Risk factors, prevention and obstetric outcome related to preeclampsia: an integrative review

Fatores de risco, prevenção e desfecho obstétrico relacionados à pré-eclâmpsia: uma revisão integrativa

Factores de riesgo, prevención y resultados obstétricos relacionados con la preeclampsia: una revisión integradora

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RESUMO

Objetivo: o presente estudo visa explorar a relação entre a Pré-Eclâmpsia e seus fatores de risco, bem como sua profilaxia e desfecho obstétrico relacionado. **Método**: realizou-se uma pesquisa nas bases de dados National Library of Medicine (PubMed), Biblioteca Virtual em Saúde (BVS) e Scientific Electronic Library Online (SciELO), utilizando descritores DeCS/MeSH "Pré-Eclâmpsia", "Fatores de Risco", "Trabalho de Parto" e "Prevenção". Foram selecionados estudos publicados entre 2013 e 2023. **Resultados**: a nuliparidade, a idade materna e a história familiar de pré-eclâmpsia estão entre os maiores fatores de risco para o desenvolvimento da doença, sendo a associação de carbonato de cálcio e ácido acetilsalicílico a melhor alternativa para sua prevenção. A condição hipertensão gestacional apresenta forte relação com o parto por via alta, principalmente em primíparas. **Conclusão**: o desenvolvimento da Pré-Eclâmpsia possui contexto multifatorial, sendo a identificação destes precipitantes fundamental para que se impementem as medidas preventivas, embora sejam necessários esforços contínuos para aprimorar a compreensão e o manejo dessa condição clínica comum.

Palavras-chave: Fatores de Risco; Pré-Eclâmpsia; Prevenção; Trabalho de Parto.

ABSTRACT

Objective: This study aims to explore the relationship between preeclampsia and its risk factors, as well as its prophylaxis and related obstetric outcomes. **Method**: A search was conducted in the National Library of Medicine (PubMed), Virtual Health Library (VHL), and Scientific Electronic Library Online (SciELO) databases, using the DeCS/MeSH descriptors "Preeclampsia," "Risk Factors," "Labor," and "Prevention." Studies published between 2013 and 2023 were selected. **Results**: Nulliparity, maternal age, and a family history of preeclampsia are among the greatest risk factors for the development of the disease, with the combination of calcium carbonate and aspirin being the best alternative for its prevention. Gestational hypertension has a strong association with upper airway delivery, especially in primiparous women. **Conclusion**: the development of Pre-eclampsia has a multifactorial context, and the identification of these precipitants is essential for implementing preventive measures, although continuous efforts are needed to improve the understanding and management of this common clinical condition.

Keywords: Risk Factors; Preeclampsia; Prevention; Labor.

RESUMEN

Objetivo: Este estudio busca explorar la relación entre la preeclampsia y sus factores de riesgo, así como su profilaxis y los resultados obstétricos relacionados. **Método**: Se realizó una búsqueda en las bases de datos de la Biblioteca Nacional de Medicina (PubMed), la Biblioteca Virtual en Salud (BVS) y la Biblioteca Electrónica Científica en Línea (SciELO), utilizando los descriptores DeCS/MeSH "Preeclampsia", "Factores de Riesgo", "Parto" y "Prevención". Se seleccionaron estudios publicados entre 2013 y 2023. **Resultados**: La nuliparidad, la edad materna y los antecedentes familiares de preeclampsia se encuentran entre los principales factores de riesgo para el desarrollo de la enfermedad, siendo la combinación de carbonato de calcio y aspirina la mejor alternativa para su prevención. La hipertensión gestacional tiene una fuerte asociación con el parto por vía aérea superior, especialmente en mujeres primíparas. **Conclusión**: El desarrollo de la preeclampsia tiene un contexto multifactorial, y la identificación de estos factores precipitantes es esencial para implementar medidas preventivas, aunque se requieren esfuerzos continuos para mejorar la comprensión y el manejo de esta afección clínica común..

Descriptores: Factores de Riesgo; Preeclampsia; Prevención; Trabajo de Parto.

