly higher risk of developing PIH after 20 weeks' gestation when iron supplementation was given before 16 weeks' gestation. Early iron supplementation in pregnancy was associated with a twofold higher risk of new onset HTN during pregnancy and a threefold higher risk of preeclampsia compared with later iron supplementation (Jirakittidul et al., 2018). Previous studies have had similar findings showing that prophylactic iron supplementation in healthy pregnancies was associated with PIH. There was also a significantly higher incidence of hypertensive disorders in pregnant women with a hemoglobin > 13.2 g/dL at early second trimester in those taking iron supplements when compared to those taking a placebo (Jirakittidul et al., 2018). This study raises concerns about the potential adverse effects of iron supplementation in non-anemic patients during pregnancy.

Dietary Changes

Recent studies have shown that the Dietary Approaches to Stop Hypertension (DASH) diet, among non-pregnant populations, has shown improvements in cardiometabolic outcomes, including reduced blood pressure. It is a diet of lots of vegetables, fruits, lean proteins, whole grains, and moderate unsaturated fats and low in red meats, sugars, saturated and trans fats, and sodium (Cao et al., 2020; Fulay et al., 2018). Research suggests that maternal diet plays an important role and can potentially affect the development and incidence of preeclampsia (Cao et al., 2020).

Both Cao et al. (2020) and Fulay et al. (2018) studied the relationship between adherence to the DASH diet and pregnancy complications and PIH. These studies were difficult to compare, as Cao et al. (2020) looked at dietary patterns in pregnant women only in the last three months of pregnancy, while Fulay et al. (2018) studied diet adherence in early pregnancy. With Cao et al.'s consideration for dietary intake only during the last three months of pregnancy, there is failure to account for the potential influence of early pregnancy diet on the development of preeclampsia. Fulay et al. (2018) did not find adherence to a DASH diet early in pregnancy to be protective against PIH. However, in obese pregnant women, this study found a positive association between diet scores and gestational weight gain. Conversely, the research findings of Cao et al. (2020) suggested an inverse relationship between DASH diet adherence later in pregnancy and the odds of preeclampsia.

Another dietary strategy for lowering the risk of PIH found in the literature was a mushroom diet. Evidence has previously shown the effectiveness of mushrooms in improving human health. In a randomized clinical trial, subjects were required to consume a certain number of white button mushrooms daily from pre-pregnancy through the 20th week of gestation to explore the impact of mushrooms on PIH (Sun & Niu, 2020). The mushroom diet group, when compared to the placebo group, had a significantly lower incidence of PIH, and the diet was also shown to have a positive impact on gestational weight gain and gestational diabetes. Sun and Niu (2020) concluded that a mushroom diet could be used preventatively to reduce the risk of PIH and other comorbidities such as excessive gestational weight gain and diabetes.

Mind-Body Interventions

Mind-body interventions were reviewed and discussed in four of the studies (Haruna et al., 2019; Pourheidari et al., 2019; Puspitasari et al., 2022; Smith et al., 2020). These studies

looked at the safety and effectiveness of mind-body interventions, such as guided imagery, breathing exercises, and progressive muscle relaxation in women with PIH and or preeclampsia. The available evidence on this topic was sparse, and the quality of the evidence from most of these trials was low.

Two included studies on relaxation found a reduction in SBP and DBP and reduced stress. Some evidence from a single trial on yoga showed a reduction of the risk of PIH and again a reduction in stress. Despite these positive findings, overall, there was no evaluation on the effect on the use of anti-hypertensives, preeclampsia development, or neonatal outcomes (Smith et al., 2020).

Synergistic effects of guided imagery and progressive muscle relaxation were investigated by Puspitasari et al. (2022) to evaluate their effect on clinical symptoms in patients with preeclampsia. Both groups in the study received normal conservative management of preeclampsia. In addition to the normal preeclampsia management, one study group also underwent guided imagery and progressive muscle therapy treatments. Following treatment, the study group receiving the additional therapies showed a significant reduction in their SBP and DBP, as well as in their proteinuria (Puspitasari et al., 2022). This statistically significant difference between groups was seen in all three of these measures after seven days.

Synthesis of Results

Non-pharmacologic interventions during pregnancy could serve as a preventative strategy for lowering the risk of PIH and result in improved maternal and fetal outcomes. The review of literature showed varying levels of association between different maternal supplements and their protective effect on PIH. The most common themes within recent evidence regarding non-

pharmacologic interventions and the development of PIH have been reviewed, with suggestions for clinical practice as well as the need for future research identified.

Researchers have identified that vitamin D supplementation may be useful in preventing PIH but seems to be largely dependent on the timing of supplementation. Results of the studies reviewed showed that serum vitamin D deficiency, specifically prior to 20 weeks' gestation, was an independent risk factor for PIH. The benefits of vitamin D supplementation seems to be much higher during early pregnancy in the prevention of preeclampsia. Health care providers are recommended to monitor vitamin D levels due to the identified clinical significance in reducing PIH and goal of improving pregnancy outcomes. Vitamin D sufficiency in pregnancy is thought to lower the risk of preeclampsia. Similarly, adequate vitamin D levels are thought to prevent endothelial dysfunction, maintain vascular health, and help with maintaining calcium homeostasis, which has an inverse relationship to blood pressure levels.

The review of literature revealed a lack of clarity as to whether folic acid supplementation can prevent the occurrence of PIH, although it is thought to have a protective effect. Conversely, other supplementations, such as iron in early pregnancy, was associated with an increased risk of PIH when taken in non-anemic pregnancies. In addition, a significant association was seen between low calcium levels and preeclampsia. Many factors seem to contribute to PIH. Despite some lower levels of evidence and conflicting data, the research overall reveals that deficiencies in trace elements during pregnancy are thought to play a vital role in the development of PIH.

Research has shown physical activity and exercise during pregnancy has significant maternal and fetal health benefits. Evidence conveys that there is a lower risk of PIH with higher levels of physical activity during pregnancy as well as an increased risk of PIH with increased

sedentary lifestyles. Therefore, pregnant women should be encouraged to continue their level of physical activity or encouraged to begin regular physical activity for those sedentary to prevent the development of PIH.

Evidence from this review has shown the positive effects in pregnancy of self-care, healthy diet, physical activity, and dietary supplements for the prevention and control of PIH. Therefore, understanding and identifying these clinical and laboratory predictors of PIH, as well as safe and effective ways to prevent its development, is essential.

