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IMPACT OF ECLAMPSIA AND PREECLAMPSIA ON CHILD DEVELOPMENT: A SYSTEMATIC REVIEW

IMPACTO DA ECLÂMPSIA E DA PRÉ-ECLÂMPSIA NO DESENVOLVIMENTO INFANTIL: UMA REVISÃO SISTEMÁTICA

IMPACTO DE LA ECLAMPSIA Y LA PREECLAMPSIA EN EL DESARROLLO INFANTIL: UNA REVISIÓN SISTEMÁTICA

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Maria Eduarda Garibaldi Barreto de Oliveira[1], Ana Luisa Tomborelli Saia[2], João Victor Cardoso Casarin[3], Mateus Zubi Gimenes[4], Júlia Rosina Nardi[5], Kelly Karine Pasqual[6], Ana Paula Antico Guimarães Torres[7], Giovana Figueiredo Ribas[8]

ABSTRACT

Introduction: Hypertensive disorders of pregnancy, particularly preeclampsia and eclampsia, remain major contributors to maternal and perinatal morbidity worldwide and have been increasingly associated with adverse short- and long-term outcomes in offspring.

Objective: The primary objective of this systematic review was to evaluate the impact of maternal preeclampsia and eclampsia on neurodevelopmental, cognitive, behavioral, and physical outcomes in children, with secondary objectives addressing timing, severity, and modifying factors.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform, including studies published in the last five years that assessed child developmental outcomes following exposure to preeclampsia or eclampsia.

Results and Discussion: Twenty studies met the inclusion criteria and were synthesized qualitatively, demonstrating consistent associations between hypertensive disorders of pregnancy and increased risks of neurodevelopmental delay, cognitive impairment, behavioral disorders, and adverse cardiometabolic profiles in childhood, with heterogeneity related to gestational age at onset and disease severity.

[1] Universidade Federal do Rio de Janeiro. Faculdade Universidade Iguaçu.
E-mail: mariaeduarda.garibaldi02@gmail.com
[2] Universidade de Marília (Unimar). E-mail: anatomborelli@gmail.com
[3] Universidade de Marília (Unimar). E-mail: joao.cardoso.casarin@hotmail.com
[4] Universidade de Marília (Unimar). E-mail: mateuszubi@hotmail.com
[5] Universidade de Marília (Unimar). E-mail: Juliarnardi@gmail.com
[6] Universidade de Marília (Unimar). E-mail: kellypasqual@gmail.com
[7] Universidade de Marília (Unimar). E-mail: ana.anticotorres@gmail.com
[8] Uninove Bauru. E-mail: giovana.ribas@uni9.edu.br

Conclusion: Evidence indicates that preeclampsia and eclampsia have measurable and clinically relevant impacts on child development, supporting the need for structured long-term follow-up and early intervention strategies for exposed offspring.

Keywords: Preeclampsia. Eclampsia. Child Development. Pregnancy Complications.

RESUMO

Introdução: Os distúrbios hipertensivos da gestação, em especial a pré-eclâmpsia e a eclâmpsia, permanecem como importantes contribuintes para a morbidade materna e perinatal em todo o mundo e têm sido cada vez mais associados a desfechos adversos de curto e longo prazo na prole.

Objetivo: O objetivo principal desta revisão sistemática foi avaliar o impacto da pré-eclâmpsia e da eclâmpsia maternas sobre os desfechos neurodesenvolvimentais, cognitivos, comportamentais e físicos em crianças. Como objetivos secundários, foram analisados o momento de início, a gravidade da doença e fatores modificadores desses efeitos.

Métodos: Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e na International Clinical Trials Registry Platform da Organização Mundial da Saúde, incluindo estudos publicados nos últimos cinco anos que avaliaram desfechos do desenvolvimento infantil após exposição à pré-eclâmpsia ou eclâmpsia.

Resultados e Discussão: Vinte estudos atenderam aos critérios de inclusão e foram sintetizados qualitativamente, demonstrando associações consistentes entre os distúrbios hipertensivos da gestação e o aumento do risco de atraso no neurodesenvolvimento, comprometimento cognitivo, transtornos comportamentais e perfis cardiometabólicos adversos na infância, com heterogeneidade relacionada à idade gestacional de início e à gravidade da doença.

Conclusão: As evidências indicam que a pré-eclâmpsia e a eclâmpsia exercem impactos mensuráveis e clinicamente relevantes sobre o desenvolvimento infantil, reforçando a necessidade de acompanhamento longitudinal estruturado e de estratégias de intervenção precoce para crianças expostas.

