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Risk prediction for preeclampsia in pregnant women with chronic kidney disease

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ABSTRACT

Preeclampsia can have long-term effects on kidney function in women with chronic kidney disease (CKD). Women with a history of preeclampsia have an increased risk of CKD and end-stage renal disease (ESRD) later in life. Regular check-ups are needed for preeclamptic women, especially those with persistent hypertension or proteinuria. Therefore, prediction models incorporating renal function and pregnancy outcomes in the first trimester can help assess pregnancy risk in CKD patients. Risk stratification models consider disease activity, major organ involvement, maternal risk factors and comorbidities, previous pregnancy complications, teratogenic drugs, and laboratory tests.

Keywords: Preeclampsia, End-stage renal disease, Chronic kidney disease

Mini-Review

Implication for health policy/practice/research/medical education:
Preeclampsia significantly impacts long-term kidney health, increasing a woman's risk for various renal complications later in life. This condition illustrated by new-onset hypertension and proteinuria after 20 weeks of gestation, which leads to both short-term kidney injury and heightened susceptibility to chronic kidney disease (CKD) and even end-stage renal disease (ESRD).
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Introduction

Preeclampsia, characterized by hypertension and proteinuria following 20 weeks of gestation, creates significant risks for women with renal dysfunction (1). Prediction of preeclampsia in this population is crucial for improving maternal and fetal outcomes (2). Preeclampsia also can lead to several complications, including cerebral disturbance, pulmonary edema, visual disturbance, impaired liver function, cardiovascular disease, and thrombocytopenia (2,3). Chronic kidney disease (CKD) itself is a significant risk factor for preeclampsia (4). Pregnant women with CKD have a higher risk of developing preeclampsia, which can lead to superimposed acute kidney injury and adverse outcomes (5). Risk factors include age, type of glomerular diseases, and levels of blood pressure (5). Conversely, preeclampsia, particularly early preterm preeclampsia, is strongly associated with various chronic kidney illnesses later in life (6). It is also a known risk factor that can accelerate the deterioration of renal function (7). A significant proportion of preeclampsia patients may experience persistent proteinuria and reduced glomerular filtration rate up to 12 months postpartum (8). Preeclampsia can lead to chronic renal failure throughout endothelial damage and podocyte loss (4). This mini-review sough to consider the risk prediction for preeclampsia in pregnant women with chronic renal failure.

Search strategy

For this review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ) and Embase, using different keywords such as preeclampsia, acute kidney injury, chronic kidney disease and end-stage renal disease.

Mechanisms of renal damage in preeclampsia

The mechanisms contributing to renal complications and proteinuria in preeclampsia consisted of angiogenic/anti-angiogenic factors, immune cells, inflammatory cytokines, and AT1-AA (agonistic Ang II [angiotensin II] type 1

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receptor autoantibody), across with systemic endothelial dysfunction (9). This disease can cause direct kidney injury, leading to proteinuria and hypertension which mediates subsequent injuries (10). Moreover, damage to the podocytes also occurs (11). Glomerular endotheliosis, a characteristic renal change in preeclampsia, is usually fully reversible but can sometimes lead to persistent renal damage (12). Previous studies have identified residual focal segmental glomerular lesions, focal global glomerular sclerosis, focal interstitial scarring, and arteriolosclerosis in kidney biopsies of patients with a history of preeclampsia (13). Moreover, preeclampsia commonly leads to acute kidney injury, since acute renal failure is also a known risk factor for the development of CKD outside of pregnancy (14).

Key risk factors of preeclampsia

Both pre-existing and poorly controlled blood pressure increase risk substantially preeclampsia in CKD (15). Moreover, elevated 24-hour urinary protein, especially at higher quantity, is a strong independent risk factor and is incorporated in predictive nomograms (16). Additionally, higher values of serum creatinine and blood urea nitrogen reflect reduced renal function and elevating the risk of renal failure (17). Higher mean arterial pressure at baseline also increases risk (12,18). Previous studies found that advanced CKD stages (particularly 3–5) are associated with higher preeclampsia risk (19). Along with above risk factors, elevated uric acid is an independent predictor (20,21). Accordingly low-serum albumin, identified as a risk factor, especially (20). Other factor is diabetic nephropathy increases preeclampsia risk independently (7). Advanced maternal age and increased body mass index are associated with risk, but the impact is less than kidney-related factors (15). Finally, high plasma fibrinogen concentration may contribute, to CKD (21,22).