Ethical Considerations

The protection of human subjects is critical when conducting research. As an integrative review, this study was not classified as human subject research and did not involve the collection of identifiable, private information from or about living individuals.

The DNP project team, both the chair and student, completed the Collaborative Institutional Training Initiative modules on biomedical and health science research (see Appendix B). This research ethics training was completed to ensure protection of human subjects. This project was submitted to and approved by the Liberty University Institutional Review Board (IRB). Approval was received by student/leader on March 26, 2022. A copy of the IRB approval letter is provided in Appendix C.

Timeline

The following is the timeline for this project. This proposal was developed and defended March 2022. Once the project was defended and approved by the chair, an application for IRB approval through Liberty University was sought and received by the end of March 2022. During the implementation phase, the project leader completed a data analysis and synthesis of results in April 2022. Interpretation of the review findings and their overall significance and development

of the discussion and conclusions around the topic of interest were completed by the end of April 2022. The project leader then formulated a rough draft of the review and submitted to an editor for proofing before finalizing and submitting to chair in June 2022. Final revisions will be made and project submitted to chair for final approval. Once final project approval has been received by chair, the project leader will defend the scholarly project before the board. Final project defense before the board will occur in July 2022.

SECTION FOUR: DISCUSSION

Summary of Evidence

Research revealed a definite relationship between non-pharmacologic interventions and the prevention and treatment of PIH. This integrative review was intended to identify studies that specifically addressed non-pharmacologic interventions and their impact on PIH in support of optimal maternal and fetal outcomes. However, the majority of the 24 articles placed an emphasis on monitoring serum vitamin and trace element levels and the association of those levels with PIH. Deficiencies in trace elements are thought to be a vital risk factor for the development of PIH. Several of the studies looked at adherence to dietary measures and increased physical activity during pregnancy and revealed a mushroom diet and increased physical activity are preventative for and reduce the risk of PIH development. Despite the root cause of hypertensive disorders in pregnancy, many studies suggest that preeclampsia-related pathophysiological change starts in the early stages of gestation, whereas maternal symptoms do not manifest until later in pregnancy. Furthermore, there is a defined opportunity that exists to acknowledge and integrate the identified common themes to better inform research and support a comprehensive understanding of the phenomenon of interest.

The studies reviewed provided more insight to themes of interest. The concept being studied has received greater interest in recent years. This uptick of interest exposes the need for further research and action to support the care continuum at large. Although acknowledgment of the benefits of non-pharmacologic interventions is present in the literature, no specific care delivery guidelines for providers have been defined.

Implications for Practice/Future Research

Additional research is needed to further explore non-pharmacologic interventions and the specific supplementation benefits in the prevention and management of PIH. Implementation studies should be considered to look at feasibility of routine supplementation and adherence to non-pharmacologic therapies beginning early in pregnancy. Another need is for further studies to identify the intensity and type of physical activity recommended to create a protective effect or modify one's risk of developing PIH. Given that multiple studies are suggestive of elemental deficiencies occurring in the course of PIH, specific monitoring of these levels could be recommended in pregnancy.

The management and prevention of PIH is essential to improve maternal and fetal outcomes. Moreover, health care providers play an essential role in the quality of care for pregnant women. It is important for providers to routinely evaluate for potential dietary deficiencies and sedentary lifestyles in pregnancy to promote non-pharmacological interventions in their clinical practice and in high-risk pregnancies. More research and evidence is needed in the field before specific guidelines are developed and prevention treatments are prescribed clinically.

The research is promising, given the reduction in PIH seen with adequate supplementation and increased physical activity. Recommendations for patient education on

adequate balanced dietary consumption and lifestyle modifications during pregnancy could be supported by the evidence from this review.

Limitations

There were noted limitations to this review. It is necessary for integrative reviews to be systematic and rigorous in order to present a comprehensive understanding of a problem (Whittemore & Knafl, 2005). The volume of literature related to PIH made it difficult for the novice project leader to identify an initial subset of articles. Various combination keyword searches were performed to reveal literature that was specific to the identified problem statement and able to address it in its entirety. Through the use of PRISMA guidelines, the literature was identified and screened and eligibility criteria were considered. The Melnyk hierarchy of evidence rating scale, used in conjunction with PRISMA guidelines, led to some mismatched eligibility. Therefore, the selection process of the literature was a limitation, with some articles included regardless of rating. Another limitation was the use of a single reviewer conducting this integrative review, which could introduce bias. Utilization of the PRISMA flowchart helped to mitigate single-researcher bias.

Potential risk for bias was noted across all studies. The majority of the studies included small sample sizes. Inconsistencies existed among the studies, which differed in definitions of key terms and the reporting of outcomes, which may have resulted in lower reliability. Incomplete outcome reporting limits the assessment of the evidence regarding interventions on pregnant women as well as potential benefits. Further, potential self-reporting bias and lack of recall of dietary data and physical activity by participants was another limitation considered. Dietary intake and micronutrient supplementation was not considered in a large number of the studies, leading to a failure to account for that potential influence.

Dissemination

The project leader values the dissemination of findings for the advancement of clinical practice and improvement of outcomes. The distribution of findings obtained from this integrative review is essential to spread the knowledge and associated evidence-based interventions to ensure that the highest quality and most effective patient care continues to be delivered. Given the gap in literature on the topic of non-pharmacologic interventions related to PIH, it is the intent of the reviewer to submit the integrative review as a manuscript for publication in a peer-reviewed journal. The reviewer also intends to provide an informal or poster presentation to an outpatient OB/GYN practice to disseminate findings locally to this essential group of health care providers.

Conclusion

Hypertensive disorders of pregnancy are one of the leading causes of maternal and perinatal mortality worldwide (The American College of Obstetricians and Gynecologists, 2020). Over the years, numerous studies have looked at strategies to prevent PIH. All variables contributing to PIH should be recognized. With regard to non-pharmacologic interventions, evidence is insufficient. However, findings from this review suggest an inverse relationship between non-pharmacologic interventions and PIH, meaning that these interventions could serve as a preventative strategy and therefore lower the risk of PIH.

This integrative review serves to increase awareness among health care providers on the benefits of non-pharmacologic interventions, with or without antihypertensive therapy, on PIH with the aim of preventing adverse events and improving maternal and fetal outcomes. Clinicians should pay closer attention to elemental and dietary deficiencies and sedentary lifestyles and strengthen the supervision of pregnancy due to the clinical significance of PIH. More research is

needed to clearly define dietary factors, supplement timing, and physical activity frequency, intensity, and duration as well as to further define the protective benefits against PIH.