Introduction

Preeclampsia (PE) is defined as a specific condition of pregnancy characterized by the onset of arterial hypertension and proteinuria after the 20th week in a previously normotensive pregnant woman, with blood pressure equal to or greater than 140/90 mmHg in two distinct measurements with a minimum interval of 4 hours and a maximum of 7 days, while proteinuria is identified by the presence of 300 mg or more of protein in the urine over a 24-hour period or a proteinuria/creatininuria ratio (mg/dL) ≥0.3, or the appearance of at least one cross in the albuminuria evaluation on a dipstick (30 mg/dL).[2,5,6] More current concepts also include the diagnosis when, in the absence of proteinuria, target organ dysfunction occurs.[1,2]

The pathophysiology of preeclampsia is complex and multifactorial, involving interactions between genetic, immunological, and environmental factors, with the compromise of the second wave of trophoblastic invasion being one of the main proposed mechanisms, with a consequent reduction in placental blood flow.[3,4,7,8] Furthermore, the presence of the gestational hypertensive condition is strongly related to failures in inducing labor and its resolution via cesarean section, showing that not only the identification of risk factors but also their prevention are of extreme importance in the scope of obstetric outcome.[14,15]

In this context, the study aims to address the contributing aspects to the development of Preeclampsia, offering a comprehensive view of current knowledge, with a focus on the prevention of this common obstetric condition.

Methods

The present integrative literature review brings an exploratory and descriptive approach, of a qualitative nature, based on scientific articles, aiming to offer a current view on the relevant factors in the approach and development of Preeclampsia, in order to reduce its incidence, improve maternal and fetal outcomes, and avoid disease-related deaths.

The methodology used was the analysis of the Virtual Health Library (VHL), National Library of Medicine (PubMed), and Scientific Electronic Library Online (SciELO) databases. The choice of these databases was based on the broad coverage of relevant scientific works in the area of Gynecology and Obstetrics and health in general.

The descriptors used in the search for articles were “Pre-Eclampsia,” “Risk Factors,” “Labor,” and “Prevention,” in Portuguese, Spanish, and English, combined with the Boolean operators AND and OR, in order to ensure simultaneous approaches to the main topics and include synonyms and variations of the descriptors, respectively, aiming to expand the results.

The inclusion criteria covered articles published between 2013 and 2023, with only one systematic literature review from 2005 selected due to presenting relevant conclusions consistent with the most current works. Studies available in Portuguese, Spanish, or English that directly addressed delivery routes, risk factors, and/or prophylaxis related to Preeclampsia were selected. Publications unrelated to

the theme were considered as exclusion criteria. After selection, 7 articles were included to compose this review.

Results

The systematic review by Kirsten Duckitt and Deborah Harrington (2005) concluded that women aged ≥40 had almost double the risk of developing Preeclampsia, whether primiparous or multiparous (RR 1.68, CI 95%1.23 to 2.29 and 1.96, 1.34 to 2.87, respectively), with nulliparity capable of almost tripling this risk (2.91, 1.28 to 6.61), as well as a family history of PE (2.90, 1.70 to 4.93).[9]

Twin gestation (RR 2.93, CI 2.04 to 4.21), high body mass index (RR 2.47, CI 1.66 to 3.67), and pre-existing medical conditions, such as insulin-dependent diabetes (RR 3.56, CI 2.54 to 4.99), constitute factors capable of tripling, doubling, and quadrupling, respectively, the overall risk of PE.[9]

Ticianne da Cunha Soares et al. (2019) also demonstrated, in their literature review, that maternal age configures a triggering factor for some intercurrences in the gestational period, as do black women, who present a possible hereditary failure in cellular uptake and renal transport of calcium and sodium, with a sodium-sparing gene that promotes the cellular influx of sodium and calcium efflux, facilitating the development of hypertension.[10] Primiparity was pointed out as a risk factor due to being related to a situation of atypical stress.[10]

In the preventive scope, the systematic review by Darwin Ciro Nascimento de Moura (2023) gathered a population of 152,506 pregnant women at risk of PE, confirming the efficacy of prophylactic use of acetylsalicylic acid (AAS) at a dosage of 150 mg/day and calcium 1.5 g/day in relation to the decrease in the incidence of PE (67.2%) if started before the 16th week until the 36th week.[11] However, satisfactory results were not obtained as a protective measure against the disease if the medication started late.[11]

The isolated use of AAS was demonstrated by Jillian Henderson et al. (2021) in 26,952 participants at risk for PE, recruited from the analysis of 23 randomized clinical trials, with Aspirin® doses ranging from 50 mg/day to 150 mg/day, being significantly associated with a lower risk of PE (RR 0.85, CI 95%0.75 to 0.95), perinatal mortality (RR 0.79, CI 0.66 to 0.96), premature birth (RR 0.80, CI 0.67 to 0.95), and intrauterine growth restriction (RR 0.82, CI 0.68 to 0.99).[12] There were no notorious associations between the use of the medication and the risk of postpartum hemorrhage (RR 1.03, CI 0.94 to 1.12) and other bleeding-related harms, or with rare perinatal harms.[12]

