Risk of Preeclampsia in Women with CKD, Dialysis or Kidney Transplantation

Noriko Hirose, Akihide Ohkuchi*, Rie Usui, Shigeki Matsubara, and Mitsuaki Suzuki
Department of Obstetrics and Gynecology, Jichi Medical University School of Medicine, Japan

Abstract

**Aim:** In women with chronic kidney disease (CKD), dialysis, and kidney transplantation, the occurrence rate of preeclampsia is increased. We collected articles on pregnant women with CKD, dialysis, and kidney transplantation, and summarized the occurrence rates of preeclampsia.

**Methods:** We searched for articles on pregnant women with CKD, dialysis, and kidney transplantation in PubMed and in review articles.

**Results:** We found 6 articles on pregnant women with CKD which reported the incidence rate of preeclampsia; preeclampsia occurred in >20%. We found 4 articles on pregnancy with dialysis which reported the incidence rate of preeclampsia; preeclampsia occurred in >19%. One meta-analysis reported in 2011 summarized the overall pooled incidence rate of preeclampsia in women with kidney transplantation; preeclampsia occurred in an average of 27%.

**Conclusion:** Preeclampsia risk in pregnant women with CKD, dialysis, and kidney transplantation appears to be very high, >19%.

INTRODUCTION

In 2007, the Japan Society of Nephrology published practical guideline for pregnant women with kidney diseases [1]. The editor stated that there were few randomized controlled trials for the treatment of pregnant women with kidney diseases, so the guideline was developed mainly according to meta-analysis [1]. However, in the guideline, the occurrence rate of preeclampsia (PE) in pregnant women with CKD, dialysis, and kidney transplantation was not systematically reviewed [1]. Since then, several large systematic reviews of pregnant women with CKD [2], dialysis [3], and kidney transplantation [4] have been published. Our aim was to evaluate the occurrence rates of PE in pregnant women with CKD, dialysis, and kidney transplantation by searching for articles in PubMed.

METHODS


RESULTS

Pregnant women with CKD

In 2011, Piccoli et al. [2] attempted to systemically review the literature for 2000-2009 on pregnancy in CKD; 26 eligible studies on over 2000 pregnancies were collected. In 9 studies of pregnant women with CKD, the incidence rate of PE was reported in 2 studies [5,6]. Trevisan et al. [5] compared 25 patients (sCr ≥1.5 mg/dL) and 50 controls, and revealed that PE...
occurred in 40% of patients, whereas it occurred in only 5.7% of controls. Bar et al. [6] reported 46 pregnant women with mild CKD (sCr<1.4 mg/dL), moderate CKD (sCr: 1.4-2.4 mg/dL), severe CKD (sCr>2.5 mg/dL); PE occurred in 22% (10/46) of all subjects and 25% (1/4) of moderate or severe CKD patients. By searching for articles in PubMed from 2010 to 2014, we found four other articles reporting the incidence rate of PE in women with CKD. Masuyama et al. [7] reported 90 pregnant women with CKD; superimposed PE occurred in 23.3% (21/90) of all subjects. Maruotti et al. [8] reported 93 pregnant women with CKD; the incidence rate of PE in women with sCr ≥125 μmol/L (Group 2) was significantly higher than in those with sCr ≤125 μmol/L (Group 1) (78.6% vs. 25.3%); the mean gestational age at diagnosis of PE was significantly lower in Group 2 than in Group 1 (29 ± 2 vs. 33 ± 1 weeks; p < 0.04), and gestational age at delivery was 30 ± 2 and 34 ± 1 weeks, respectively (p < 0.04). Alsuwaida et al. [9] reported 98 pregnant women with CKD; PE occurred in 20.8% (21/98) of all subjects; the prevalence of PE was 12.9% in stage 1, 47.4% in stage 2, and 44.4% in stage 3/4 (p = 0.002); and women with elevated systolic or diastolic BP in the first trimester were more prone to develop PE. Bramham et al. [10] reported that 22 women with mild CKD (sCr: 101-124 μmol/L) had high rates of PE (40%), and 30 women with proteinuria (≥2+) had a concomitant risk of PE (60%).

**Pregnant women with lupus nephropathy**

As for lupus nephropathy (LN), the incidence rate of PE was reported in 3 studies [11-13] in the review by Piccoli et al. [2]. Imbasciati et al. [11] reported 113 pregnant women with LN with histology according to the WHO classification; PE occurred in 9.7%. Camona et al. [12] reported 42 pregnant women with the most severe forms of LN (proliferative or class III-IV); PE occurred in 28.1%, whereas it occurred in only 4.6% of women with SLE, but without LN. Moroni et al. [13] reported 13 women in whom LN developed during pregnancy and 38 patients with known LN; PE occurred in 38.5% of women whom LN developed during pregnancy, whereas it occurred in 9.8% of patients with known LN. Although we searched for articles in PubMed from 2010 to 2014, we found no other articles reporting the incidence rate of PE in women with LN.

