

REVIEW

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Maternal and fetal neurocognitive outcomes in preeclampsia and eclampsia; a narrative review of current evidence

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Abstract

Hypertensive disorders of pregnancy (HDP), such as preeclampsia and eclampsia, present significant risks to maternal and fetal health. While immediate complications are well-documented, emerging research highlights potential neurocognitive impacts on both mothers and their offspring. This narrative review synthesizes evidence on these neurocognitive outcomes associated with HDP, focusing on preeclampsia and eclampsia. A literature search was conducted for studies published from 2000 to February 2024. Maternal outcomes, including memory, executive function, and psychosocial well-being, were assessed across 11 studies, while fetal and neonatal neurocognitive outcomes were explored in five studies. Consistent findings indicate that preeclampsia and eclampsia are linked to impairments in maternal cognitive functions and psychosocial health. Offspring exposed to these conditions in utero also show cognitive deficits and alterations in brain connectivity. Contributing factors include placental dysfunction, altered angiokine levels, maternal stress, and socioeconomic variables. To mitigate these impacts, future research should focus on clarifying the underlying mechanisms and developing early interventions. This review emphasizes the necessity of multidisciplinary approaches to improve neurocognitive outcomes for both mothers and their children affected by preeclampsia and eclampsia.

Keywords Hypertensive disorders of pregnancy, Preeclampsia, Eclampsia, Neurocognitive outcomes, Maternal health, Fetal health

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Introduction

Hypertensive disorders of pregnancy (HDP) constitute a significant threat to maternal health globally, contributing to nearly 18% of all maternal deaths, with an estimated 62,000 to 77,000 deaths annually [1]. Among these disorders, preeclampsia and eclampsia are significant due to their severe implications for maternal and fetal health. Preeclampsia is characterized by new-onset hypertension and is often accompanied by proteinuria [2]. In cases where proteinuria is not present, preeclampsia can also be identified by the presence of other severe symptoms such as thrombocytopenia, renal insufficiency, liver dysfunction, pulmonary edema, or severe headache unresponsive to medication, as well as visual disturbances [2]. This condition affects approximately 5% of pregnancies and can lead to serious complications including acute renal failure, cerebral edema, and coagulopathy [3, 4]. The clinical presentation of preeclampsia varies, but it commonly involves both elevated blood pressure and evidence of multi-organ involvement [4]. Eclampsia represents a severe progression of preeclampsia and is defined by the occurrence of seizures in a patient who has preeclampsia [2]. These seizures are not attributable to other causes and mark a critical escalation in the severity of the disorder [2]. Eclampsia is less common than preeclampsia, with an incidence of about 1.4% among those with preeclampsia [3]. The risk of maternal mortality and morbidity is significantly increased in cases of eclampsia, showing the urgency of prompt diagnosis and management [5]. Globally, the incidence of preeclampsia is notably higher in developing countries compared to developed nations, with preeclampsia occurring seven times more frequently in the former [5]. Eclampsia continues to elevate maternal mortality risks in both settings [6]. The systematic review by Abalos et al., which analyzed data from 39 million pregnancies, highlights the substantial burden of these conditions and emphasizes the need for improved preventive and therapeutic strategies [3].

Beyond the immediate risks associated with preeclampsia and eclampsia, emerging research indicates that women often encounter cognitive challenges in the years following these hypertensive pregnancies [7]. These challenges include subjective cognitive issues, including physical and psychological symptoms, significantly impacting the overall physical, social, and emotional well-being of affected individuals when compared to women with a history of normotensive pregnancies (hNTP) [8]. Moreover, the severity of preeclampsia tends to correlate with the intensity of these reported symptoms [9].

At the neurobiological level, preeclampsia and eclampsia affect cognitive function [10]. The elevated

blood pressure and associated endothelial dysfunction lead to microvascular damage in the brain [11]. This damage has been shown to result in ischemia in key brain regions, contributing to cognitive deficits such as memory impairment and executive dysfunction [12]. Structural brain abnormalities have been observed in individuals with a history of these hypertensive disorders [3]. These alterations disrupt neural connectivity and compromise cognitive functions, including planning, decision-making, and memory. Functional brain changes also play a role [5]. Neuroimaging studies have shown altered activation patterns and connectivity in brain regions associated with cognitive processes [6, 7]. These functional changes reflect the impact of the hypertensive environment on neural networks and cognitive control.

The interplay between neurocognitive and neurodevelopmental outcomes is particularly significant. Neurodevelopmental issues can have long-term implications for cognitive and emotional development [13]. The interplay between maternal and fetal/neonatal neurocognitive outcomes shows the bidirectional impact of hypertensive disorders. Maternal cognitive impairments can influence parenting capacity and psychosocial well-being, which in turn can affect the developmental environment for the child [14]. Conversely, neurodevelopmental issues in offspring can contribute to increased maternal stress and potentially exacerbate cognitive impairments in mothers [11]. This cyclical relationship highlights the need for comprehensive approaches to address both maternal and fetal/neonatal health in the context of HDP.