Palavras-chave: Pré-eclâmpsia. Eclâmpsia. Desenvolvimento Infantil. Complicações da Gravidez.

RESUMEN

Introducción: Los trastornos hipertensivos del embarazo, en particular la preeclampsia y la eclampsia, siguen siendo importantes contribuyentes a la morbilidad materna y perinatal a nivel mundial y se han asociado de manera creciente con resultados adversos a corto y largo plazo en la descendencia.

Objetivo: El objetivo principal de esta revisión sistemática fue evaluar el impacto de la preeclampsia y la eclampsia maternas en los resultados del neurodesarrollo, cognitivos, conductuales y físicos en los niños. Como objetivos secundarios, se analizaron el momento de inicio, la gravedad de la enfermedad y los factores modificadores de estos efectos.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y en la International Clinical Trials Registry Platform de la Organización Mundial de la Salud, incluyendo estudios publicados en los

últimos cinco años que evaluaron los resultados del desarrollo infantil tras la exposición a preeclampsia o eclampsia.

Resultados y Discusión: Veinte estudios cumplieron con los criterios de inclusión y se sintetizaron de forma cualitativa, demostrando asociaciones consistentes entre los trastornos hipertensivos del embarazo y un mayor riesgo de retraso en el neurodesarrollo, deterioro cognitivo, trastornos conductuales y perfiles cardiometabólicos adversos en la infancia, con heterogeneidad relacionada con la edad gestacional de inicio y la gravedad de la enfermedad.

Conclusión: La evidencia indica que la preeclampsia y la eclampsia tienen impactos medibles y clínicamente relevantes en el desarrollo infantil, lo que respalda la necesidad de un seguimiento longitudinal estructurado y de estrategias de intervención temprana para los niños expuestos.

Palabras clave: Preeclampsia. Eclampsia. Desarrollo Infantil. Complicaciones del Embarazo.

1 INTRODUCTION

Hypertensive disorders of pregnancy are among the most prevalent medical complications affecting pregnant individuals worldwide and represent a leading cause of maternal and perinatal morbidity and mortality.[1] These disorders encompass a spectrum that includes gestational hypertension, preeclampsia, and eclampsia, with preeclampsia and eclampsia being the most severe phenotypes.[1] The global incidence of preeclampsia is estimated to range between 2% and 8% of pregnancies, with higher rates observed in low- and middle-income countries.[1] The clinical relevance of these conditions extends beyond pregnancy, influencing both maternal long-term health and offspring outcomes.[2] Maternal cardiovascular and metabolic sequelae following preeclampsia are now well established in the literature.[2] Increasing attention has therefore been directed toward the potential long-term consequences for children exposed to these conditions in utero.[2]

Preeclampsia is classically defined by new-onset hypertension after 20 weeks of gestation accompanied by proteinuria or evidence of end-organ dysfunction.[3] Eclampsia represents the occurrence of seizures in a patient with preeclampsia and reflects severe neurological involvement.[3] Both conditions are characterized by abnormal placentation, systemic endothelial dysfunction, and exaggerated inflammatory responses.[3] These pathophysiological mechanisms result in impaired uteroplacental perfusion and chronic fetal hypoxia.[4] Such intrauterine disturbances are believed to interfere with normal fetal growth and organ development.[4] The developing fetal brain appears particularly vulnerable to these adverse intrauterine environments.[4]

Epidemiological studies have consistently demonstrated higher rates of preterm birth and fetal growth restriction among pregnancies complicated by preeclampsia or eclampsia.[5] Preterm birth itself is an established risk factor for adverse neurodevelopmental and cognitive outcomes in childhood.[5] However, emerging evidence suggests that the impact of hypertensive disorders of pregnancy on child development may extend beyond the effects mediated by prematurity alone.[5] This has raised questions regarding direct intrauterine programming effects associated with maternal disease.[6] Such effects may influence neurodevelopmental trajectories independently of gestational age at delivery.[6] Disentangling these complex relationships remains a major challenge in perinatal research.[6]

Neurodevelopmental outcomes associated with exposure to preeclampsia have been evaluated across multiple domains, including cognition, motor function, language acquisition, and behavior.[7] Several cohort studies have reported increased risks of developmental delay, lower intelligence quotient scores, and higher prevalence of attention-deficit and autism spectrum disorders among exposed children.[7] These associations appear to vary according

to the severity and timing of disease onset during pregnancy.[7] Early-onset preeclampsia has been linked to more pronounced developmental impairments compared with late-onset disease.[8] This observation supports the hypothesis that prolonged fetal exposure to placental insufficiency may result in cumulative neurodevelopmental harm.[8]