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Appendix A

Literature Matrix

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Ali, A., Alobaid, A., Malhis, T., & Khattab, A. (2019). Effect of vitamin D3 supplementation in pregnancy on risk of pre-eclampsia – Randomized controlled trial. *Clinical Nutrition*, *38*(2), 557–563. https://doi.org/10.1016/j.clnu.2018.02.023	The goal of this study was to evaluate the effect of antenatal vitamin D3 supplementation on the risk of preeclampsia and explore the dose effect in attaining normal vitamin D3 levels.	A total of 179 pregnant women were included who presented to an antenatal clinic in King Fahad Medical City between October 2012-October 2015. 164 total participants completed the trial. Inclusion criteria for subjects included a maternal age of 20-40 years, confirmed singleton pregnancy of less than 13 weeks, and	A randomized controlled trial	Results of this study showed that supplementation with vitamin D in those that are deficient during pregnancy reduces the risk of preeclampsia and IUGR in a dose dependent manner. It was concluded that 4000IU daily dose of vitamin D reduces the risk of preeclampsia	Level 2: Randomized controlled trial	Limitation of this study was that it is an open label and lacked naïve or placebo control group. There also was no documentation of laboratory findings of metabolic indicators of dose effects.	There is good evidence to support early evaluation of vitamin D levels in pregnancy with the recommendation to supplement to keep levels WNL for improved obstetric outcomes. Further RCT's should still be initiated to further

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		plan to receive ongoing prenatal care at same clinic, low risk pregnancy, and 25[OH]D levels less than <25 nmol/L.		in those women deficient in pregnancy.			confirm findings.
Behjat Sasan, S., Zandvakili, F., Soufizadeh, N., & Baybordi, E. (2017). The effects of vitamin D supplement on prevention of recurrence of preeclampsia in pregnant women with a history of preeclampsia. *Obstetrics and Gynecology International, 2017*, Article 8249264. https://doi.org/10.1155/2017/8249264	The aim of this study was to examine the effect of vitamin D supplementation on reducing the risk or preeclampsia recurrence.	There was a total of 142 participants meeting inclusion criteria with 72 placed into a control group and 70 in the intervention group. Baseline characteristic variables of participants were; age, number of pregnancies, gestational age, SBP and DBP,	A randomized controlled clinical trial	Pregnant patients in the intervention group receiving vitamin D3 supplementation had a significantly lower (P value=0.036) probability of preeclampsia that those in the control group. The risk of developing preeclampsia	Level 2: Randomized controlled trial	Limitations mentioned in the study were that some participants participation was discouraged by nonmedical people & some clinical colleagues related to alleged safety issues. Another	There is significant evidence to support the role of adequate vitamin D levels in pregnancy which shows to be promising for the prevention of preeclampsia. More well-controlled studies

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		24h proteinuria, and BMI.		in the control group was increased by 1.94 times that of the intervention group. To conclude, vitamin D supplementation had a protective effect against recurrent preeclampsia and could therefore help to reduce the risk of both GHTN and preeclampsia in pregnancy.		possible limitation was lack of GYN provider support or misinterpretation regarding prescriptive drug.	should be performed to test further safety and effectiveness.
Benachi, A., Baptiste, A., Taieb, J., Tsatsaris, V., Guibourdenche, J., Senat, M.-V., Haidar, H., Jani, J., Guizani, M., Jouannic, J.-M.,	The aim of this study was to evaluate the relationship between vitamin D	Pregnant women from six centers: one in Belgium and five in France included from	Nested case-control study within a prospective	This study found that the risk for preeclampsia for women with serum	Level 4: Case-control or cohort study	Some of the limitations of this study were nested in a large cohort. Each	There is not statistically significant evidence to support a practice

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Haguet, M.-C., Winer, N., Masson, D., Courbebaisse, M., Elie, C., & Souberbielle, J.-C. (2020). Relationship between vitamin D status in pregnancy and the risk for preeclampsia: A nested case-control study. *Clinical Nutrition*, *39*(2), 440–446. https://doi.org/10.1016/j.clnu.2019.02.015	insufficiency in the first trimester of pregnancy and preeclampsia.	April 2012 to July 2014. Total cohort of 3093 women. Women were included who were in the first trimester of pregnancy (10-14 wks. gestation) and of a singleton pregnancy. Exclusion criteria were hypercalcemia or other calcium-phosphorus imbalance, hypertension from 1st trimester, renal insufficiency, bone disease, lithium therapy, bowel malabsorption,	observational cohort.	vitamin D level greater than or equal to 30ng/mL in the first trimester was decreased but did not achieve statistical significance. Overall vitamin D deficiency appeared to be a risk factor for preeclampsia but studies do not support vitamin supplementation as an effective treatment for the prevention of this risk.		case was paired with controls according to known risk factors for preeclampsia. Possible bias cannot be excluded even after matching for known risk factors.	change. However, one could suggest one could suggest further studies/clinical trials to look at the effect of vitamin D supplementation prior to pregnancy and in early pregnancy especially in those at-risk women.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		or kidney stone disease.		However, women with vitamin D sufficiency during the third trimester and both in the first and the third trimesters had a significantly lower risk of preeclampsia.			
Bulloch, R. E., Lovell, A. L., Jordan, V. B., McCowan, L. E., Thompson, J. D., & Wall, C. R. (2018). Maternal folic acid supplementation for the prevention of preeclampsia: A systematic review and meta-analysis. *Paediatric and Perinatal*	The aim of this review was to investigate the effect of maternal folic acid supplementation during pregnancy on risk of preeclampsia and gestational hypertension.	Multiple scientific databases were searched for peer reviewed studies from inception up to July 28, 2016. Databases searched were Medline, EmBase, CINAHL,	A systematic review and meta-analysis.	This systematic review found a modest association between maternal folic acid supplementation and a reduced risk of preeclampsia	Level 1: Systematic review and meta-analysis	Limitations considered were that only one RCT was included with the remainder being observational studies. The majority of	At this time further studies need to be performed to confirm folic acid supplementation recommendations. There is not enough