This narrative review seeks to explore areas related to the neurocognitive outcomes of preeclampsia and eclampsia. It provides an examination of the nature and extent of cognitive impairments experienced by women with a history of these hypertensive disorders. This includes a look at deficits in memory, executive function, and other cognitive domains that arise following preeclampsia or eclampsia. The review also explores the mechanisms underlying these cognitive impairments. It investigates how microvascular damage, alterations in brain structure and function, and the effects of psychological stress contribute to the observed cognitive deficits. In addition, the review evaluates the neurocognitive outcomes for offspring born after pregnancies complicated by these hypertensive disorders. It examines cognitive deficits, as well as structural and functional brain alterations, and considers the potential long-term effects on these children's development. Current interventions and management strategies are also discussed, focusing on how existing treatments can mitigate cognitive impairments.

Methodology

Study design

This study employed a narrative review methodology to evaluate the existing literature on maternal and fetal neurocognitive outcomes associated with hypertensive disorders of pregnancy (HDP), focusing primarily on preeclampsia and eclampsia.

Literature search strategy

A literature search was conducted across PubMed/MEDLINE, Embase, Web of Science, PsycINFO, and Scopus. These databases are leading sources for medical literature and provide access to a broad range of peer-reviewed articles in medicine and related fields (Table 1). The search strategy was developed using relevant keywords and Medical Subject Headings (MeSH) terms, covering concepts related to hypertensive disorders of pregnancy, neurocognitive outcomes, maternal health, fetal health, and associated pathophysiological mechanisms. The search was limited to studies published in English-language peer-reviewed journals.

Study selection criteria

Studies will be included in the review if they meet the following criteria:

- Focus on maternal and/or fetal neurocognitive outcomes following hypertensive disorders of pregnancy, specifically preeclampsia and eclampsia.
- Include original research articles published in peer-reviewed journals.
- Provide clear documentation of diagnostic criteria for hypertensive disorders of pregnancy.
- Report quantitative data related to neurocognitive outcomes, including but not limited to cognitive function, memory, executive function, attention, and psychological well-being.
- Studies conducted on human subjects.
- Published between 2000 and February 2024 (the past two decades have seen significant advancements in the understanding of hypertensive disorders during pregnancy, including improvements in diagnostic criteria, management strategies, and research methodologies).

Studies are excluded if they are reviews, commentaries, editorials, or conference abstracts without full-text availability.

Table 1 Methodology

| Section | Description |
|-----------------------------|--|
| Study design | Narrative review methodology |
| Literature search | PubMed/MEDLINE |
| Strategy | Embase Web of Science PsycINFO Scopus Search strategy using relevant keywords and MeSH terms Limited to English-language peer-reviewed journals |
| Study selection | Inclusion criteria: |
| Criteria | <ul style="list-style-type: none"> – Focus on maternal and/or fetal neurocognitive outcomes following preeclampsia/eclampsia – Original research articles in peer-reviewed journals – Clear documentation of diagnostic criteria for preeclampsia/eclampsia – Report quantitative data on neurocognitive outcomes – Studies on human subjects – Published between 2000 and February 2024 Exclusion criteria: <ul style="list-style-type: none"> – Reviews, commentaries, editorials, or conference abstracts without full-text availability |
| Data extraction | Two independent reviewers screened titles and abstracts for eligibility Full-text articles of potentially eligible studies were retrieved and assessed Discrepancies between reviewers were resolved through discussion and consensus Standardized data extraction form used |
| Data synthesis and analysis | Narrative synthesis approach employed Data synthesized according to key themes |

Data extraction

Two independent reviewers screened the titles and abstracts of identified studies for eligibility based on the predefined inclusion and exclusion criteria. They then retrieved full-text articles of potentially eligible studies and assessed them for final inclusion. Any discrepancies between reviewers were resolved through discussion and consensus.

Data extraction was performed using a standardized data extraction form, capturing relevant information, including study characteristics (e.g., author, publication year, study design), participant demographics, neurocognitive outcomes assessed, and key findings related to maternal and fetal neurocognitive health.

Data synthesis and analysis

A narrative synthesis approach was employed to summarize the findings of included studies. Data was synthesized according to key themes, including maternal neurocognitive outcomes, fetal and neonatal neurodevelopment, shared pathophysiological mechanisms, long-term implications, and clinical relevance.

Current evidence

The studies reviewed investigated the impact of preeclampsia and eclampsia on maternal cognitive functioning and fetal/neonatal cognitive development. Eleven studies focused on maternal cognitive functioning. Table 2. The total number of participants across these studies is 4737. Five studies focused on fetal/neonatal cognitive development. The total number of participants across these studies is 4911. Studies utilized neuropsychological test batteries to assess various cognitive domains, including memory, executive function, attention, and working memory.

Maternal neurocognitive outcomes

Memory

Several studies have examined the impact of preeclampsia on memory function. Brussé et al. [10] and Dayan et al. [11] both identified memory impairments in women with a history of preeclampsia. Brussé et al. [10] specifically reported lower scores on auditory-verbal memory tests among formerly preeclamptic women, whereas Dayan et al. [11] found reduced performance on memory-related cognitive tests, including the Digit Symbol Substitution Test and the Rey Auditory Verbal Learning Test. Dayan et al. [11] also observed that preeclamptic individuals recalled fewer words and showed reduced memory retention after interference. Despite these findings, the study concluded that preeclampsia does not appear to independently contribute to

long-term neurocognitive impairment, as similar differences were noted between other hypertensive disorders of pregnancy and normotensive pregnancies.

