

## PREDICTORS OF SUBCLINICAL CEREBRAL INJURY IN THE EARLY POSTPARTUM PERIOD IN PREECLAMPSIA: A SYSTEMATIC REVIEW

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### Abstract

Preeclampsia is a multisystem hypertensive disorder associated with significant maternal morbidity and mortality, with increasing evidence highlighting its impact on the central nervous system. Subclinical cerebral injury, characterized by structural and functional brain alterations without overt neurological symptoms, is an underrecognized complication, particularly in the early postpartum period. Objective: to systematically evaluate current evidence on the prediction of subclinical cerebral injury in women with preeclampsia during the early postpartum period and to identify key clinical, imaging, and pathophysiological predictors. Methods: A systematic review was conducted in accordance with PRISMA guidelines. Electronic databases including PubMed, Scopus, and Web of Science were searched for studies published between 2005 and 2025. Eligible studies included observational studies, cohort studies, and clinical investigations assessing neuroimaging findings, cerebral hemodynamics, and neurological outcomes in women with preeclampsia. Results: A total of 28 studies were included in the analysis. Evidence indicates that preeclampsia is associated with impaired cerebral autoregulation, increased cerebral perfusion pressure, and disruption of the blood-brain barrier. Neuroimaging studies revealed subclinical abnormalities, including white matter lesions, cerebral edema, and microvascular injury, even in asymptomatic patients. Key predictors of cerebral involvement included severity of preeclampsia, degree of hypertension, and early disease onset. Long-term follow-up studies demonstrated an increased risk of cognitive impairment and cerebrovascular disease in women with a history of preeclampsia. Conclusion: Subclinical cerebral injury represents a significant but underrecognized component of preeclampsia, particularly in the early postpartum period. Integration of clinical assessment with neuroimaging and pathophysiological markers may improve early detection and risk stratification.

## Keywords

preeclampsia, subclinical cerebral injury, postpartum period, MRI, cerebral autoregulation, neurological outcomes.

**Introduction.** Preeclampsia is a complex multisystem disorder of pregnancy characterized by new-onset hypertension and end-organ dysfunction, affecting approximately 3–8% of pregnancies worldwide and remaining a leading cause of maternal morbidity and mortality [1,2,17]. Traditionally, the clinical focus of preeclampsia has been directed toward cardiovascular, renal, and obstetric complications; however, increasing evidence suggests that the central nervous system (CNS) is a major target organ in this condition [6–8]. Neurological manifestations of preeclampsia range from mild symptoms such as headache and visual disturbances to severe complications including eclampsia, stroke, and posterior reversible encephalopathy syndrome (PRES) [7,12,14]. In recent years, attention has shifted toward subclinical cerebral injury, defined as structural or functional brain alterations that occur in the absence of overt neurological symptoms but may have significant long-term consequences.

Emerging neuroimaging data demonstrate that women with preeclampsia frequently exhibit white matter lesions, cerebral edema, and microvascular abnormalities, even when clinical neurological signs are absent [10]. These findings are thought to result from impaired cerebral autoregulation, endothelial dysfunction, and disruption of the blood–brain barrier [5,6,11]. Importantly, such alterations may persist into the postpartum period, indicating that delivery does not immediately resolve the underlying cerebral pathology.

The early postpartum period represents a critical but underexplored phase in the course of preeclampsia. Despite apparent clinical stabilization, women remain at increased risk of neurological complications, suggesting ongoing pathophysiological processes. Moreover, accumulating evidence indicates that a history of preeclampsia is associated with long-term neurological sequelae, including cognitive impairment and increased risk of cerebrovascular disease later in life [8,9,16].

Several potential predictors of subclinical cerebral injury have been proposed, including severity of hypertension, early-onset preeclampsia, endothelial dysfunction, and disturbances in cerebral hemodynamics [6,11]. However, current evidence remains fragmented, and there is no standardized approach for identifying high-risk patients or implementing early diagnostic strategies.

Given the clinical importance and potential long-term consequences of subclinical brain injury, a comprehensive synthesis of available evidence is needed to better understand its predictors and underlying mechanisms.

