

Risk factors for preterm delivery in pregnancy with Chronic Kidney Disease (CKD) : A retrospective analysis

Abstract

Objective: Advanced obstetric care in pregnancy with chronic kidney disease (CKD) has improved the perinatal outcomes. However, preterm delivery associated with high cost implications and perinatal morbidity is a matter of concern in these women. Better understanding of the risk factors for preterm delivery in these women may further help to improve the outcome by targeted interventions. The objective of our study was to evaluate the maternal and fetal outcomes and identify the risk factors for induced preterm delivery in pregnancy with CKD.

Study Design: It was a retrospective analysis of 57 pregnant women with CKD. Various biochemical and clinical factors were compared between these women with induced preterm delivery and term delivery to find out associated risk factors. P value <0.05 was considered as statistically significant.

Results: Out of 57 women, 39.59% (n=22) had term delivery, 57.89% (n=33) preterm and 3.50% (n=2) women underwent medical termination of pregnancy. The mean age (26.55±4.04 vs 27.36±4.02 years, p=0.46) and body mass index (24.91±3.23 vs 25.48±3.43 kg/m², p=0.53) were similar among term vs preterm group. Primary glomerulonephritis was commonest cause of CKD in both groups. In term group, 68.2% were stage 1, 27.3% stage 2, 4.5% stage 3 and none of the patient were in stage 4 and 5. In preterm group, 48.5% were stage 1, 3.5% stage 2, 30.3% stage 3 CKD. All women in stage 4 (12.1%) and stage 5 (6.1%) had preterm births. Anaemia (4.5% vs 33.4%, p=0.018) and hypertension (31.8% vs 72.7%, p=0.003) were significantly more in preterm as compared to term group. On univariate analysis, CKD stage ≥3 (OR 15, 95% CI 1.8-127.4), uric acid (OR 1.7, 95% CI 1.15-2.44), anaemia (OR 10.50, 95% CI 1.2-88.5) and hypertension (OR 5.71, 95% CI 1.75-18.5) were significant predictors of induced preterm delivery. On multivariate analysis, hypertension and stage of CKD were significant risk factors for induced preterm delivery.

Conclusion: Conception in earlier stage of CKD, correction of anaemia in first trimester and control of hypertension are to be especially focused during preconception counselling and antenatal care of patients with CKD. Early detection of risk factors and timely intervention may reduce induced preterm delivery and improve maternal and fetal outcomes.

Keywords: Chronic kidney disease (CKD), CKD stage, Induced preterm delivery, Hypertension, Anaemia

Introduction

Pregnancy in chronic kidney disease (CKD) patients is considered as a high risk pregnancy with a prevalence of 0.1% to 3% in women of childbearing age¹. All CKD patients are at increased risk of adverse maternal and fetal outcomes which worsen as the stage of disease advances^{2,3}. With advancement in obstetric and neonatal care, an improved fetomaternal outcome in CKD patients has been reported^{4,5}. The present retrospective study was conducted in Indian settings with an objective to evaluate the maternal and fetal outcomes in pregnancies with CKD and to compare early and late stages of CKD. We also focused on evaluating the factors associated with risk of induced preterm

delivery in these patients. Better understanding of these factors can provide an opportunity to treating physician for optimization of disease, appropriate preconception counselling and targeted intervention for improved perinatal outcomes.

Materials And Methods

It was a retrospective observational study conducted at Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi from January 2007 -December 2017. During this period, 72 pregnancies diagnosed with CKD preconceptionally or in early pregnancy were identified. Complete case records could be retrieved for 57 women. Fifteen patients with incomplete/missing data and lost to follow-up were excluded from the analysis. Estimated glomerular filtration rate (eGFR) was calculated using Cockcroft-Gault formula and CKD stage was defined according to eGFR as per National kidney foundation-Kidney disease outcome quality initiative (NKF-KDOQI) guidelines ⁶. The baseline demographic ,biochemical parameters and detailed obstetric outcomes were recorded.