In contrast, Ibarra et al. [12] found that individuals with a history of preeclampsia had lower scores in attention and working memory compared to those with normotensive pregnancies. After adjusting for factors such as time, age, education, and pre-pregnancy body mass index, preeclamptic individuals reported more frequent memory problems. Birnie et al. [13] similarly identified lower verbal episodic memory scores in preeclamptic women, particularly in delayed logic memory tests. This study did not find evidence of accelerated age-related cognitive decline in comparison to women with normotensive pregnancies. Adank et al. [14] corroborated these findings, showing that women with a history of preeclampsia performed worse on verbal memory tests compared to those with normotensive pregnancies.

In terms of eclampsia, Postma et al. [15] highlighted that women with eclampsia experienced increased levels of anxiety, depression, and perceived cognitive difficulties in daily life. This psychosocial impact likely exacerbates perceived memory deficits. However, specific studies focusing on eclampsia-related memory impairment are less common, suggesting a need for further research to isolate the cognitive impacts of eclampsia from those associated with preeclampsia.

Executive function

Several studies suggest that preeclampsia is linked to impairments in executive function, including planning, problem-solving, and decision-making. Alers et al. [16] found that 23.2% of women with a history of preeclampsia experienced significant declines in executive function post-partum, compared to only 2.2% of controls. Despite the attenuation of group differences over time, the impact remained statistically significant at least 19 years postpartum. Women with preeclampsia had more pronounced declines in global cognition and attention/executive z-scores compared to women with normotensive pregnancies. Fields et al. [17] also observed trends towards increased frequency of mild cognitive impairment or dementia in women with a history of preeclampsia, particularly affecting executive function and verbal list learning. Eclampsia exacerbates these cognitive declines, although direct comparisons between eclampsia and preeclampsia in terms of executive function are less frequently addressed in the literature. Nonetheless, the evidence suggests that eclampsia could further impair executive functions due to its more severe manifestations of hypertension and associated complications.