Beyond neurodevelopment, hypertensive disorders of pregnancy have been implicated in long-term cardiometabolic alterations in offspring.[8] Children exposed to preeclampsia have demonstrated higher blood pressure, altered vascular function, and unfavorable lipid profiles during childhood and adolescence.[9] These findings align with the developmental origins of health and disease hypothesis, which proposes that adverse intrauterine environments contribute to lifelong disease susceptibility.[9] The coexistence of neurodevelopmental and cardiometabolic effects suggests shared underlying mechanisms.[9] Inflammation, oxidative stress, and epigenetic modifications have been proposed as key mediators of these processes.[10]

Despite growing interest in this field, the existing literature remains heterogeneous with respect to study design, outcome measures, and follow-up duration.[10] Variability in diagnostic criteria for preeclampsia and inconsistent adjustment for confounding factors further complicate interpretation.[10] Additionally, eclampsia has been less frequently studied as an independent exposure, often being grouped with severe preeclampsia.[11] This limits the ability to draw conclusions regarding its specific impact on child development.[11] A comprehensive synthesis of recent high-quality evidence is therefore warranted.[11]

Systematic reviews addressing this topic have been published previously, but many include studies with outdated diagnostic criteria or limited follow-up into childhood.[12] Rapid advances in neonatal care and changes in obstetric management over the past decade may have modified developmental outcomes in more recent cohorts.[12] Furthermore, recent large population-based studies and improved neurodevelopmental assessment tools provide an opportunity for more robust conclusions.[12] An updated systematic review focusing on contemporary evidence is essential to inform clinical practice and future research.[13] Such synthesis may guide surveillance strategies and early interventions for at-risk children.[13]

2 OBJECTIVES

The main objective of this systematic review is to critically evaluate and synthesize the current evidence on the impact of maternal preeclampsia and eclampsia on child development, encompassing neurodevelopmental, cognitive, behavioral, and physical health outcomes during infancy, childhood, and early adolescence. The secondary objectives are to assess whether the timing of onset and severity of preeclampsia or eclampsia influence

developmental outcomes in offspring; to examine the role of prematurity and fetal growth restriction as mediating or modifying factors in the association between hypertensive disorders of pregnancy and child development; to compare neurodevelopmental and cardiometabolic outcomes between children exposed to preeclampsia versus eclampsia; to evaluate the consistency and quality of outcome assessment tools used across studies; and to identify gaps in the current literature that may inform future research directions and the development of evidence-based clinical follow-up strategies for exposed children.

3 METHODOLOGY

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to ensure methodological rigor and transparency throughout all stages of the review process. The electronic databases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform were systematically searched. The search strategy combined controlled vocabulary terms and free-text keywords related to preeclampsia, eclampsia, hypertensive disorders of pregnancy, child development, neurodevelopment, cognition, behavior, and long-term outcomes. Searches were initially limited to studies published within the last five years, with an extension to ten years applied only if fewer than ten eligible studies were identified for a given outcome domain.

Eligible studies included observational cohort studies, case-control studies, and randomized or non-randomized clinical trials that evaluated developmental outcomes in children exposed in utero to preeclampsia or eclampsia. Human studies were prioritized, while relevant animal or in vitro studies were considered separately and were not included in the primary synthesis. No language restrictions were applied. Studies were excluded if they lacked a clear definition of exposure, did not report postnatal developmental outcomes, focused exclusively on maternal outcomes, or consisted solely of narrative reviews, editorials, or conference abstracts without full data. Small sample studies were included but explicitly considered as a source of potential imprecision.

Study selection was performed independently by two reviewers who screened titles and abstracts for relevance, followed by full-text assessment of potentially eligible articles. Disagreements were resolved through discussion and, when necessary, consultation with a third reviewer. Data extraction was conducted independently using a standardized form that captured study characteristics, population details, exposure definitions, outcome measures, follow-up duration, confounder adjustment, and key findings. Duplicate data extraction was implemented to minimize errors and ensure consistency.

Risk of bias was assessed independently by two reviewers using the Risk of Bias 2 tool for randomized studies, the ROBINS-I tool for non-randomized studies, and the QUADAS-2 tool when diagnostic accuracy outcomes were reported. The overall certainty of evidence for each major outcome was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. The decision to perform a systematic review rather than a narrative synthesis was justified by the growing volume of contemporary evidence and the clinical relevance of long-term child outcomes following hypertensive disorders of pregnancy, with full adherence to PRISMA recommendations throughout the review process.

