Review Article

Chronic Kidney Disease and Pregnancy

Dr Manik Kataruka[1]

Introduction

Incidence of chronic kidney disease (CKD) is increasing worldwide. Similarly, incidences of renal diseases are increasing in pregnant and pre-pregnant women. Presence of renal disease may alter the course of pregnancy and both maternal and fetal outcome. Increase in incidence may be due to increase use of screening test and increase in risk factors in the pregnant and pre-pregnant women. Many women are diagnosed to have renal disease during their pregnancy due to universal screening of blood pressure and proteinuria. Pre-eclampsia and eclampsia occurs at a higher incidence in patients with kidney disease and occurrence of both the condition may deteriorate the pre-existing kidney disease in pregnant women. Incidence of CKD in women aged between 20-39 years in United States is estimated to be 3%[1] and in UK, it is estimated to be 2% (Health and Social Care Information Centre, 2010). Incidence of CKD in Indian subcontinent is not available due to lack of central registry. Pregnant women with CKD are at a higher risk of complication and adverse outcome compare to healthy pregnant women.[2] Advances in the knowledge and treatment of CKD has resulted in better pregnancy and fetal outcome compared to past, consequently now most of the pregnant females with CKD had a successful pregnancy outcome.

Factors Affecting Pregnancy Outcomes

Predictors of adverse events in pregnancy include:

- Severity of renal disease
- Severity of proteinuria
- Severity of hypertension
- Development of pre-eclampsia
- Previous poor obstetric history

Proteinuria

Proteinuria is a known risk factor for CKD progression. In pregnancy, proteinuria in CKD patients is associated with worse outcome. During pregnancy, in CKD patients, proteinuria may aggravate due to increased renal blood flow and cessation of ACE inhibitors. About 30% of non proteinuric CKD patients may start excreting significant amount of protein during pregnancy. Both pregnancy and proteinuria are a pro-thrombotic condition. So anti-coagulation therapy with low molecular heparin may be considered in patients with proteinuria more than 2gm per day or serum albumin less than 2gm/dl.

Hypertension

Incidence of chronic hypertension in general population is increasing. Pregnant women with chronic hypertension have a poorer pregnancy outcome compared to the normotensive pregnant woman. New onset hypertension is common in normotensive CKD patients during pregnancy. Previously hypertensive CKD patients have higher incidence of pre-eclampsia and eclampsia during pregnancy compared to non CKD control. Target blood pressure control in CKD pregnant patient has not been validated but experts

1. DM (Nephrology), Calcutta National Medical College & Hospital, Kolkata

recommends a target of 120-139/70-85 mmHg for all women with CKD.[3]

Pre-eclampsia

Diagnosis of pre-eclampsia in pregnant lady with pre-existing CKD is difficult. Both CKD and pre-eclampsia can present with hypertension and proteinuria. Diagnosis of superimposed pre-eclampsia in CKD patients can be suspected by sudden aggravation of proteinuria or decline in renal function after 20 week of pregnancy. Decrease platelet count and deranged LFT also points towards superimposed pre-eclampsia in CKD patients.[4] Soluble fms-like tyrosine kinase receptor (s-Flt) and placental growth factor (PlGF) concentration ratios are lower in women with CKD compared to women with pre-eclampsia.[5] Thus, these markers can be used to distinguish between CKD and pre-eclamsia.

Incidence of pre-eclampsia increases with decline in renal function. Presence of hypertension and proteinuria also increases the risk of superimposed pre-eclampsia in CKD patients. Women with lupus nephritis, renal transplants and reflux nephropathy appear to be at increased risk of pre-eclampsia. Women with CKD and pre-eclampsia should be admitted for assessment of maternal and fetal assessment. Multi disciplinary consultation should be done to assess the maternal risk of deteriorations of renal function and neonatal risk of preterm delivery.