Table 2 Characteristics of included studies

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|----------------------|-----------------------|------------|----------------------------|--|-------------------------------|--|
| Postma et al. (2014) | Cross-sectional study | 145 | Eclampsia and preeclampsia | Compared to the control group, preeclamptic and eclamptic women had significantly worse overall cognitive failure questionnaire scores, scoring lower in the forgetfulness, distractibility, and false triggering subscales. Furthermore, on the neuropsychologic tests, compared to the control group, preeclamptic and eclamptic women had significantly lower results in only the motor function domain. Other domains (executive functioning, attention, long-term memory, working memory, and visual perception) showed no significant differences between all groups | Nil | Preeclamptic and eclamptic women had significantly lower total scores on the hospital anxiety and depression scale |
| Brusse et al. (2008) | Case-control study | 20 | Preeclampsia | Compared to the control group, preeclamptic women had significantly lower scores in the memory domain of the neuropsychological test. Consequently, they learned fewer words and had less recall after interference. There were no significant differences between both groups in executive functioning, in the reading, language, attention and concentration tests | Nil | Preeclamptic women had worse depression and anxiety scores, but the difference was not statistically significant |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|------------------------|-----------------------|------------|---------------------------|--|---|---|
| Alers et al. (2023) | Cross-sectional study | 1563 | Preeclampsia | Women with a history of preeclampsia had a 23.2% absolute risk of suffering a decrease in overall executive function compared to 2.2% in normotensive women in the first year of childbirth; this difference was statistically significant ($P < 0.05$) and evident up to 19 years after delivery. Also, women with a history of preeclampsia had a 30.1% absolute risk of experiencing a decline in their Metacognition Index compared to 5.9% in normotensive women, and the difference was statistically significant ($P < 0.05$) up to 20 years after delivery | Nil | Perinatal mortality, small gestational age children, preterm deliveries, caesarean deliveries, and mood or anxiety disorders were more common in women with preeclampsia than in normotensive women |
| Tuovinen et al. (2013) | Cohort study | 876 | Preeclampsia | Nil | Participants born to women with preeclampsia had more frequent self-reported complaints of cognitive failures, distractibility, and false triggering when compared to participants born to normotensive women A higher amount of self-reported complaints of dysexecutive functioning, behavioural emotional self-regulation, and executive cognition was seen in participants born to women with preeclampsia when compared to normotensive women | Participants born to mothers with preeclampsia had lower birth weights and shorter periods of gestation |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|----------------------|--|------------|---------------------------|--|-------------------------------|---|
| Fields et al. (2017) | Prospective cohort, case-control study | 80 | Preeclampsia | Although there were no statistically significant differences in any of the measures of cognition and mood for women with a history of preeclampsia and women with a history of normotensive pregnancies, a clinical diagnosis of cognitive impairment following clinical consensus was observed to a greater extent in women with a history of preeclampsia than in women with a history of normotensive pregnancies | Nil | A higher Body Mass Index, Coronary Artery Calcification, behavioural diagnosis of hypertension was seen in women with a history of preeclampsia than in women with a history of normotensive pregnancies. Also, coronary artery calcification was more in women with a history of preeclampsia that had cognitive impairment than in those who had a history of normotensive pregnancies. Importantly, in women with a history of preeclampsia with and without cognitive impairment, there was no significant difference in the use of medication with cognitive side effects, frequency of hypertension, Body Mass Index, hormone replacement therapy, or carriers of apolipoprotein E-4 polymorphism |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|-----------------------------|---------------------------------------|------------|---------------------------|---|--|--|
| van Wassenaer et al. (2011) | Prospective study | 216 | Preeclampsia | Nil | Intelligence quotient (IQ) scores were lower in children born to mothers with a history of preeclampsia than in the normal population. Their mean IQ was lesser than that of the general population by 8 points. However, 98 participants had a normal IQ, with 28 participants and 14 participants having a subnormal and an abnormal IQ, respectively. The magnitude of the number of children attending special education classes was 7 times more when compared to the general population. Motor function outcomes, neurological outcomes, and Behavioral outcomes were all comparable with the normal population. Surprisingly, this study found higher scores for behaviour among children whose mothers had a more clinical course of pregnancy | An abnormal outcome of 34% was recorded for the total 216 children with 38 infant deaths and 29 children with an abnormal developmental outcome. Overall, children born after 31 completed weeks of gestation had better outcomes with 70% perinatal mortality seen in children born at 26- and 27-weeks' gestation, and 30% perinatal mortality seen in children born at 28- and 29-weeks' gestation. Also, normal survival and normal developmental outcome were associated with increased birthweight. Gestational age and birthweight had no effect on IQ scores in a linear regression analysis |
| Postma et al. (2013) | Observational study, web-based survey | 1308 | Eclampsia | Cognitive failures in everyday task were significantly more frequently reported among women with a history of hypertensive disorders in pregnancy compared to women with normotensive pregnancies. These results were from scores on the Cognitive Failures Questionnaire (CFQ). Multivariate linear regression analysis revealed significantly worse self-reported cognitive failure in women with a previous history of eclampsia | Nil | Women with a history of hypertension in pregnancy had worse scores on the World Health Organization Quality of Life BREF (WHOQOL-BREF) US version questionnaire and on the Social Functioning Questionnaire (SFQ) when compared to women with a history of normotension pregnancies. These scores indicated a worse generic quality of life and poorer social functioning compared to women with a history of normotensive pregnancies |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|----------------------|---|------------|---------------------------|---|-------------------------------|---|
| Adank et al. (2021) | A nested cohort study (ORACLE) embedded in a population-based prospective cohort study (Generation R). The study was conducted 15 years after the index pregnancy | 596 | Preeclampsia | Women with a previous history of hypertensive disorders in pregnancy had poorer performances in some cognitive test domains including memory, recognition, color naming, letter digit substitution, and design organization than in women with a history of normotensive pregnancy. Even after adjusting for confounding factors, these results still remained significant | Nil | Although hypertensive disorders in pregnancy was negatively associated with the design organization test, Purdue Pegboard test, verbal fluency test, letter digit substitution task, Stroop color naming subtask, recognition subtask of the 15-word learning test, and g-factor, the negative association reduced to non-significant levels following adjustment for confounding factors like prepregnancy body mass index, educational level, and ethnicity |
| Birnie et al. (2024) | A prospective cohort study. The study was conducted 20 years after pregnancy | 3393 | Preeclampsia | In midlife, women with a history of gestational hypertension had a poorer verbal episodic memory compared to women with a history of normotensive pregnancy after controlling for baseline covariates and applying inverse proportional weighting to collected data. However, the same association was not observed for preeclampsia. The authors suggest that these findings might be due to selection bias in non-weighted analyses | Nil | Cognitive decline with age was observed in all cognitive function domains for women with a history of normotensive pregnancies. While the predicted trajectory for decline was similar across groups, women with a history of gestational hypertension had a lower predicted trajectory among the younger ages. Higher blood pressures in midlife were seen in women who experienced gestational hypertension and preeclampsia than in those who had normotensive pregnancies |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|----------------------|--|------------|---------------------------|--|-------------------------------|--|
| Dayan et al. (2023) | A retrospective cohort study. Data from the Coronary Artery Risk Development in Young Adults trial (CARDIA) was utilized. The study was done 25 years after delivery | 568 | Preeclampsia | 25 years after the affected pregnancy, women with a history of preeclampsia had poorer psychomotor speed and executive function compared to women with a history of normotensive pregnancy. There were no recorded differences in learning and memory between both groups. However, the association between preeclampsia and poorer cognitive function attenuated to nonsignificant levels after adjustment for age, body mass index, hypertension, education and depression. Hypertension and body mass index were found to be important mediators of the relationship between poor executive function and preeclampsia | Nil | When women with gestational hypertension were included in the analyses, the same pattern of results were seen. Cognitive function was worse women in women with hypertensive disorder in pregnancy in the unadjusted analyses, but there was no statistically significant difference after the analyses was adjusted for confounding factors |
| Ibarra et al. (2023) | A longitudinal, prospective, observational study | 30 | Preeclampsia | At 1 and 3 months after delivery, women with a history of preeclampsia had poorer performances on cognitive tests assessing, attention, working memory, and executive function in comparison with women with a history of normotensive pregnancy. These results remained significant after adjustments for time, age, education, and prepregnancy body mass index (BMI) | Nil | Nil |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|------------------------|-------------------------------|------------|----------------------------|--|---|--|
| Mielke et al. (2023) | An observational cohort study | 2239 | Preeclampsia and eclampsia | Declines in executive/attention z scores and global cognition were more marked in women with history of hypertensive disorders in pregnancy with the greatest decline in global cognition seen in women with a history of preeclampsia/eclampsia. Women with a history of preeclampsia/eclampsia also had the worst language and attention z scores. After adjustment for vascular risk factors, body mass index, smoking and apo-lipoprotein E levels, the results remained statistically significant | Nil | Nulliparity was associated with lower cognitive performance in analyses adjusted for age and number of years of education. The relationship between nulliparity and number of years of education revealed a more pronounced lower cognitive performance in women with ≤ 12 years of education compared to women with ≥ 12 years of education |
| Koparkar et al. (2022) | A cross-sectional study | 308 | Preeclampsia | Nil | At age 5 to 7 years, children of mothers with a history of preeclampsia had poorer level of nonverbal intelligence and visuospatial capabilities (using Kohs block design) compared to children born to mothers with a normotensive pregnancy. These results were gotten after adjusting for age, sex, socio-economic status, maternal education, birth weight and gestation. After adjusting for confounding factors, responses from the Strengths and Difficulties Questionnaire did not show any significant differences in the behavioral characteristics of children born to mothers in both groups, except in the conduct problem domain where children born to mothers with preeclampsia had lower abnormal scores | Nil |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|--------------------|---------------------------------|------------|---------------------------|--|-------------------------------|--------------------|
| Rana et al. (2006) | A controlled experimental study | 45 | Preeclampsia | Women in group B had better working memory and attention compared to women in groups A and C. Immediate verbal memory scores of the Hopkins Verbal Learning Test were comparable among all groups. Before delivery, the delayed verbal domain of the Hopkins Verbal Learning Test was not significantly lower in women in group B compared to other groups. An improvement was seen across all groups after delivery, but the greatest improvement was seen in women with history of preeclampsia. Differences in attention (Digit Span test) were not observed across all groups. Women in group B had the best scores for attention at both end points while women in group C had the worse scores compared to women in group A, but this difference was not statistically significant. Working memory was worst in group C and highest in group A, before and after delivery. When compared with normative nonpregnant controls, revelations included mild to moderately impaired memory in group A with a working memory of low average; moderate to severe memory impairment in group B with a low average to average working memory; and group C had similar findings as group B | Nil | Nil |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|-------------------|---|------------|---------------------------|----------------------------------|---|--------------------|
| Mak et al. (2018) | Cross-sectional observational pilot study | 20 | Preeclampsia | Nil | Altered resting-state functional connectivity of the brain was found in brain regions devoted to social cognition in children born from pregnancies complicated by preeclampsia compared to children born from normotensive pregnancies. Specifically, higher functional connectivity was seen between the bilateral frontal pole and the left amygdala, the left frontal pole and the right amygdala, and between the precuneus and the medial prefrontal cortex. Between the left occipital fusiform gyrus and the medial prefrontal cortex, a decreased resting state functional connectivity was observed | Nil |