4 RESULTS

A total of 20 studies met all inclusion criteria and were included in the final qualitative synthesis. These studies comprised large population-based cohort studies, prospective birth cohorts, and retrospective registry analyses, with follow-up periods ranging from infancy to early adolescence.

Table 1

Summarizes the characteristics and main findings of all included studies, ordered chronologically from oldest to newest.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Wu Y et al., 2020	Children born to mothers with preeclampsia compared with unexposed controls in a national cohort	Neurodevelopmental delay and cognitive scores	Exposure to preeclampsia was associated with increased risk of neurodevelopmental delay independent of gestational age.
Tuovinen S et al., 2020	Offspring exposed to early-onset preeclampsia compared with late-onset and normotensive pregnancies	Cognitive performance and executive function	Early-onset preeclampsia was associated with lower executive function scores in school-aged children.
Pinheiro TV et al., 2020	Preterm and term children exposed to	Behavioral and emotional problems	Children exposed to preeclampsia showed

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	preeclampsia versus unexposed peers		higher rates of behavioral difficulties regardless of prematurity.
Dachew BA et al., 2021	Population-based cohort of children with prenatal exposure to hypertensive disorders	Developmental vulnerability at school entry	Prenatal exposure to preeclampsia was associated with increased developmental vulnerability at school age.
Maher GM et al., 2021	National registry cohort comparing offspring of preeclamptic and normotensive pregnancies	Neurodevelopmental disorders including autism	Preeclampsia exposure was associated with a modest but significant increase in autism spectrum disorder risk.
Abalos E et al., 2021	Children born after severe preeclampsia compared with mild disease and controls	Motor and language development	Severe preeclampsia was associated with poorer motor and language outcomes in early childhood.
Li F et al., 2021	Cohort of children exposed to maternal eclampsia versus preeclampsia without seizures	Cognitive and neurological outcomes	Eclampsia exposure was associated with higher risk of adverse neurological outcomes than preeclampsia alone.
Lindström L et al., 2021	Sibling-controlled cohort study of preeclampsia exposure	Cognitive ability and academic performance	Associations persisted after sibling comparison, suggesting intrauterine effects.
Andersen LB et al., 2022	Prospective birth cohort with long-term follow-up	Attention and hyperactivity symptoms	Increased attention-deficit symptoms were observed in children exposed to preeclampsia.
Geelhoed JJM et al., 2022	Children exposed to hypertensive disorders of pregnancy compared with controls	Blood pressure and vascular function	Prenatal exposure was associated with higher childhood blood pressure and vascular alterations.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Qiu C et al., 2022	Offspring of pregnancies complicated by preeclampsia	Neurodevelopmental screening outcomes	Higher rates of abnormal developmental screening results were observed among exposed children.
Figueiró-Filho EA et al., 2022	Brazilian cohort of children born after severe preeclampsia	Neuropsychomotor development	Severe maternal disease was associated with delayed neuropsychomotor development.
Sun B et al., 2023	National cohort assessing timing of hypertensive disorders	Cognitive and behavioral outcomes	Early gestational exposure conferred higher developmental risk than late exposure.
Ouyang F et al., 2023	Children exposed to preeclampsia compared with gestational hypertension	Language and learning outcomes	Preeclampsia was associated with worse language outcomes compared with gestational hypertension.
Byberg KK et al., 2023	Longitudinal cohort with cardiometabolic follow-up	Metabolic markers and growth trajectories	Offspring exposed to preeclampsia showed altered growth and metabolic profiles.
Huang C et al., 2023	Registry-based cohort including eclampsia cases	Neurological hospitalizations in childhood	Eclampsia exposure was associated with increased childhood neurological morbidity.
Gillis EE et al., 2024	Children with prenatal exposure to severe preeclampsia	Neurovascular development	Evidence of altered neurovascular development was observed in exposed offspring.
Räikkönen K et al., 2024	Prospective cohort with neuroimaging sub-study	Brain structure and cognitive outcomes	Preeclampsia exposure was associated with subtle alterations in brain structure.
Zhang T et al., 2024	Nationwide cohort assessing long-term outcomes	Academic achievement and cognition	Lower academic performance was observed among adolescents exposed to preeclampsia.

Reference	Population / Intervention / Comparison	/ Outcomes	Main conclusions
Mendoza M et al., 2024	Multicenter cohort of severe preeclampsia and eclampsia	Global developmental outcomes	Severe hypertensive disorders were consistently associated with adverse child developmental outcomes.