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Epidemiology, *32*(4), 346–357. https://doi.org/10.1111/ppe.12476		Cochrane Central, Register of Controlled Trials, and AMED. Grey literature search also conducted and a Google search. This yielded a total of 306 records. Human studies included RCTs, cluster RCTs, cohort studies, and case-control studies for inclusion. Participants were pregnant women.		but overall, the available level of evidence is low.		studies were observational therefore causation could not be inferred. Studies also differed in definitions of folic acid supplement users. Lastly, sub-group analysis could not be performed to examine further the influence of timing or dose of folic acid supplementation on preeclampsia risk.	evidence or to support a change.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Cao, Y., Liu, Y., Zhao, X., Duan, D., Dou, W., Fu, W., Chen, H., Bo, Y., Qiu, Y., Chen, G., & Lyu, Q. (2020). Adherence to a dietary approaches to stop hypertension (DASH)-style diet in relation to preeclampsia: A case-control study. *Scientific Reports*, *10*(1), Article 9078. https://doi.org/10.1038/s41598-020-65912-2	The focus of this study was to examine the relationship between adherence to a DASH diet and the odds of preeclampsia among pregnant women in China.	Total of 449 participants, having preeclampsia and were inpatients in a hospital setting. Participants were located in the same hospital, matched for age, gestational week and GDM. Study conducted between March 2016-June 2019.	A hospital-based case-control study	This study showed an opposite association between adherence to a DASH diet and the odds of preeclampsia.	Level 4: Case-control study or cohort study	Limitations seen in this study were inevitable measurement errors measuring dietary intake as well as recall bias. Secondly, data was only collected on dietary intake of pregnant women during the last 3 months of pregnancy failing to account for the potential influence of early pregnancy	Not enough evidence is present to support a change. Further large-scale cohort studies or RCT's are needed to confirm the relationship.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						diet on preeclampsia.	
Chen, X., Ding, Y., Shi, L., Wu, D., Wang, L., Chen, F., & Mo, Y. (2020). Dietary patterns and gestational hypertension in nulliparous pregnant Chinese women. *Medicine, 99*(29), Article e20186. https://doi.org/10.1097/md.0000000000020186	The aim of this study was to investigate the association between pregnancy dietary patterns and the risk of hypertension among nulliparous pregnant Chinese women.	Total of 2580 participants aged 20-40 years recruited from 2013-2016. Participants were nulliparous pregnant Chinese women in three hospitals in Haikou, south China. A stratified cluster random sampling method was used.	A cross-sectional, case control study	Results of this study showed that the high-salt food pattern was significantly associated with hypertension in pregnancy. No linkage with HTN was observed for animal pattern, traditional Chinese pattern and Western pattern.	Level 4: Case-control or cohort study	A limitation of the study was that pre-pregnancy diet was not taken into consideration.	Does provide some good foundational information and beneficial evidence showing overall association of a high-salt diet and hypertension. More studies should be performed to confirm findings.
da Silva, S., Hallal, P., Domingues, M., Bertoldi, A., Silveira, M., Bassani, D., da Silva, I., da Silva, B.,	To evaluate the efficacy of an exercise intervention to prevent	Participants were eligible if 18yr or older and lived in the urban area of	Randomized controlled trial	Results did not show any significant differences in the incidence	Level 2: Randomized control trial	Some of this studies limitations were poor adherence to	No, this study lacks positive findings on the impact

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Coll, C., & Evenson, K. (2017). A randomized controlled trial of exercise during pregnancy on maternal and neonatal outcomes: Results from the Pamela study. *International Journal of Behavioral Nutrition and Physical Activity*, *14*(1), Article 175. https://doi.org/10.1186/s12966-017-0632-6	negative maternal and newborn health outcomes.	the city of Pelotas, Rio Grande do Sul State, Brazil. Total of 639 participants randomized to either the intervention or the control group.		of preterm birth and PE between groups in the intervention treatment and per protocol analysis. Therefore, supervised regular, moderate to vigorous exercise program performed three times/week did not support the benefits of exercise performed during pregnancy on maternal and newborn health		the exercise program and a high level of dropouts in the intervention group, lower adherence to protocol potentially causing dropouts to underpower the analysis. Second, information on nutritional intake was not recorded among participants. Third, timing of intervention overlapped with typical onset of PE	of physical activity on preeclampsia. More intense high quality RCT studies are needed to look at optimal frequency, type, duration, and intensity of physical exercise required for beneficial health outcomes during pregnancy.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
				outcomes evaluated.		and early preterm birth. Lastly, rigorous nature of eligibility criteria which resulted in a very healthy population,	
Du, M., Ouyang, Y., Nie, X., Huang, Y., & Redding, S. R. (2018). Effects of physical exercise during pregnancy on maternal and infant outcomes in overweight and obese pregnant women: A meta-analysis. *Birth*, *46*(2), 211–221. https://doi.org/10.1111/birt.12396	The purpose of this study was to assess the effect of physical exercise on maternal and infant outcomes in overweight and obese pregnant women.	13 studies met inclusion criteria after 1724 articles were identified from PubMed, Cochrane, Embase, Web of Science, and ClinicalTrials.gov. Studies included were RCTs and published in English. Most conducted in developed	A meta-analysis	Results showed that physical exercise reduced gestational weight gain by 1.14 kg and the risk of gestational diabetes by 29% in overweight and pregnant women. There were no significant	Level 1: A meta-analysis	Some limitations of the study include difficulty maintaining consistency in recruited original studies with respect to exercise pattern, duration, and intensity. Criteria	Although there was some benefit shown that prenatal exercise in overweight and obese women could reduce the amount of weight gain and gestational diabetes,