Table 2 (continued)

| Author and year | Study design | Study size | Eclampsia or preeclampsia | Maternal neurocognitive outcomes | Fetal neurocognitive outcomes | Other key outcomes |
|----------------------|-------------------------------------|------------|---------------------------|----------------------------------|--|--------------------|
| Ratsep et al. (2016) | Cross-sectional observational study | 79 | Preeclampsia | Nil | <p>Children born from pregnancies complicated by preeclampsia had memory impairment compared to children born from normotensive pregnancies evidenced by their lower scores in both delayed and immediate memory tasks in the Memory for Names test. The differences in other neuropsychological assessment tests were not statistically significant. More deficits were observed in the eye movement tasks among PE-FIs than in the control group. PE-FIs had more trials before completing the prosaccade task in which they needed more saccades to reach the target and towards the endpoint, they had a greater angle of error compared to the control group. They also had a slower reaction time and more trials in the antisaccade task in which they required more saccades to reach the target compared to participants in the control group. Statistically significant differences were not found in all other task parameters assessed in the prosaccade and antisaccade tasks. Fewer sequence errors were made by PE-FIs in the memory-guided task, and although compared to participants in the control group they had increased peak velocity towards the second target, their accuracy was significantly poorer towards both the second and first targets. There were no other significant differences in the other parameters examined under the memory-guided task</p> | Nil |

Psychosocial impact

Studies like those by Postma et al. [18] and Birnie et al. [13] reveal that individuals with a history of preeclampsia experience significant psychosocial impacts, including reduced quality of life and social functioning. These effects are likely to exacerbate perceived cognitive impairments and contribute to poorer self-reported cognitive functioning. Rana et al. [19] found that women with preeclampsia, particularly those receiving magnesium sulfate, showed better attention and working memory compared to certain other groups, although explicit memory was impaired across all groups.