Comment [pc1]: Please mention about the ethical approval

Comment [pc2]: Clarify: The patient drop out in retrospective study?

Comment [pc3]: Mention the list of recorded parameters

Adverse maternal outcome were defined as development of any of complication like presence of anaemia, hypertensive disorders of pregnancy, caesarean delivery, prolonged hospital stay, intensive care unit (ICU) admissions or maternal death. Anaemia was defined as haemoglobin (Hb) level less than 11g/dl. Hypertensive disorders were defined according to National High Blood Pressure education programme working group on high blood pressure during pregnancy, 2000 ⁷. Chronic hypertension was defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg, or on anti-hypertensive therapy before 20 weeks of gestation. Preeclampsia was defined as new onset hypertension after 20 weeks of pregnancy with/without proteinuria. Superimposed preeclampsia was defined as CKD with hypertension with new onset or sudden increase in proteinuria, sudden increase in blood pressure, thrombocytopenia or deranged liver or kidney function. In this study, patients with superimposed preeclampsia were included in preeclampsia group. Eclampsia was defined as development of seizures in a patient of preeclampsia. Adverse fetal outcomes were defined as presence of any of the factors like small for gestational age (SGA, infants <10th percentile of birth weight for given gestation), oligohydramnios (amniotic fluid index <5), preterm births (<37 weeks gestation), low Apgar score (<7 at 5 min), intrauterine death or stillbirths.

For comparing different biochemical parameters and outcomes, three categories were defined. Early stage CKD was divided into stage 1, stage 2 and late stage included stage 3-5. To analyse risk factors for induced preterm delivery, two groups were defined based on period of gestation at time of delivery. Women delivered at <37 weeks were included into preterm group and who delivered at ≥ 37 weeks into term group. Various biochemical parameters and pregnancy complications were also compared between these groups.

Comment [pc4]: Define the stages

Comment [pc5]: Mention the parameters

Data analysis was carried out using SPSS software version 22.0. Continuous variables were tested for normality assumption using Kolmogorov-SMIRNOV. Descriptive statistics such as mean, standard deviation and range values were calculated for normally distributed data. Group-wise mean were compared using student t-independent/one-way analysis of variance test as appropriate. Categorical data were expressed as frequency and percentage values. Frequency data was compared between the categories using chi-square/fischer's exact test as appropriate. To assess significant variables for primary outcome, univariate logistic regression was carried out and variables found to be significant were included for multivariate logistic regression to calculate adjusted odd's ratio with 95% confidence interval. P- value<0.05 was considered as statistically significant.

Results

Baseline demographic and biochemical parameters

Majority of women in our study population were in early stages of CKD (stage I, 57.9% and stage II, 12.3%) and 29.82% of the women had a significant reduction in kidney function (Stage 3-5) (Table 1). The mean age and BMI of the study population were 27.09±3.95years and 25.22±3.37 kg/m² respectively. Majority (80.70%) of women were diagnosed to have CKD before pregnancy with a mean duration of disease 3.7 years while 19.29% were diagnosed de novo in pregnancy (Table 2). Glomerulonephritis was the commonest cause of CKD followed by nephrotic syndrome and lupus nephritis respectively.

TABLE 1: Stage-wise distribution of study population

CKD Stage	GFR(ml/min/1.73m ²)	n (%)
Stage 1	≥90	33 (57.9%)
Stage 2	60-89	7 (12.3%)
Stage 3	30-59	11 (19.3%)
Stage 4	15-29	4 (7.0%)
Stage 5	<15 or dialysis	2 (3.5%)

Table 2 depicts the comparison of biochemical parameters among three groups based on CKD stages i.e Stage 1, Stage 2 and Stage 3-5. The baseline haemoglobin (Hb) levels at the beginning of pregnancy (< 12 weeks of gestation) was similar in three groups . As the pregnancy advanced, a significant decline in mean Hb level was observed in late stage CKD only. In CKD stages 1 and 2, the serum creatinine levels did not increase with advancing pregnancy while in late stages (≥3) the serum

creatinine levels increased significantly. Similar trend was observed for serum urea levels as it did not change much with advancing gestation in early stages while increase in serum urea over each trimester was significant in late stage disease. Serum uric acid levels also increased significantly with advanced stage. Though there was significant increase in urinary protein excretion in late stage CKD but serum albumin levels were not significantly different.