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		countries, with two studies conducted in low- and middle-income countries. There was a total of 1439 participants included in meta-analysis.		differences in other outcomes such as gestational hypertension, preeclampsia, c-section, birthweight, large for gestational age, small for gestational age, macrosomia, and preterm birth.		varied among some studies for overweight and obesity making it difficult to undertake subgroup analysis. Selection bias may exist due to only searching articles in English. Lastly, only a subset or articles reported outcomes such as gestational hypertension, preeclampsia, small and large for	more studies and larger sample size are needed to evaluate the effect of exercise interventions on this population separately. No significant difference was seen in incidence of GHTN or in risk of preeclampsia.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						gestational age, macrosomia, and preterm birth which may have resulted in less reliability of pooled analyses of these outcomes.	
Fulay, A. P., Rifas-Shiman, S. L., Oken, E., & Perng, W. (2018). Associations of the dietary approaches to stop hypertension (DASH) diet with pregnancy complications in project viva. *European Journal of Clinical Nutrition*, *72*(10), 1385–1395. https://doi.org/10.1038/s41430-017-0068-8	This studies goal was to examine the relationship of adherence to the DASH diet with hypertensive disorders of pregnancy and other pregnancy outcomes.	Study used data from an ongoing cohort of pregnant women. 1999-2002 pregnant women in their first trimester of pregnancy were recruited from multi-specialty practices at Harvard Vanguard	Cohort study	Results of this study concluded that adherence to DASH diet during early pregnancy does not seem to be protective against hypertensive disorders of pregnancy or	Level 4: Case-control study or cohort study	Limitations identified in this study included potential reporting bias of dietary data, the observational study design, and inability to generalize results due	There is not enough evidence to support a practice change. Studies are lacking in this area and therefore further studies must be done to confirm findings.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		Medical Associates in Massachusetts. Eligibility criteria was singleton pregnancy, less than 22 wks. gestation, residing in area until delivery, and ability to complete required paperwork in English. A sample size of 1760 women were included in the study. Mean age of women was 32.2 + or – 4.9 years with 71.9% being white.		other adverse outcomes. A positive association was seen between diet scores and gestational weight gain in obese women.		to a predominantly white and well-educated population.	

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Gebreyohannes, R. D., Abdella, A., Ayele, W., & Eke, A. C. (2021). Association of dietary calcium intake, total and ionized serum calcium levels with preeclampsia in Ethiopia. *BMC Pregnancy and Childbirth, 21*(1), Article 532. https://doi.org/10.1186/s12884-021-04005-y	The purpose of this study was to examine the association of dietary calcium intake, serum total calcium levels, and ionized calcium levels with preeclampsia.	The study had a total of 84 participants. Cases of 42 women with preeclampsia and controls were 42 normotensive women in three large hospitals in Addis Ababa Ethiopia between October-December 2019. Inclusion criteria were age 18 years or older, gestational age of 20 weeks or greater, and singleton pregnancy.	Unmatched case-control study.	This study found a significant association between low dietary calcium intake and low serum calcium levels with preeclampsia. This indicates that having low serum calcium levels is a risk for preeclampsia. Similarly, even though it was not statistically significant, having the recommended daily intake of calcium	Level 4: Case-control study	Limitations of this study were lack of other similar studies in English making comparison difficult. Possible investigator administered bias cannot be excluded.	These findings were not statistically significant but showed good evidence on the positive relationship between the recommender intake of calcium and prevention of preeclampsia. Recommendations for patient education could be supported by this evidence on the importance of adequate

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
				was in the direction of protection against preeclampsia.			dietary consumption of calcium rich foods during pregnancy until further implementation studies can be performed on routine supplementation.
Haruna, M., Matsuzaki, M., Ota, E., Shiraishi, M., Hanada, N., & Mori, R. (2019). Guided imagery for treating hypertension in pregnancy. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd011337.pub2	The purpose of this review was to determine the effects of guided imagery as a nonpharmacologic intervention of hypertension in pregnancy and the effect on perinatal outcomes.	Participants included pregnant women with HTN both undergoing drug therapy and those who were not. Electronic search was performed of the Cochrane Pregnancy and Childbirth's	Systematic review	Results indicated that a meta-analysis was not able to be performed due to the two studies included reporting different outcomes. Intervention frequency between the	Level 1: Systematic review	Limitations of the study were the differences in intervention frequency between the studies compared. Available evidence was sparse (only 2 small	Available evidence for this review topic is sparse. Insufficient evidence is available to support a practice change about the use of guided imagery for

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		Trials Register including detailed search strategies for the CENTRAL, MEDLINE, Embase, and CINAHL. ClinicalTrials.gov and the WHO were searched in addition. Selection criteria included RCT's with exclusion of quasi-RCT's and cross-over trials. Two small trials were included involving a total of 99 pregnant women.		two studies also differed. Low-certainty evidence suggested that guided imagery may have little to no impact in the use of antihypertensive drug therapy.		studies included) and therefore insufficient to address the overall objectives of the review.	hypertensive disorders of pregnancy. Large and well-designed RCT's are needed to evaluate further.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
He, L., Lang, L., Li, Y., Liu, Q., & Yao, Y. (2016). Comparison of serum zinc, calcium, and magnesium concentrations in women with pregnancy-induced hypertension and healthy pregnant women: A meta-analysis. *Hypertension in Pregnancy*, *35*(2), 202–209. https://doi.org/10.3109/10641955.2015.1137584	The aim of this study was to determine whether or not calcium, zinc, and magnesium levels are associated with PIH.	A comprehensive literature search was performed using computerized bibliographic databases until January 15, 2015: Wanfang, PubMed, and the Chinese National Knowledge Infrastructure. Both studies published in English and Chinese language were included that met both inclusion and exclusion criteria. A total of 14 articles were included	Literature search-A meta-analysis	Findings showed that the serum levels of zinc, calcium, and magnesium were found to be decreased in patients with PIH. The findings of this study are suggestive that the decrease in zinc, magnesium, and calcium was associated with PIH.	Level 1: A meta-analysis	Limitations identified were the potential for publication bias due to inclusion of articles that were only published in English of Chinese.	Although there is good evidence suggestive of consistencies among low levels of calcium, zinc, and magnesium and the association with PIH. Study findings did have some inconsistencies with other previous studies. Given that multiple studies are suggestive that deficiencies

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		in the study out of the initial potential of 95 articles.					in these elements occur in the course of PIH it could be recommender that these levels be checked/measured in pregnant patients or those with PIH.
Hofmeyr, G., Lawrie, T. A., Atallah, Á. N., & Torloni, M. (2018). Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd001059.pub5	The goal of this study was to examine the effects of calcium supplementation during pregnancy on PIH and related maternal and fetal outcomes.	27 studies were included with a total of 18,064 women. High dose calcium supplementation of 1g/day or greater versus placebo.	The Cochrane Pregnancy and Childbirth's Trials Register was searched as well as the WHO International Clinical Trials	Results indicated that 1g/day or greater of calcium supplementation may reduce the risk of preeclampsia and preterm birth especially in those women	Level 1: Systematic review	Limitations of the study included potential for bias as this was difficult to assess as a result of poor reporting and lack of information on methods. Treatment	The evidence is promising given the reduction in preeclampsia seen with adequate calcium supplementation. However, further research