The exclusive intake of calcium in the prevention of gestational hypertensive disorders, in turn, was studied by Hyo Kyozuka et al. (2020), who, through data from the Japan Environment Children's study (JECS), recruited 33,894 Japanese normotensive primiparous women between January 2011 and March 2014, with them being categorized into five quartiles (Q) according to the daily calcium intake before pregnancy; the median (interquartile) of each group from Q1 to Q5 was 199 (154−235), 321 (295−347), 430 (401−460), 567 (529−613), and 899 (755−1253) mg/day, respectively.[13]

The percentage of participants who presented a dietary calcium intake greater than 500 mg/day, 550 mg/day, 650 mg/day, 700 mg/day, 1,000 mg/day, 1,500 mg/day, and 2,000 mg/day were 38.9%, 32.1%, 21.6%, 18.0%, 7.9%, 3.3%, and 2.0%, respectively.[13] Regarding the obstetric outcome, no significant differences were found in the occurrence of gestational hypertension (GH) (p=0.719), early GH (p=0.739), and late GH (p=0.655) in primiparous women with any limit of pre-pregnancy calcium intake, requiring more studies to examine the effect of other pre-gestational dietary factors on obstetric outcomes for the formulation of earlier preventive strategies for primigravidae.[13]

In the analytical and retrospective study by José Juvenal Linhares (2014), delivery by cesarean section was significantly associated with women with PE, mainly in those with previous cesarean sections and obesity.[14] In this study, compared to patients without hypertensive history, pregnant women with a history of PE or chronic arterial hypertension had 2.5 times more chance of evolving to cesarean delivery, in addition to age over 35 years being an independent risk factor for cesarean sections in women with PE (rates of 50%).[14]

Rosa Marcela Castellón Pasos (2013) concluded that in 96% of severe PE cases, resolution occurred via cesarean section, a value justified by blood pressure levels that were difficult to control (44%), fetal growth restriction (30%), hypertensive encephalopathy (19%), HELLP syndrome (11%), and oliguria (7%).[15]

Discussion

Controlled cohort studies showed that women with a previous history of Preeclampsia and/or with antiphospholipid antibodies, pre-existing diabetes, multiple pregnancy (twin), nulliparity, family history, previous elevated blood pressure (diastolic ≥80 mmHg), high body mass index before pregnancy, and maternal age ≥40 years constitute increased risk factors for the development of the disease (Table 1), a risk that, according to individual studies, also increases with an interval ≥10 years since a previous pregnancy, autoimmune and kidney diseases, and chronic hypertension.[9]

Table I - Risk factors related to the occurrence of pre-eclampsia

Característica clínica	Risco relativo	
Hipertensão arterial crônica (PAD 80-89 na 1ª consulta pré-natal)	1,38	1,01-1,87
Idade > 40 anos e primípara	1,69	1,23-2,29
Idade > 40 anos e multípara	1,96	1,34 -2,87
IMC > 30 na primeira consulta pré-natal	2,12	1,56-2,88
História familiar de pré-eclâmpsia (mãe, avó, irmã)	2,90	1,70-4,93
Nuliparidade	2,91	1,28-6,61
Gestação múltipla	2,93	2,04-4,21
Diabetes melito preexistente	3,56	2,54 4,99
História pregressa de pré-eclâmpsia	7,19	5,85-8,83
Síndrome de anticorpo antifosfolípide	9,72	4,34-21,75

Source: Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. Duckitt K, Harrington D., 2005.

Aiming at prevention, the recommended interventions capable of resulting in a reduction in the risks of developing preeclampsia are the use of acetylsalicylic acid (AAS) at a dose of 100 to 150 mg/day taken at night and calcium supplementation in doses ≥1 g/day, both initiated between the 12th and 16th weeks and suspended from the 36th week, obtaining better results in patients identified as at risk and with low daily calcium intake.[12,16-18]

Final Considerations

Preeclampsia has a multifactorial context, and the early identification of risk factors is essential in order to minimize them, in addition to the prophylactic implementation for the disease, when possible, aiming for better maternal-fetal outcomes and reduction of morbidity and mortality in this population.

Another point to highlight is that little is known about the associations between risk factors, which have been mainly studied in isolation.

Furthermore, new research is needed regarding the interaction between precipitating factors, pre-gestational dietary factors, and labor induction techniques, especially in women over 35 years of age, aiming for better obstetric outcomes in pregnant women with Preeclampsia.

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