TABLE 2 : Comparison of biochemical parameters among different CKD stages

Comment [pc6]: Mention in methodology the timing of biochemical parameter. In which gestational week they were checked? How many times?

Characteristic	Stage 1 (n=33) Mean ±SD or number (percentage)	Stage 2 (n=7) Mean ±SD or number (percentage)	Stage 3-5 (n=17) Mean ±SD or number (percentage)	p value
Mean Age (in years)	27.24±3.94	25.71±2.28	27.35±4.54	0.623
Mean body mass index (in kg/m ²)	25.67±3.94	24.98±2.84	24.45±2.17	0.478
Obstetric History				
Primigravidae	7 (21.2%)	1(14.3%)	6 (35.3%)	0.547
Multigravidae	26 (78.8%)	6 (85.7%)	11 (64.7%)	
H/O Abortions	20(60.61%)	3(42.9%)	8(47.06%)	0.516
Referred early	27 (81.8%)	7 (100%)	12 (70.6%)	
Referred late	6 (18.2%)	0 (0%)	5 (29.4%)	0.340
Cause of CKD				
Primary GLN	22 (66.67%)	3(42.85%)	13(76.47%)	
Nephrotic syndrome	7(21.21%)	2(28.57%)	1(5.88%)	
Lupus nephritis	3(9.09%)	1(14.28%)	1(5.88%)	
Vascular or Diabetic nephropathy	1(3.03%)	1(14.28%)	2 (11.76%)	
Mean Haemoglobinlevel(in gram%)				
First trimester	10.7±1.74	10.7±1.45	10.1±1.73	0.527
Second trimester	10.6±1.44	9.8±1.54	9.4±1.31	0.021

Comment [pc7]: What is considered early? And what is considered late?

Third trimester	10.8±1.48	10.7±1.52	9.3±1.56	0.005
Mean Serum Creatinine (in mg/dL)				
First trimester	0.78±0.76	1.24±0.44	2.06±0.74	0.001
Second trimester	0.73±0.47	1.28±0.32	2.20±0.74	0.001
Third trimester	0.76±0.57	1.21±0.48	2.87±1.69	0.001
Mean Serum Uric acid levels (in mg/dL)	6.01±1.38	5.91±2.28	8.24±1.92	0.001
Mean 24 hour Urinary Protein (mg/24hrs)	0.300±0.43	0.611±0.94	1.295±1.14	0.001
Mean 24 hour urinary creatinine (mg/24hrs)	0.444±0.86	0.494±0.25	0.701±0.25	0.456
Mean Serum Urea Levels (in mg/dL)				
First trimester	31.21±17.23	39.14±4.88	53.41±18.18	0.001
Second trimester	29.68±13.2	44.71±12.9	63.12±23.19	0.001
Third trimester	30.57±15.25	42.85±13.60	81.41±39.57	0.001
First trimesterBP (at 8 weeks)				
Systolic blood pressure	121.45±12.52	122.83±9.51	124.93±10.6	0.647
Diastolic blood pressure	78.00±10.55	78.00±8.27	79.47±7.60	0.743
Second trimesterBP (at 24 weeks)				
Systolic blood pressure	123.24±15.91	131.67±18.4	135.13±24.4	0.139
Diastolic blood pressure	79.31±11.58	84.83±9.74	88.07±19.15	0.149
Third trimesterBP (at 32 weeks)				
Systolic blood pressure	121.08±15.41	124.80±11.8	130.18±11.0	0.212
Diastolic blood pressure	76.64±10.33	78.20±12.73	86.45±6.33	0.028