**Pregnant women with diabetic nephropathy**

As for diabetic nephropathy (DN), the incidence rate of PE was reported in 3 studies [14-16] in the review by Piccoli et al. [2]. Carr et al. [14] reported 43 pregnant women with DN; when pregnant women with DN were complicated with mean arterial pressure of ≥100 mmHg, PE occurred in 42.9%, whereas when pregnant women with DN had their mean arterial pressure controlled to <100 mmHg, PE occurred in 27.3%. Khoury et al. [15] reported 72 pregnant women with DN; in pregnant women with DN with sCr of ≤1.0 mg/dL, 1.1-1.5 mg/dL, and >1.5 mg/dL, PE occurred in 41%, 33.3%, and 44.4%, respectively. Ekbom et al. [16] reported 240 pregnant women with type 1 diabetes; in pregnant women with diabetes, but showing normal albuminuria, PE developed in 6%; in those showing micro albuminuria, PE developed in 42%, and in those with DN, PE developed in 64%. By searching for articles in PubMed from 2010 to 2014, we found one other article reporting the incidence rate of PE in women with DN. Young et al. [17] reported 11 pregnant women with DN; PE occurred in 63.6%.

**Pregnant women undergoing dialysis**

In 2010, Piccoli et al. [3] attempted to systematically review the literature for 2000-2008 on pregnancy while undergoing dialysis; 10 eligible studies on over 90 pregnancies were collected. The incidence rate of PE was reported in two studies [18,19]. Malik et al. [18] reported 12 pregnant women undergoing dialysis; PE occurred in 66%. Eroglu et al. [19] reported 7 pregnant women receiving dialysis; PE occurred in 29%. By searching for articles in PubMed from 2010 to 2014, we found two other articles reporting the incidence rate of PE in pregnant women undergoing dialysis [20,21]. Luders et al. [20] reported 52 pregnant women receiving dialysis; PE occurred in 19.2%; and PE was associated with a poor prognosis compared with pregnant women without PE: a successful delivery rate of 60% versus 92.9% (p = 0.02), an extremely premature delivery rate of 77.8% versus 3.3% (p< 0.001), lower gestational age (p< 0.001), and birth weight (p< 0.001). Shahir et al. [21] reported 49 pregnant women undergoing dialysis; PE occurred in 19.4% (6/31).

**Pregnant women with kidney transplantation**

Deshpande et al. [4] attempted to systematically review the literature for 2000-2010 on pregnancy with kidney transplantation (KT). Fifty eligible studies of 4706 pregnancies in 3570 KT recipients were collected, with meta-analyses of the outcomes of live birth, miscarriage, gestational diabetes, PE, caesarean section, preterm birth, gestational age at delivery, birth weight, and acute rejection rate during post-KT pregnancies, and the post-transplantation graft loss rate. The overall pooled incidence rate of PE was 27%, and in all 34 studies, the PE occurred in ≥3.8%, which is the PE rate in the general US population, suggesting that KT is a very high risk factor for the occurrence of PE.

**DISCUSSION**

PE occurred in 21-79% of pregnant women with CKD, in 10-38% with LN; in 27-64% with DN; in 20-66% pregnant women on dialysis; and in an average of 27% with KT. Thus, PE occurs frequently in women with kidney diseases.

In the Clinical Practice Guidebook for the diagnosis and treatment of chronic kidney disease in 2012 in Japan [22], CKD is defined as either renal dysfunction such as proteinuria, and/or renal dysfunction with glomerular filtration rate of <60 mL/min/1.73m² for more than 3 months. The concept of CKD has been widely accepted in clinical practice [22]. However, in clinical practice, for women with kidney disease, the relatively old guideline published in 2007 in Japan are used [1]. In the current review, we found that the incidence rate was very high in women with CKD. Although there is little evidence, PE appears to occur more frequently in high-stage CKD than in mild CKD [6,8,9]. Meta-analysis of the occurrence rate of PE according to the grade of CKD is therefore warranted. As for LN, PE occurred in 10-38%, especially in pregnant women with the most severe forms of LN (proliferative or class III-IV), almost 6-fold higher than in pregnant women with SLE but not with LN [8]. Therefore, pregnancy with a high class of LN is a very high risk factor for PE. As for DN, PE occurred in 20-66%. Since the progression of diabetes is mainly due to bad control of blood glucose, if women with DN become pregnant, strict control of blood glucose levels during pregnancy and the puerperal period is necessary to prevent the progression to end-stage DN and the occurrence of PE.
As for pregnancy while on dialysis, not only PE, but also severe hypertension, often occur [3]. However, the success rate of pregnancies while on dialysis is growing and is approaching 75% [3]. Now, in most cases, daily dialysis is introduced, resulting in the improved outcomes observed in the past decade [3].

As for pregnancy with KT, PE occurred in an average of 27%. The reasons why PE occurs at such a high rate have not been elucidated. Close monitoring of home blood pressure may be useful for early detection of hypertension in pregnancy.

In conclusion, pregnant women with CKD, dialysis, and kidney transplantation are at very high risk for the occurrence of PE. In a survey of articles on kidney disease in pregnancy, meta-analysis existed only for a review on pregnancies in women with KT. However, in the evaluation of short- and long-term prognoses of renal function in women with kidney diseases, clinical studies are lacking on the prognosis of pregnant women with kidney diseases, especially CKD, LN, DN and on dialysis. The accumulation of case series, case-control studies, and cohort studies is therefore urgent. In the future, meta-analyses of the occurrence rates of PE in women with CKD, LN, DN, dialysis and KT should be summarized, and recommendations for enabling and continuing pregnancy should be published.

CONTRIBUTORS

N.H. systemically searched for articles, and selected eligible articles; A.O. wrote manuscript; and R.U, S.M. and M.S. critically reviewed the manuscript.

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