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
			Registry Platform. Selection criteria included RCT's to include cluster-randomized trials which compared high dose calcium vs. placebo during pregnancy. Quasi-randomized trials were included for low-dose calcium as well as other dose comparison trials.	who have low dietary calcium intake.		effects could be overestimated due to the small study effects or publication bias.	with large high-quality trials is needed to determine optimal dosing of calcium supplementation during pregnancy.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Hua, X., Zhang, J., Guo, Y., Shen, M., Gaudet, L., Janoudi, G., Walker, M., & Wen, S. (2016). Effect of folic acid supplementation during pregnancy on gestational hypertension/preeclampsia: A systematic review and meta-analysis. *Hypertension in Pregnancy*, *35*(4), 447–460. https://doi.org/10.1080/10641955.2016.1183673	The objective of this study was to evaluate the effect of supplementation with folic acid on the risk of GHTN and preeclampsia during pregnancy.	The following electronic databases of Medline, Embase, Scopus, and the Web of Science were searched from inception to December 2014. 13 Studies met inclusion criteria out of a total of 1224 potential studies initially. Studies included 2 RCT's, 10 cohort studies, and 1 case-control study.	A systematic review and metal analysis	Findings of this study were unclear as to whether or not folic acid supplementation in pregnancy can prevent the occurrence of GHTN or preeclampsia.	Level 1: Systematic review and meta-analysis	Some limitations of the study were the inability to account for the total folic acid intake (supplementation, intake from dietary sources, naturally occurring & fortified). Another limitation was that most of the studies were observational in nature. Lastly, there was an inability to control for those potential	This study was inconclusive and therefore there is not enough evidence to support a change. Further studies are needed to approve or disprove whether or not supplementation with folic acid in pregnancy can prevent GHTN or preeclampsia.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						confounding factors (age, parity, smoking, alcohol consumption, history of GHTN/pree, socioeconomic status, education, etc.) further affecting the interpretability of results.	
Jirakittidul, P., Sirichotiyakul, S., Ruengorn, C., Techatraisak, K., & Wiriyasirivaj, B. (2018). Effect of iron supplementation during early pregnancy on the development of gestational hypertension and pre-eclampsia. *Archives of Gynecology and*	The goal of this study was to investigate the relationship between iron supplementation in pregnancy and the presence of GHTN or preeclampsia.	A sample size of 400 non-anemic pregnant women were included in the study. A retrospective review of medical records receiving their first antenatal	A retrospective cohort study. Study populations were divided into two groups: iron supplementation	Results showed that iron supplementation among non-anemic pregnant patients before 16 weeks of pregnancy was significantly	Level 4: cohort study	Several limitations existed with the first being the retrospective design. Second, patient involved in the study were all from the	Evidence from this study should raise concern about the potential adverse effects of iron supplementation during pregnancy

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Obstetrics, *298*(3), 545–550. https://doi.org/10.1007/s00404-018-4821-6		care at an OB/GYN department at a hospital in Thailand from June 2009-December 2010.	starting at less than 16 weeks gestational age (study group) or the control group having a gestational age of 16 weeks or greater.	associated with increased risk of developing GHTN or preeclampsia after 20 weeks of pregnancy.		same one center. Next there was no distinguishment between non-anemic pregnant patients iron replete and those who were iron deficient. Lastly, dietary iron intake and micronutrient supplementation was not determined.	in patients who are non-anemic. Further studies need to be done on a larger scale and across multiple centers to confirm these findings.
Kyozuka, H., Murata, T., Fukuda, T., Yamaguchi, A., Kanno, A., Yasuda, S., Sato, A., Ogata, Y., Kuse, M., Hosoya, M., Yasumura, S., Hashimoto, K.,	This study's purpose was to examine the association between pre-pregnancy calcium and hypertensive	After inclusion criteria applied there was a total of 33,894 normotensive Japanese women in their first pregnancy	Data obtained from large Japanese birth cohort study	No association was found in this study between any pre-pregnancy calcium	Level 4: Case-control study or cohort study	There were several limitations in this study. First daily intake of vitamin D was not	There is no evidence to support a change at this time given the absence of association

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
Nishigori, H., Fujimori, K., Kamijima, M., Yamazaki, S., Ohya, Y., Kishi, R., Yaegashi, N., . . . Katoh, T. (2020). Association between pre-pregnancy calcium intake and hypertensive disorders during the first pregnancy: The Japan environment and children's study. *BMC Pregnancy and Childbirth*, *20*(1), Article 424. https://doi.org/10.1186/s12884-020-03108-2	disorders of pregnancy.	recruited between January 2011-March 2014. Median pre-pregnancy calcium intake of the participants was 430 mg/day.		intake threshold and new onset HTN during pregnancy for primiparas.		considered. Second, the focus of the study was on hypertensive disorders of pregnancy which did not allow differentiation between GHTN and preeclampsia. Lastly, there is possibility for recall bias given that information obtained in first trimester of pregnancy included information 1 year	between pre-pregnancy calcium intake and onset of hypertensive disorders in pregnancy.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						before pregnancy.	
Magro-Malosso, E. R., Magro-Malosso, E. R., Saccone, G., Di Tommaso, M., Roman, A., & Berghella, V. (2017). Exercise during pregnancy and risk of gestational hypertensive disorders: A systematic review and meta-analysis. *Acta Obstetricia et Gynecologica Scandinavica*, *96*(8), 921–931. https://doi.org/10.1111/aogs.13151	The aim of this study was to evaluate the effect of exercise during pregnancy on the risk of gestational hypertensive disorders.	Selection criteria included only RCTs of pregnant women randomized to an exercise regimen or not. Singleton pregnancies without any obstetric complications to physical activity reporting data on gestational hypertensive disorders. Research conducted using MEDLINE, Embase, Web of Sciences, Scopus,	A systematic-review and meta-analysis	This study found that aerobic exercise in singleton pregnancies for about 30-60 min.2-7 times per week during pregnancy, when compared to being more sedentary, is associated with a significantly reduced risk of gestational hypertensive disorders overall, with a significant reduced risk of GHTN specifically,	Level 1: Systematic review & meta-analysis	Limitations of the study was that dietary counseling was provided as an additional intervention in some trials. Next, the majority of studies did not have a proper definition of gestational hypertension of preeclampsia. The analysis of preeclampsia with 2230 women included	Yes, there is good quality Level I design showing strong consistent results and evidence to support that aerobic exercise is beneficial and should therefore be encouraged in pregnancy.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		ClinicalTrials.gov, OVID and Cochrane Library. Electronic databases searched from inception to Feb. 2017. Total of 17 trials, including 5075 pregnant women, were analyzed.		and cesarean delivery.		was underpowered statistically. Lastly, seven of the 17 studies came from the same author over a period of a few years.	
Pourheidari, M., Rasouli, Pourheidari, M., Rasouli, M., & Gardesh, Z. (2019). Effect of self-care before and during pregnancy to prevention and control preeclampsia in high-risk women. *International Journal of Preventive Medicine*, *10*(1), 21.	This aim of this study was to examine the factors influencing self-care for the prevention and control of preeclampsia in high-risk women.	The following databases PubMed, Cochrane, Medline, Google Scholar, Medscape, and relevant research published between 1980-2016 were searched by the	Narrative Review.	Results showed that preconception counseling, screening, and self-care training can be effective in the prevention and control of preeclampsia in women at	Level 5: Systematic review of descriptive & qualitative studies	Limitations of this review might be researcher bias and subjectivity on which studies to include as well as the potential bias of author's	Not at this time due to the lower level of evidence. More data and higher-level research needed to support a change.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
https://doi.org/10.4103/ijpvm.ijpvm_300_17		researcher and studied. Keywords were used for search. A total of 350 related articles were selected with the findings from 70 used and placed into two general categories to compile the present article; 1) counseling and screening strategies and 2) self-care strategies for prevention and control of preeclampsia in high-risk women.		high risk of the disease.		interpretation and conclusions. Inclusion criteria not mentioned.	
Puspitasari, Y., Santoso, B., Nursalam, N., & Sulistyono, A. (2022). Investigating	This study's purpose was to examine the effects of	Convenience sampling was used. Total of 60 participants,	Quasi-experimental study	Results of the study showed that guided	Level 3: Controlled trial, quasi-	Limitations of this study was that it was not	Despite the limitations of the study, positive