*p value <0.05 is considered significant

Comparison of adverse pregnancy outcomes among different stages

Hypertensive disorders of pregnancy was the most common medical complication observed in 45.61% of CKD patients (Table 3). Even in early stages (stage1&2), preeclampsia was seen in 40% of patients while in 58.82% of patients with advanced disease (stage 3-5). Anaemia was the second most common association which was significantly more in late stage disease as compared to early stages. In our study population, 23 (40.35%) women had normal vaginal delivery, 32 (56.14%) had caesarean delivery and 2 (3.50%) underwent medical termination of pregnancy. It was observed that Stage 3-5 CKD patients had increased rate of preterm and low birth weight deliveries with mean period of gestation 32 -33 weeks at delivery and mean birth weight of 1.4 kg . There was no significant difference in apgar score among different stages. Late stage CKD required prolonged hospitalization as compared to early stages.

TABLE 3: Comparison of adverse maternal and fetal outcome among different CKD stages

Outcome Measure	Stage 1 (n=33)	Stage 2 (n=7)	Stage 3-5 (n=17)	p-value
Preeclampsia, n (%)	13 (39.39%)	3 (42.85%)	10 (58.82%)	0.437
Chronic hypertension, n(%)	6 (18.18%)	3 (42.85%)	7 (41.17%)	0.131
Anaemia, n (%)	3 (9.1%)	1 (14.3%)	8 (47.1%)	0.007
FGR, n (%)	5 (15.2%)	2 (28.6%)	7 (41.2%)	0.114
POG at Delivery (Mean ±S.D)	35.4±2.95	36.7±3.49	32.8±3.81	0.014
Preterm (n,%)				
Late (34-36.6 weeks)	11(33.34%)	0	7(41.17%)	0.147
Early(32-33.6 weeks)	2(6.06%)	0	4(23.52%)	0.067
Extremely preterm(<32weeks)	3(9.09%)	1(14.28%)	5(29.41%)	0.171
Term (n,%)	15(45.45%)	6(85.71%)	1(5.88%)	0.001

Baby Weight in Kg (Mean \pm S.D)	2.1 \pm 0.806	2.3 \pm 0.931	1.4 \pm 0.524	0.011
Low Birth Weight(<2.5 kg)	16(48.48%)	2(28.57%)	9(52.94%)	0.641
Extremely Low Birth Weight (<1.5 kg)	7(21.21%)	1(14.29%)	8(47.06%)	0.105
Normal birth weight.(>2.5 kg)	8(24.24%)	4(57.14%)	0(%)	0.004
Apgar of newborn				
at 1 minute	8	8	7	0.509
at 5 minute	8	8	8	0.427
Duration of hospital stay (Mean \pm S.D)	20.50 \pm 18.21	19.86 \pm 31.8	35.47 \pm 25.43	0.078
Mode of Delivery				
Vaginal delivery	12(36.36%)	5(71.42%)	6(35.29%)	0.425
Caesarean delivery				
MTP	19(57.58%)	2(28.57%)	11(64.70%)	
	2(6.06%)	0	0	

*p value <0.05 is considered significant

Comparison of biochemical parameters and adverse pregnancy outcomes based on period of gestation at delivery

The difference in the biochemical parameters and obstetric outcomes between preterm and term group is summarized in Table 4 and 5. In our analysis, 33(57.89%) women had preterm births while 22(38.59%) delivered at term. Primary glomerulonephritis was the commonest cause of CKD among both groups. There was no significant difference in mean age and BMI among two groups. In preterm group, first trimester Hb was significantly lower than the term group (10.24 \pm 1.62 vs 11.18 \pm 1.59;

p=0.03). Blood urea, serum creatinine and serum uric acid were significantly higher in each trimester in preterm delivery group as compared term group. In late CKD stages 3-5, majority 16 (94.11%) women had preterm delivery while only 1(4.5%) delivered at term. Most (95.46%) of the women who delivered at term belonged to early disease (Stage 1&2). Medical complications such as anaemia (33.4% vs 4.5%) and hypertension (72.7% vs 31.8%) were significantly more in preterm as compared to term group. We also found that preterm group had significantly higher mean systolic blood pressure than term delivery (126.34±11.83 vs 118.62±10.02) even at first trimester (8 weeks).On follow up, difference in second trimester mean systolic and diastolic BP was also significant among two groups . At 32 weeks, difference in SBP remained significant (128.95±15.43 vs 118.75±10.98; p value =0.020).