Long-term renal implications of preeclampsia

Preeclampsia is a risk factor for the development of CKD and end-stage renal disease (ESRD) (23). Women with a history of preeclampsia have a significantly higher risk of developing CKD (24). A prior systematic review found a 5-fold higher risk of end-stage kidney disease for affected women (23). The recent analysis on over five million women across 23 different studies by Kristensen et al, revealed that a history of preeclampsia doubles a woman's risk for kidney disease later in life. In addition, the hazard of developing chronic kidney dysfunction is particularly elevated with earlier onset of preeclampsia (7). The risk of any chronic renal disorder almost quadruples for females with a history of early preterm preeclampsia (delivery <34 weeks), compared to women without preeclampsia who delivered at the same gestational age (7). Kristensen et al also found that the associations between preeclampsia and CKD and glomerular/proteinuric disease are especially strong within five years of the latest pregnancy, with hazard ratios of 6.11 and 4.77 respectively (7). They accordingly found that, even five years or further following the newest pregnancy, women with a history of preeclampsia still face a 100% higher risk of CKD and a 50% higher chance of glomerular disease compared to those without a history of preeclampsia (7). Similarly, the study by Vikse et al demonstrated that preeclampsia is a marker for an increased risk of subsequent ESRD, even if the absolute risk is low (25). Vikse et al also detected that for women who had preeclampsia during their first pregnancy, the relative risk of ESRD was 4.7 (25). They showed, if preeclampsia occurred in both the first and second pregnancies, the relative risk for ESRD was 6.4 (25). Likewise, women with a history of preeclampsia experience an approximate 5-12-fold increased risk of ESRD (26).

Biomarkers for preeclampsia prediction

Several biomarkers have been investigated for their potential in predicting preeclampsia, particularly in high-risk populations like those with renal failure (27). An imbalance of circulating angiogenic and antiangiogenic factors, such as increased soluble fms-like tyrosine kinase-1 (sFlt-1) and decreased placental growth factor (PlGF), is associated with preeclampsia (28). The PROGNOSIS study was designed to investigate the use of the sFlt-1/PlGF ratio for the short-term prediction of preeclampsia/eclampsia/HELLP syndrome (29). This ratio can effectively predict and improve the diagnostic accuracy for preterm preeclampsia in patients with chronic renal failure (29,30). Pre-partum sFlt-1 levels have been found to correlate with impaired renal function parameters postpartum, though sFlt-1 alone may not be sufficient to predict renal impairment after preeclampsia (8). Additionally, low levels of PlGF tend to drop during pregnancy in asymptomatic individuals who later develop preeclampsia (31). The PlGF test can be offered between 20 and 35 weeks of gestation if preeclampsia is suspected (32). Furthermore, elevated endogenous marinobufagenin levels have been described early in preeclamptic patients, and an algorithm dealing with marinobufagenin plasma levels might be established in the future to help predict preeclampsia risk (33). In women with suspected preeclampsia, elevated serum level of cystatin C (Cysc) have been observed in preeclampsia-positive patients (34). Recent studies also found, plasma value of pregnancy-associated plasma protein-A tend to decrease in asymptomatic individuals who later develop preeclampsia (35).

Angiogenic biomarkers

Angiogenic biomarkers like SDF-1 (stromal cell-derived factor 1) and VEGF (vascular endothelial growth factor) may have diagnostic and prognostic value in women with preeclampsia and pregnancy-related acute kidney injury (36). These biomarkers can help evaluate the severity and predict the progression of kidney injury and obstetric

complications (36). An imbalance of angiogenic factors plays a key role in the development of renal damage in preeclampsia (37).

Conclusion

Risk prediction for preeclampsia in CKD incorporates both clinical and laboratory variables, including blood pressure, proteinuria, renal function markers, albumin, uric acid, and select biomarkers. Models using these factors demonstrate strong discriminative ability, supporting proactive, personalized pregnancy care in women with CKD.

Authors' contribution

Conceptualization: Samaneh Saghafian Larijani and Tahereh Zabihi.
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Investigation: Roya Biglarifar and Samaneh Saghafian Larijani.
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Visualization: Roya Biglarifar.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized Perplexity to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

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