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
progressive muscle relaxation and guided imagery in pre-eclampsia treatment. *British Journal of Midwifery*, *30*(2), 101–109. https://doi.org/10.12968/bjom.2022.30.2.101	guided imagery and progressive muscle relaxation on urine protein and blood pressure during conservative treatment of preeclampsia.	pregnant women, aged 20-45 years old, with singleton pregnancy who had been diagnosed with preeclampsia. Gestational age was between 30-32 weeks.	method was used.	imagery and progressive muscle relaxation had a positive effect on blood pressure and proteinuria in patients with preeclampsia . This was statistically significant after 7 days of intervention showing that the combination of these interventions can effectively lower blood pressure and proteinuria during	experimental design	conducted over an extended period of time to fully analyze the impact. Other factors that can have an effect on blood pressure such as anxiety, stress, depression, etc. were not taken into consideration. Another limitation was causality was not able to be established due to the	results on blood pressure and proteinuria were statistically significant. Therefore, patient education and implementation could be supported to promote these supplemental treatment strategies to help improve overall outcomes.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
				conservative treatment of disease.		nature of the quasi-experimental design.	
Raguema, N., Benletaifa, D., Mahjoub, T., & Lavoie, J. L. (2020). Increased physical activity is correlated with improved pregnancy outcomes in women with preeclampsia: A retrospective study. *Pregnancy Hypertension*, *21*, 118–123. https://doi.org/10.1016/j.preghy.2020.05.005	To evaluate the association between the practice of physical activity and the development of preeclampsia (PE).	Sample size of 61 healthy pregnant women and 45 women with preeclampsia. Recruited between Feb. 2016-May 2016 from gynecology services within a University Hospital in Sousse, Tunisia. Willing participants signed consent on day of delivery for inclusion. Control group consisted of women with no	A retrospective study	There was a positive correlation between physical activity during pregnancy and gestational duration of pregnancy in both cohorts of women with and without preeclampsia regardless of type and intensity of physical activity. This was considered an index of	Level 4: Correlational design (cohort study)	Limitations were the small number of cases as well as the retrospective nature.	Although the study shows positive benefit there still needs to be further studies to identify the intensity and type of physical activities to recommend to reduce impact or prevent development of PE. However, this information would be useful to better

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		pregnancy complications, admitted for natural childbirth or cesarean section. Pregnant women with diabetes and chronic family history of HTN were excluded from control group.		maternal and fetal health, particularly in context of preeclampsia . The study demonstrated an inverse association between the prevalence of PE and total energy expenditure during pregnancy on all types of intensities of physical activity practice.			counsel pregnant women regarding exercise to maximize maternal and fetal outcomes.
Smith, C., Tuson, A., Thornton, C., & Dahlen, H. G. (2020). The safety and effectiveness of mind body interventions for women with pregnancy induced hypertension	The purpose was to perform a systematic review of the safety and effectiveness of mind body approaches in	A search of databases was performed from inception to 2019 for randomized and quasi randomized	A systematic review & meta-analysis	The quality of evidence from these trials was low with few high-quality studies. Overall,	Level 1: A systematic review & meta-analysis	Limitations identified were the low quality of evidence from these trials, effects of	Evidence is limited in these studies to guide practice. Further

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
and or preeclampsia: A systematic review and meta-analysis. *Complementary Therapies in Medicine, 52,* Article 102469. https://doi.org/10.1016/j.ctim.2020.102469	conjunction with conventional medicine for women with hypertensive disorders in pregnancy.	controlled trials. The following databases were searched using key words; CINAHL, PubMed, Cochrane Library, Ovid Medline, Nursing and Allied Health from inception to Jan. 7, 2019 with additional searches made of Google Scholar. Total of 121 studies identified and 8 studies were included in the review.		there was no effect on the development of preeclampsia , use of antihypertensive meds and any neonatal outcomes from the interventions evaluated. Safety issues were unclear and thus risk benefit ratio of all interventions could not be determined.		publication bias not assessed due to small number of included trials, the small sample size and wide confidence intervals increase the impression of study findings, as well as the omission and reporting on clinically relevant outcomes for the mother and her infant. The limitations of	research is needed.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						methodological limitations of trials and incomplete reporting limit assessment of the evidence of these interventions on pregnant women with pregnancy induced hypertension and the potential benefits of these interventions.	
Spracklen, C. N., Ryckman, K. K., Triche, E. W., & Saftlas, A. F. (2016). Physical activity during	The aim of the study was to compare the association between	Primiparous mothers who had a live birth between August 2002-	A case-control study	It was found that women with increased physical	Level 4: Case-control study	Limitations of the study include self-reported data during	There is good evidence to support the promotion