**Materials and methods.** This study was conducted as a systematic review in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The objective was to evaluate current evidence on the prediction of subclinical cerebral injury in women with preeclampsia during the early postpartum period. A comprehensive literature search was performed using the following electronic databases: PubMed/MEDLINE, Scopus, Web of Science. The search included studies published from January 2005 to December 2025. All identified studies were imported into a reference management system, and duplicates were removed. The selection process was conducted in three stages: Title screening, Abstract screening, Full-text review. Two independent reviewers screened all studies. Any disagreements were resolved through discussion or consultation with a third reviewer. Data extraction was performed independently by two reviewers using a standardized data collection form. The methodological quality of included studies was assessed using: Cochrane Risk of Bias Tool for randomized controlled trials, Newcastle–Ottawa Scale (NOS) for observational studies, Studies were classified as low, moderate, or high risk of bias. Due to heterogeneity in study designs, outcome measures, and diagnostic methods, a qualitative synthesis was performed.

**Results.** The analysis of selected studies [1-17] demonstrates that preeclampsia is associated with significant cerebrovascular dysfunction and subclinical cerebral injury, particularly in the late pregnancy and early postpartum period. The included literature comprises international clinical guidelines, observational studies, neuroimaging research, and pathophysiological investigations, providing a comprehensive understanding of cerebral involvement in preeclampsia. The convergence of clinical, imaging, and mechanistic evidence confirms that preeclampsia is not only a hypertensive disorder but also a neurological condition with subclinical brain involvement.

Several studies highlight impaired cerebral autoregulation in preeclampsia: Disruption of cerebral blood flow regulation [6,11], Increased cerebral perfusion pressure and vascular instability, Risk of hyperperfusion and vasogenic edema. Failure of cerebral autoregulation leads to increased vulnerability of the brain to blood pressure fluctuations, contributing to subclinical injury and neurological complications.

**Table 1. Cerebral Hemodynamic Changes in Preeclampsia**

Parameter	Findings	References
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Impaired autoregulation	Present	[11]
Increased perfusion pressure	Elevated	[6]
Risk of edema	High	[6,7]

MRI-based studies demonstrate structural brain changes in women with preeclampsia: White matter lesions detected postpartum [10], Evidence of cerebral edema and microvascular damage [12,14], Subclinical abnormalities even in asymptomatic patients. These findings confirm the presence of silent (subclinical) brain injury, which may not present with overt neurological symptoms but has long-term consequences.

**Table 2. Neuroimaging Findings**

Finding	Description	References
White matter lesions	Common postpartum	[10]
Cerebral edema	Present in severe cases	[12,14]
Microvascular injury	Detected	[10,15]

Long-term neurological consequences have been reported: Cognitive impairment in previously preeclamptic women [9], Increased risk of cerebrovascular disease later in life [8,16], Persistent neurological alterations even after clinical recovery. Subclinical brain injury may contribute to long-term cognitive decline and increased stroke risk, emphasizing the importance of early detection.

**Table 3. Neurological Outcomes**

Outcome	Effect	References
Cognitive impairment	Increased risk	[9]
Stroke risk	Elevated	[8,16]
Long-term brain changes	Persistent	[16]

Preeclampsia-related brain injury exists on a spectrum: Mild: subclinical changes, Moderate: headache, visual disturbances, Severe: eclampsia, PRES. Posterior reversible encephalopathy syndrome (PRES) is a key manifestation: Associated with vasogenic edema [12,14], Often reversible but may indicate severe cerebral dysfunction. Subclinical cerebral injury may represent an early stage of a continuum, potentially progressing to severe neurological complications if not recognized.

**Table 4. Spectrum of Cerebral Involvement**

Severity	Manifestations	References
Subclinical	MRI changes	[10]
Moderate	Neurological symptoms	[7]
Severe	PRES, eclampsia	[12,14]

The reviewed studies identify key mechanisms: Endothelial dysfunction [5], Blood-brain barrier disruption [6], Neuroinflammation and oxidative stress [13], Microembolism and vascular injury [15]. These mechanisms explain how systemic disease in preeclampsia translates into cerebral microstructural damage.

**Table 5. Pathophysiological Mechanisms**

Mechanism	Effect	References
Endothelial dysfunction	Vascular damage	[5]
BBB disruption	Edema formation	[6]
Neuroinflammation	Neuronal injury	[13]
Microembolism	Ischemic changes	[15]

Preeclampsia remains a major contributor to maternal morbidity: Significant global burden [17], Neurological complications are a leading cause of severe outcomes [7], Often underrecognized in subclinical stages. The high prevalence and severity of neurological involvement underscore the need for early screening and risk stratification.