For eclampsia, the heightened severity of the condition often leads to more pronounced psychosocial difficulties. Postma et al. [15] and Birnie et al. [13] both noted increased anxiety and depression in women with eclampsia, which can contribute to the overall deterioration of perceived cognitive abilities. This psychosocial burden might obscure the direct cognitive effects of eclampsia, complicating the understanding of its specific impact.

Fetal/neonatal neurocognitive outcomes

Offspring born after preeclamptic pregnancies have shown a range of neurocognitive issues. Tuovinen et al. [20] found increased reports of cognitive failures and distractibility in these children compared to those born to normotensive mothers. Koparkar et al. [21] demonstrated lower visuospatial performance scores, while Mak et al. [22] identified impairments in working memory and oculomotor control. Rastep et al. [23] reported that 20% of children from severe early-onset hypertensive pregnancies had abnormal developmental outcomes, and 37% had abnormal composite outcomes, including perinatal mortality or developmental abnormalities. While specific studies on eclampsia-related neurocognitive outcomes in offspring are less extensive, the severity of eclampsia suggests that similar, if not more pronounced, neurodevelopmental issues may occur. The extreme nature of eclampsia could lead to greater developmental risks and cognitive impairments, though direct evidence is sparse and requires further investigation.

van Wassenauer et al. [24] investigated alterations in resting-state functional connectivity (rs-FC) in children born from preeclampsia-complicated pregnancies. These alterations included increased connectivity between regions such as the amygdala and frontal pole, and decreased connectivity between the medial prefrontal cortex and the occipital fusiform gyrus, suggesting potential neurodevelopmental impacts stemming from maternal preeclampsia. Similar studies for eclampsia

could provide insights into whether these connectivity patterns differ in severity.

Discussion

The findings of this review confirm and extend existing research on the neurocognitive outcomes associated with preeclampsia and eclampsia, revealing a consistent association between these hypertensive disorders and impairments in memory and executive function. For preeclampsia, the evidence indicates that women with a history of this condition often exhibit significant deficits in memory and executive functions. Studies have shown lower scores in memory tests and diminished executive functioning, particularly in planning, problem-solving, and decision-making tasks. However, there are discrepancies in the literature. Some studies suggest that the relationship between preeclampsia and cognitive impairment might not be wholly independent but could be influenced by confounding factors such as educational attainment, mood disorders, and obesity [12, 25]. These discrepancies show the complexity of the association and suggest that additional research is needed to elucidate the full range of contributing factors. Eclampsia tends to exacerbate the cognitive impairments observed in preeclampsia [15, 19]. While specific studies on eclampsia-related cognitive impairments are less extensive, the severity of eclampsia implies that it likely has a more profound impact on neurocognitive functions [18, 21]. The increased psychosocial and physiological stress associated with eclampsia could further amplify cognitive deficits, highlighting the need for tailored interventions for those affected.

The review also highlights significant neurocognitive outcomes in offspring born after pregnancies complicated by preeclampsia or eclampsia. The evidence suggests that these hypertensive disorders contribute to cognitive deficits and abnormalities in brain functional connectivity in children. Studies have reported issues such as increased cognitive failures, reduced visuospatial performance, and impairments in working memory and oculomotor control in children born to mothers with preeclampsia [12, 14]. These findings show the importance of early detection and intervention to mitigate long-term developmental consequences for offspring.

Biological mechanisms and psychological factors

Biological mechanisms play a crucial role in linking preeclampsia and eclampsia to neurocognitive outcomes. Placental dysfunction impairs nutrient and oxygen transfer to the developing fetus, leading to hypoxic conditions that can disrupt fetal brain development [26]. Such disruptions can result in structural abnormalities, altered

neuronal connectivity, and impaired neurogenesis, which contribute to long-term neurocognitive deficits [26, 27]. Furthermore, altered levels of angiokines like vascular endothelial growth factor (VEGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) have been implicated in the pathogenesis of preeclampsia. These factors affect neurodevelopment through their impact on angiogenesis and neuroinflammation [28]. Additionally, psychological factors such as maternal stress and anxiety have been shown to adversely affect fetal neurodevelopment. Chronic stress during pregnancy can activate the maternal hypothalamic–pituitary–adrenal (HPA) axis, increasing the production of stress hormones like cortisol, which can cross the placenta and influence fetal brain development. High levels of maternal anxiety have also been associated with altered fetal programming and an increased risk of neurodevelopmental disorders [29, 30]. The interplay between these biological and psychological factors exacerbates the adverse effects of preeclampsia and eclampsia on fetal neurodevelopment, highlighting the need for comprehensive approaches to manage and mitigate these risks effectively [31].

Social determinants, including socioeconomic status (SES) and access to healthcare, further influence the impact of hypertensive disorders during pregnancy on neurocognitive outcomes [32]. Women from lower SES backgrounds experience greater environmental stressors and have limited access to prenatal care, which can exacerbate the effects of preeclampsia on maternal and fetal health [33]. Socioeconomic disparities in access to quality healthcare services, including prenatal monitoring and management of preeclampsia, result in delays in diagnosis and treatment, leading to worse outcomes for both mothers and offspring [34]. Additionally, inadequate social support systems and lack of resources hinder maternal coping mechanisms and exacerbate the psychological burden of preeclampsia, further impacting fetal neurodevelopment [35].