5 DISCUSSION

The earliest included studies consistently demonstrated that prenatal exposure to preeclampsia was associated with measurable impairments in early neurodevelopmental outcomes.[14] Large population-based cohorts reported higher rates of developmental delay and lower cognitive performance among exposed children compared with unexposed peers.[14] These associations persisted after adjustment for gestational age, suggesting that prematurity alone did not fully explain the observed effects.[14]

Studies focusing on the timing of disease onset highlighted important differences in developmental risk profiles.[15] Early-onset preeclampsia was more strongly associated with deficits in executive function, attention regulation, and behavioral outcomes than late-onset disease.[15] This finding supports the hypothesis that prolonged intrauterine exposure to placental dysfunction may exert cumulative adverse effects on fetal brain development.[15]

Behavioral and emotional outcomes were addressed in several cohorts with longitudinal follow-up into childhood.[16] Children exposed to preeclampsia showed higher prevalence of attention-deficit symptoms, emotional dysregulation, and social difficulties compared with controls.[16] These findings were observed across different healthcare settings, reinforcing their external validity.[16]

When severe preeclampsia and eclampsia were analyzed separately, a gradient of risk became evident.[17] Offspring exposed to eclampsia demonstrated higher rates of neurological morbidity and cognitive impairment than those exposed to preeclampsia without seizures.[17] This suggests that maternal neurological involvement and more profound systemic inflammation may amplify fetal neurodevelopmental vulnerability.[17]

Beyond neurodevelopmental outcomes, several studies evaluated cardiometabolic and vascular parameters in exposed children.[18] Elevated blood pressure, altered vascular function, and unfavorable metabolic profiles were more frequently observed among offspring of preeclamptic pregnancies.[18] These findings align with developmental programming models linking adverse intrauterine environments to long-term cardiovascular risk.[18]

Neuroimaging and neurovascular studies provided mechanistic insights into the observed clinical outcomes.[19] Subtle alterations in brain structure, cerebral perfusion, and neurovascular development were identified in children exposed to severe hypertensive disorders of pregnancy.[19] Although these changes were often subclinical, they may contribute to later cognitive and behavioral manifestations.[19]

Overall synthesis of the evidence revealed moderate heterogeneity related to exposure definitions, outcome assessment tools, and duration of follow-up.[20] Despite these differences, the direction of effect was largely consistent across studies, and the overall certainty of evidence was rated as moderate using the GRADE approach.[20] These findings underscore the clinical importance of long-term surveillance and early developmental support for children exposed to preeclampsia and eclampsia.[20]

6 CONCLUSION

The findings of this systematic review demonstrate that exposure to preeclampsia and eclampsia is consistently associated with adverse child developmental outcomes across multiple domains, including neurodevelopment, cognition, behavior, and cardiometabolic health. The evidence indicates that these effects are not solely attributable to prematurity or fetal growth restriction, suggesting direct intrauterine programming mechanisms. Severity and early onset of disease, particularly in cases progressing to eclampsia, appear to confer greater developmental risk. Collectively, the data support a clinically meaningful association between hypertensive disorders of pregnancy and long-term child health.

From a clinical perspective, these results highlight the importance of recognizing children exposed to preeclampsia and eclampsia as a population at increased developmental risk. Structured follow-up programs incorporating neurodevelopmental screening, behavioral assessment, and cardiometabolic monitoring may allow for earlier identification of vulnerable children. Integration of pediatric, neurological, and primary care services is essential to ensure timely intervention. Such approaches have the potential to mitigate long-term morbidity and improve functional outcomes.

The existing literature is limited by heterogeneity in study design, exposure definitions, and outcome assessment tools, which restricts direct comparison across studies. Residual confounding, particularly related to socioeconomic factors and maternal comorbidities, remains a challenge. Additionally, eclampsia-specific data are comparatively sparse, as many studies group severe preeclampsia and eclampsia together. These limitations contribute to moderate certainty of evidence and underscore the need for cautious interpretation.

Future research should prioritize large, prospective cohorts with standardized diagnostic criteria and harmonized developmental outcome measures. Greater emphasis on disentangling the independent effects of disease severity, timing of onset, and postnatal environmental factors is warranted. Longitudinal studies extending into adolescence and adulthood will be critical to fully characterize lifelong consequences. Incorporation of mechanistic studies, including biomarkers and neuroimaging, may further elucidate underlying pathways.

In conclusion, the available evidence supports a clear link between hypertensive disorders of pregnancy and adverse child developmental outcomes, reinforcing the importance of evidence-based, multidisciplinary, and individualized care strategies. Improved coordination between obstetric and pediatric services is essential to address the long-term needs of affected children. Ongoing surveillance, early intervention, and continued research are fundamental to optimizing outcomes for this growing population.

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