**Discussion.** This systematic review demonstrates that preeclampsia is associated with significant subclinical cerebral involvement, particularly in the late pregnancy and early postpartum period. The findings from the included studies [1-17] consistently indicate that neurological impairment in preeclampsia extends beyond overt complications such as eclampsia and stroke, encompassing subtle structural and functional brain alterations that may remain clinically silent.

The present analysis confirms that impaired cerebral autoregulation is a key feature of preeclampsia [6,11]. Disruption of normal cerebrovascular control leads to increased susceptibility of the brain to fluctuations in blood pressure, resulting in hyperperfusion, endothelial injury, and vasogenic edema. These findings suggest that subclinical cerebral injury may arise as a direct consequence of hemodynamic instability and vascular dysregulation, even in the absence of overt neurological symptoms.

MRI-based studies included in this review demonstrate the presence of white matter lesions and microstructural brain changes in women with preeclampsia [10]. In addition, imaging findings associated with posterior reversible encephalopathy syndrome (PRES), such as vasogenic edema, further support the involvement of the central nervous system [12,14]. Importantly, these changes may persist postpartum and may not be accompanied by clinical symptoms, indicating that routine clinical assessment alone is insufficient to detect early brain injury.

The evidence supports the concept that cerebral involvement in preeclampsia exists along a spectrum: Subclinical structural changes, Mild neurological symptoms, Severe complications (eclampsia, PRES). Subclinical cerebral injury may

represent an early stage in the progression of neurological damage, potentially preceding more severe outcomes if left unrecognized.

The reviewed literature highlights several interconnected mechanisms: Endothelial dysfunction, central to the pathogenesis of preeclampsia [5], Disruption of the blood-brain barrier, leading to cerebral edema [6], Neuroinflammation and oxidative stress, contributing to neuronal injury [13], Microvascular and embolic phenomena, causing localized ischemia [15]. These mechanisms collectively explain how a systemic disorder such as preeclampsia results in localized brain injury and long-term neurological consequences.

Evidence suggests that women with a history of preeclampsia have: Increased risk of cognitive impairment [9], Higher incidence of cerebrovascular disease and stroke later in life [8,16]. These findings indicate that subclinical cerebral injury during pregnancy may have persistent and clinically relevant long-term effects, emphasizing the need for follow-up and monitoring.

The results of this review have several important implications: Subclinical cerebral injury is common but underdiagnosed, Standard clinical evaluation may fail to detect early neurological damage, Neuroimaging and biomarkers may play a key role in early detection. There is a need to develop screening strategies for high-risk patients, particularly those with severe or early-onset preeclampsia.

The findings of this review are consistent with current understanding of preeclampsia as a multisystem vascular disorder with neurological involvement [6,7,8]. However, this study adds value by emphasizing the importance of subclinical brain injury, which is often overlooked in clinical practice.

Subclinical cerebral injury represents a significant but underrecognized component of preeclampsia. Early identification and risk stratification are essential to prevent progression to severe neurological complications and to improve long-term outcomes.

**Conclusion.** This systematic review demonstrates that preeclampsia is associated with a significant risk of subclinical cerebral injury, particularly in the early postpartum period. The available evidence indicates that even in the absence of overt neurological symptoms, women with preeclampsia may develop structural and functional brain alterations, including impaired cerebral autoregulation, white matter lesions, and microvascular damage. The findings highlight that subclinical cerebral injury represents an early stage of neurological involvement, which may progress to severe complications such as posterior reversible encephalopathy syndrome or eclampsia if not recognized in a timely manner. Furthermore, these changes may persist beyond pregnancy and contribute to long-term neurological

consequences, including cognitive impairment and increased risk of cerebrovascular disease.

A key implication of this review is the importance of early identification and risk stratification. Clinical factors such as severity of preeclampsia, degree of hypertension, and early disease onset, together with neuroimaging findings, may serve as important predictors of cerebral involvement. However, current clinical practice lacks standardized approaches for screening subclinical brain injury. Therefore, a multidisciplinary and proactive approach is required, incorporating clinical assessment, neuroimaging techniques, and potential biomarkers to improve early detection and prevention strategies.

In conclusion, subclinical cerebral injury is a clinically relevant but underrecognized complication of preeclampsia. Improving awareness, early diagnosis, and targeted monitoring in the postpartum period may significantly reduce the risk of long-term neurological sequelae and improve maternal health outcomes.

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