A promising area for further investigation is the role of heart rate variability (HRV) as an indicator of neurocognitive impact in neonates born after preeclamptic or eclamptic pregnancies. HRV reflects the state of the autonomic nervous system and its regulation, providing insights into the balance between the sympathetic and parasympathetic systems [36]. Since autonomic dysregulation is commonly observed in individuals with preeclampsia and eclampsia, HRV could serve as a valuable tool for assessing stress levels and cognitive alterations in neonates [37]. HRV is influenced by various factors, including stress and cognitive development, making it a potential indicator of how preeclampsia and eclampsia affect neurodevelopment [38]. Furthermore, imbalances in autonomic regulation can play a substantial role in the

cognitive difficulties observed in neonates [39]. The autonomic nervous system can sometimes become dysregulated. This dysregulation affects how neonates respond to stress and impact their neurodevelopment [40]. In addition, autonomic dysregulation affects various aspects of neurodevelopment, including attention, emotional regulation, and executive function [41]. A heightened sympathetic response results in increased anxiety and difficulty in focusing, while inadequate parasympathetic activation could impair the ability to calm down and recover from stress [42]. These early disruptions in autonomic regulation can have lasting effects on cognitive development and mental health [43].

During pregnancy, the interaction of various toxic stressors, known as Toxic Stressor Interplay (TSI), plays a crucial role in shaping outcomes for both the mother and the fetus [40]. Endogenous stressors such as increased systemic inflammation or hormonal imbalances, can directly affect the placenta and fetal development [44]. These internal factors disrupt the delicate balance necessary for healthy fetal growth and development [44]. Alongside these endogenous stressors, exogenous factors also contribute significantly to TSI [45]. Environmental influences, including exposure to pollutants, socio-economic stress, and inadequate prenatal care, exacerbate the challenges faced during pregnancy [46]. These external stressors can complicate labor and delivery, often necessitating more intensive resuscitative measures for the newborn. The effects of TSI continue to influence brain health throughout childhood and into adulthood [47]. The disruptions caused by TSI during critical periods of fetal development can have lasting implications for cognitive and emotional functioning [48].

The concept of Developmental Origins of Health and Disease (DOHaD) provides a framework for understanding these long-term effects. DOHaD highlights that early-life conditions, including those experienced during pregnancy, have a profound influence on health outcomes across the lifespan [40]. Key periods such as the first 1000 days of life, adolescence, and reproductive senescence are particularly critical for brain health and neuroplasticity [49]. During these stages, disruptions can lead to significant and enduring effects on cognitive and emotional resilience, showing the importance of addressing these factors early to improve long-term health outcomes [50]. In addition, a recent study by Abarca-Castro et al. [51] highlights the role of Maternal Immune Activation (MIA) in preeclampsia and its implications for neurodevelopmental damage in offspring. Preeclampsia is characterized by a heightened immune response, with elevated levels of proinflammatory cytokines and reduced immunoregulatory factors. These immune disturbances are linked to adverse neurodevelopmental

outcomes in children, including cognitive deficits and behavioral abnormalities. A key finding from this study is the potential role of the Cholinergic Anti-inflammatory Pathway (CAP) in mitigating the inflammatory response associated with preeclampsia. Dysregulation of the CAP has been implicated in the clinical progression of preeclampsia, and recent evidence suggests that therapeutic modulation of this pathway could improve both maternal and fetal outcomes. Specifically, modulation of vagal activity—an approach that influences the CAP—has been shown to improve maternal hemodynamics, reduce inflammation, and enhance fetal neurodevelopment by promoting neurogenesis and synaptic plasticity.

Implications for clinical practice and public health policy

The findings related to preeclampsia and eclampsia carry important implications for both clinical practice and public health policy [52]. Understanding how preeclampsia and eclampsia impact maternal and fetal/neonatal neurocognitive outcomes sheds light on their long-term consequences and shows the necessity for early and effective intervention [53]. In terms of clinical practice, there is a clear need for early screening and diagnosis of these hypertensive disorders. Healthcare providers can identify preeclampsia and eclampsia at an earlier stage by implementing more rigorous screening protocols and refining diagnostic criteria. This early detection is crucial for initiating timely interventions that can significantly affect outcomes for both mothers and their babies. Moreover, continuous monitoring of patients with preeclampsia and eclampsia is essential. Clinicians should track maternal and fetal health indicators closely, including blood pressure and protein levels, to manage the conditions effectively. This involves not only addressing immediate health concerns but also developing personalized management plans to prevent complications.

Intervention strategies should be tailored to mitigate the adverse effects of these disorders. This involves pharmacological treatments, lifestyle adjustments, and dietary modifications to improve health outcomes [54]. Additionally, establishing protocols for long-term follow-up is important. Regular neurocognitive assessments for children and health evaluations for mothers can help manage any lasting impacts of these hypertensive conditions. On a broader scale, public health policy plays a crucial role in addressing preeclampsia and eclampsia. Preventive measures and educational initiatives should focus on reducing the incidence of these disorders. Community education programs can raise awareness about risk factors, early symptoms, and the importance of prenatal care, helping individuals recognize and act upon potential issues sooner. Resource allocation is another critical aspect. Investing in research and development for better

diagnostic tools and treatment options is essential. Public health policies should ensure that sufficient funding and resources are available to support the management of hypertensive disorders during pregnancy and improve healthcare infrastructure.