Management

Pregnant women with CKD should be managed by obstetrician along with consultation of nephrologist and neonatologist. When a CKD woman becomes pregnant, her medication prescription should be reviewed and all teratogenic medicines like ACE inhibitors and others should be stopped. Blood pressure should be strictly controlled with systolic blood pressure less than 140 mm of Hg. Diastolic pressure less than 70 mm of Hg should be avoided due to risk of fetal compromise. All patients should be started on aspirin 75mg daily. Thrmboprophylaxis with low molecular heparin should be considered in patient with serum albumin less than 2 gm/dl or having proteinuria more than 2 gm per day. Vitamin D deficiency should be corrected with cholecalciferol and/or 1-alpha-calcidol depending on level of renal impairment. UTI should be promptly treated with proper antibiotic and antibiotic prophylaxis should be continued after one episode of UTI. Hemoglobin should be maintained around 10-11 gm/dl. Oral or intravenous iron therapy should be continued. Erythropoietin should be started or dose should be increased if desired haemoglobin is not maintained with iron therapy. Creatinine should be monitored every monthly till 32 week and then every fortnightly. Dialysis should be initiated if blood urea > 20 mmol/L, or problems with hyperkalemia or acidosis or fluid balance are detected. Hemodialysis in pregnant women are given in gentle manner with slower blood flow and dialysate flow. More frequent hemodialysis (5 times a week) are required in pregnant patients. Patients who are on peritoneal dialysis can be continued in peritoneal dialysis if there is no problem in inflow and outflow. Babies of women on peritoneal dialysis have higher birth weights and patients have fewer episodes of pre-eclampsia but are more likely to deliver preterm.[6] If there are problems in flow or adequate dialysis is not achieved with peritoneal dialysis, patients can be shifted to hemodialysis. Fetal growth should be regularly monitored. It is unusual for CKD to be a valid indication for cesarean section; however, operative deliveries are common. Water soluble vitamins including 5 mg folic acid should be prescribed to compensate dialysis loss. New fistula should not be created during pregnancy due to possible combined effects of increased cardiac output and circulating relaxin.

In the post natal period, aspirin can be stopped if no other indication. Thromboprophylaxis should be continued up to 6 week post natal. Blood pressure should be rigorously controlled and post natal renal function should be monitored.

Maternal Renal Outcomes According to Pre-pregnancy Serum Creatinine

Pre-pregnancy serum creatinine <1.5 mg/dl (130 μmol/l): Progression to dialysis and remain dialysis dependent post nataly is seen in less than 10% women. Uncontrolled hypertension, proteinuria > 500 mg/day and GFR < 40ml/min/ m2 are associated with higher renal decline. There is 40% risk of pre-eclampsia if baseline proteinuria >500 mg/day.

Pre-pregnancy serum creatinine 1.5-2.5 mg/dl (130-220 μmol/l): Decline or permanent loss of GFR in 30% of women. Chances of renal function

decline increases to 50% if hypertension remains uncontrolled. Nearly 10% will have ESRD soon after pregnancy.

Pre-pregnancy serum creatinine more than 2.5 mg/dl (>220 μmol/l): Almost every patients progresses to ESRD near term or post pregnancy and remains dialysis dependent.

Fetal Outcomes According to Pre-pregnancy Serum Creatinine

Pre-pregnancy serum creatinine <1.5 mg/dl (130 μmol/l): 90% of female will have a live birth. But 50% will have premature labor and 60% will have small for gestational age babies.

Pre-pregnancy serum creatinine 1.5-2.5 mg/dl (130-220 μmol/l): 85% will have live birth but 60% will have premature birth. Complication rates are higher with uncontrolled hypertension and pre eclampsia.

Pre-pregnancy serum creatinine more than 2.5 mg/dl (>220 μmol/l): Fetal loss is high but exact estimate is unknown.

Pre-pregnancy Counselling

Advances in treatment had improved the outcome of pregnancy in CKD patients with successful outcomes. However, all women with CKD remain at higher risk of complications compared with healthy pregnant ladies. all women with CKD should be offered pre-pregnancy counselling in order to discuss the following:

- The effect of renal disease on pregnancy, including maternal and fetal complications
- The effect of pregnancy on renal disease
- Safety of medication

All women with CKD who are preparing for pregnancy should be counselled for accelerated decline in renal function, increased risk of pre-eclampsia and flare up of glomerulonephritis. They should also be counselled for risk of pre maturity and other fetal complications. Women with advanced renal failure (serum creatinine more than 2.5 mg/dl) should be counselled for use of contraceptives.

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