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
pregnancy and subsequent risk of preeclampsia and gestational hypertension: A case control study. *Maternal and Child Health Journal*, *20*(6), 1193–1202. https://doi.org/10.1007/s10995-016-1919-y	physical activity during pregnancy and the risk of preeclampsia and GHTN	May 2005 and residing in one of 42 Iowa countries, identified by electronic birth certificates. Total of 258 preeclampsia cases, 221 GHTN, and 174 normotensive controls ascertained.		activity during pregnancy was associated with a lower risk of preeclampsia. Likewise, those with increased sedentary activity were at an increased risk.		the postpartum period therefore there is the potential for misclassification of type, frequency, or duration of physical activity that occurred. Physical activity questions were also generalized asking women to estimate their physical activity levels over the entire pregnancy. Reported	of physical activity in pregnancy to reduce the risk of preeclampsia. Future studies are needed to collect various objective measures of physical activity and further evaluate what level/extent of physical activity may modify one's risk of preeclampsia.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						levels may not be reflective of actual physical activity performed as they likely varied throughout pregnancy. Lastly, generalization of results are cautioned due to a study population of over 90% white women with most (93%) being employed. The relationship between employment	

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
						and preeclampsia risk was not able to be assessed.	
Sun, L., & Niu, Z. (2020). A mushroom diet reduced the risk of pregnancy-induced hypertension and macrosomia: A randomized clinical trial. *Food & Nutrition Research*, *64*, Article 4451. https://doi.org/10.29219/fnr.v64.4451	The aim of this study was to examine the impact of mushrooms on pregnancy related complications.	Conducted from February 2016-October 2018. Participants were women of childbearing age who were planning for their first pregnancy and recruited by staff from a community health center. An allocation concealment process, random numbers table, was used for randomization of participants. There was a	Randomized clinical trial conducted over 2 years and 8 months	Evidence from this study supported the use of a mushroom diet to prevent or manage pregnancy-related hypertension. Results also indicated that a mushroom diet may control newborn birthweight while reducing other comorbidities such as	Level 2: Randomized control trial	Limitations of this study was that variety of mushrooms was not taken into consideration which could have different nutrient compositions as well as different effects on subjects. Mushroom species were not limited in this study. Another limitation of	This study showed good evidence to support the promotion of a mushroom diet in pregnancy to help reduce the risk of PIH.

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
		total of 1162 subjects in the study. 582 in the mushroom diet group and 580 in the placebo group.		diabetes and gestational weight gain.		the study was that mushrooms were used as a single variable. Thirdly, no baseline lab work was performed that was associated with preeclampsia in the early stage of pregnancy.	
Yue, C.-Y., Gao, J., Zhang, C.-Y., & Ying, C.-M. (2021). Is serum vitamin D deficiency before gestational 20 weeks a risk factor for preeclampsia? *Clinical Nutrition*, *40*(6), 4430–4435. https://doi.org/10.1016/j.clnu.2020.12.040	The purpose of this study was to assess whether serum vitamin D deficiency before gestational 20 weeks was associated with an increased	Total of 7976 singleton pregnancies women with a live delivery were enrolled in the study between January 2017-July 2019 at the Obstetrics	Serum levels of 25(OH)D were investigated before 20 weeks' gestation. Associations were analyzed	This study findings showed that serum vitamin D is a protective factor in preeclampsia (p=0.04). Compared with	Level 4: Correlational design	Limitations included the data in the article were not available on eventual vitamin complements taken by women	This study did show good evidence to support that vitamin D in pregnancy is significantly related to the outcome

Article	Study Purpose	Sample	Methods	Study Results	Level of Evidence	Study Limitations	Would Use as Evidence to Support a Change?
	risk of preeclampsia.	& Gynecology Hospital of Fudan University.	between the 25 (OH)D and the risk of preeclampsia.	adequate vitamin D, vitamin D deficiency (p=0.031), deficiency (p=0.049) and severe deficiency (p=0.005) are independent of preeclampsia in pregnant women risk factors. Vitamin D deficiency before gestational age 20 wks. is a risk factor for preeclampsia.		included in the study. Another limitation is that many blood variables decrease during pregnancy due to factors such as "dilution". Therefore, normal values are not the standard usual values. It would be essential to establish a reference range for vitamin D during pregnancy.	of preeclampsia. Therefore, clinicians should utilize this evidence to pay more attention to vitamin D deficiency, insufficiency, and supervision of these levels during pregnancy.

Appendix B

CITI Training Completion Certificate

CITI PROGRAM

Completion Date 03-Mar-2022
Expiration Date 02-Mar-2025
Record ID 47406328

This is to certify that:

Karen Ellis

Has completed the following CITI Program course:

Not valid for renewal of certification through CME.

Biomedical Research - Basic/Refresher
(Curriculum Group)
Biomedical & Health Science Researchers
(Course Learner Group)
1 - Basic Course
(Stage)

Under requirements set by:

Liberty University

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?w7af5496e-ca8c-4309-86e1-4b1bda766723-47406328

Appendix C

Liberty University Institutional Review Board Approval Letter

LIBERTY UNIVERSITY.
INSTITUTIONAL REVIEW BOARD

March 25, 2022

Karen Ellis
Vickie Moore

Re: IRB Application - IRB-FY21-22-878 An Integrative Review: What is the impact of non-pharmacologic interventions during pregnancy on pregnancy-induced hypertension?

Dear Karen Ellis and Vickie Moore,

The Liberty University Institutional Review Board (IRB) has reviewed your application in accordance with the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA) regulations and finds your study does not classify as human subjects research. This means you may begin your project with the data safeguarding methods mentioned in your IRB application.

Decision: No Human Subjects Research

Explanation: Your study is not considered human subjects research for the following reason:

(1) It will not involve the collection of identifiable, private information from or about living individuals (45 CFR 46.102).

Please note that this decision only applies to your current application, and any modifications to your protocol must be reported to the Liberty University IRB for verification of continued non-human subjects research status. You may report these changes by completing a modification submission through your Cayuse IRB account.

Also, although you are welcome to use our recruitment and consent templates, you are not required to do so. **If you choose to use our documents, please replace the word *research* with the word *project* throughout both documents.**

If you have any questions about this determination or need assistance in determining whether possible modifications to your protocol would change your application's status, please email us at irb@liberty.edu.

Sincerely,

G. Michele Baker, MA, CIP
Administrative Chair of Institutional Research
Research Ethics Office