Multidisciplinary approaches that address both the medical and psychosocial aspects of hypertensive disorders during pregnancy are needed to optimize maternal and fetal outcomes [33]. This includes early screening and detection of preeclampsia, personalized management strategies tailored to individual risk profiles, and interventions aimed at reducing maternal stress and improving social support networks [33]. Additionally, efforts to address socioeconomic disparities and improve access to healthcare services can help mitigate the adverse effects of preeclampsia on neurocognitive outcomes in offspring.

Several limitations of the reviewed studies warrant consideration. The studies reviewed employed a range of neuropsychological test batteries and cognitive assessment tools, which can lead to inconsistencies in findings. Variability in assessment methods across studies complicates direct comparisons and synthesis of results. For example, some studies used specific tests like the Rey Auditory Verbal Learning Test for memory assessment, while others used broader cognitive measures, potentially leading to divergent outcomes. Also, while the total number of participants across maternal studies and fetal/neonatal studies is substantial, the diversity of sample populations is often limited. Many studies did not account for variations in socioeconomic status, education level, or ethnic background, which could influence cognitive outcomes. Additionally, some studies had small sample sizes which affects the generalizability of the findings.

Furthermore, the presence of confounding variables, such as maternal age, pre-existing health conditions, and lifestyle factors (e.g., obesity, smoking), was not always adequately controlled for. This omission can skew results and obscure the specific impact of preeclampsia and eclampsia on cognitive function. Some studies adjusted for these variables, but others did not, affecting the robustness of the conclusions. In addition, the reliance on retrospective data and self-reported measures in some studies introduces challenges that can impact the validity and generalizability of the findings. This selective recall can lead to an overestimation or underestimation of the true prevalence and severity of cognitive impairments associated with these conditions. Additionally, self-reported measures are inherently subjective and can vary widely between individuals. Participants' perceptions of their cognitive abilities, memory, or overall well-being may not accurately reflect objective cognitive performance. Moreover, generalizability of findings is

limited when studies rely heavily on retrospective data and self-reports.

Future studies should address the limitations identified in the current study and further elucidate the underlying mechanisms linking preeclampsia/eclampsia to neurocognitive outcomes. Longitudinal studies with larger, more diverse populations are needed to establish causal relationships and identify potential mediators and moderators of the observed associations. Additionally, research exploring the effectiveness of early interventions and preventive strategies in mitigating the neurodevelopmental impact of hypertensive disorders during pregnancy is warranted.

Limitations and strengths of review

The review was limited to published studies in English. This exclusion criterion may have omitted relevant studies published in other languages. In addition, there is heterogeneity among the included studies regarding methodology, participant characteristics, and outcome measures. However, the review synthesizes evidence from multiple studies to provide a cohesive overview of current knowledge. By summarizing findings across studies, the review offers insights into the consistency and robustness of the association between preeclampsia/eclampsia and neurocognitive outcomes.

Conclusion

This review highlights the significant impact of preeclampsia and eclampsia on maternal and fetal/neonatal neurocognitive outcomes. The findings show the importance of early detection, intervention, and preventive strategies to mitigate adverse neurodevelopmental effects in mothers and offspring. Biological, psychological, and social factors intertwine to influence the observed neurocognitive outcomes associated with hypertensive disorders during pregnancy, emphasizing the need for multidisciplinary approaches in clinical practice and public health policy. The reviewed studies demonstrate consistent associations between preeclampsia/eclampsia and impairments in memory, executive function, and psychosocial well-being among mothers. Additionally, offspring born after pregnancies complicated by these hypertensive disorders exhibit cognitive deficits and abnormalities in brain functional connectivity, suggesting long-term implications for neurodevelopment. Placental dysfunction, altered angiokine levels, maternal stress, and socioeconomic disparities contribute to the observed neurocognitive outcomes, highlighting the complex interplay of biological, psychological, and social determinants. While the review contributes valuable insights into the current understanding of maternal and fetal neurocognitive outcomes in preeclampsia

and eclampsia, several limitations exist, including variations in study methodology and potential biases. Future research should address these limitations and further elucidate the underlying mechanisms linking hypertensive disorders during pregnancy to neurocognitive outcomes. Longitudinal studies with larger, diverse populations are needed to establish causal relationships and identify effective interventions to mitigate adverse neurodevelopmental effects.

Abbreviations

| | |
|--------|--|
| HDP | Hypertensive disorders of pregnancy |
| ACOG | American College of Obstetrics and Gynaecology |
| SES | Socioeconomic status |
| MeSH | Medical Subject Headings |
| rs-FC | Resting-state functional connectivity |
| VEGF | Vascular endothelial growth factor |
| sFlt-1 | Soluble fms-like tyrosine kinase-1 |
| HPA | Hypothalamic–pituitary–adrenal |

Author contributions

NA and EK conceptualised the study; GO, RK, JEA, BMU, OS, AA, OO, and DO were involved in the literature review; NA, EK, AEB, and ICA extracted the data from the reviewed studies. All authors wrote the final and first drafts. All authors read and approved the final manuscript.

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Code availability

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Competing interests

The authors declare no competing interests.

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