Table 4: Comparison of biochemical characteristics among groups based on period of gestation at delivery

Characteristic	Preterm Group (n=33)	Term Group (n=22)	p-value
Mean Age (in years)	27.36±4.02	26.55±4.04	0.46
Mean BMI (in kg/m ²)	25.48±3.43	24.91±3.23	0.53
Mean Haemoglobinlevel(in gram%)			
First trimester	10.24±1.62	11.18±1.59	0.03
Second trimester	9.94±1.43	10.68±1.46	0.06
Third trimester	10.12±1.63	11.00±1.51	0.04
Mean Serum Urea Levels (in mg/dL)			
First trimester	43.97±17.12	28.73±14.01	0.001
Second trimester	48.79±23.34	31.05±16.95	0.003
Third trimester	59.70±36.34	30.91 ±19.43	0.001

Mean Serum Creatinine (in mg/dL)			
First trimester	1.45±.93	0.77±.86	0.009
Second trimester	1.58±.93	0.82±.85	0.003
Third trimester	1.91±1.56	0.86±.99	0.008
Mean 24 hour Urinary Protein (mg/24hrs)	0.70±1.07	0.23±.68	0.075
Mean Serum Uric acid levels (in mg/dL)	7.33±1.74	5.77±1.90	.003

*p value <0.05 is considered significant

Table 5: Comparison of baseline characteristics among preterm and term group

Characteristic	Preterm (n=33)	Term (n=22)	p-value
Parity			
Primiparous (no, %)	9 (27.3%)	6 (27.3%)	1.00
Multiparous (no, %)	24(72.7%)	16 (72.7%)	
Number of abortions (no,%)			
0	15(45.5%)	12(54.5%)	
1	14(42.4%)	8 (36.4%)	0.797
2	4 (12.1%)	2 (9.1%)	
Cause of disease			
Primary GLN	27(81.8%)	13 (59.1%)	0.064
Nephrotic syndrome	1(3.0%)	5 (22.7%)	0.033
Lupus nephritis	2(6.06%)	3 (13.6%)	0.379
Vascular or Diabetic nephropathy	3(9.09%)	1 (4.5%)	0.642

Stage of disease (based on eGFR)			
Stage 1	16 (48.5%)	15(68.2%)	
Stage 2	1 (3.0%)	6 (27.3%)	
Stage 3	10(30.3%)	1 (4.5%)	0.004
Stage 4	4 (12.1%)	0 (0%)	
Stage 5	2 (6.1%)	0 (0%)	
First trimesterBP (at 8 weeks)			
Systolic blood pressure	126.34±11.83	118.62±10.02	0.019
Diastolic blood pressure	80.83±9.92	76.57±8.29	0.116
Second trimesterBP (at 24 weeks)			
Systolic blood pressure	133.93±21.85	120.48±14.23	0.017
Diastolic blood pressure	86.55±17.09	77.67±7.30	0.030
Third trimesterBP (at 32 weeks)			
Systolic blood pressure	128.95±15.43	118.75±10.98	0.020
Diastolic blood pressure	81.86±10.99	76.95±9.43	0.134
Anaemia (no,%)	11 (33.4%)	1 (4.5%)	0.018
Hypertension (no,%)	24 (72.7%)	7 (31.8%)	0.003

*p value <0.05 is considered significant

Based on univariate analysis (Table 6), CKD stage ≥ 3 (OR 15, 95% CI 1.8-127.4), serum uric acid levels (OR 1.7, 95% CI 1.15-2.44), anaemia (OR 10.50,95%CI 1.2-88.5) and hypertension(OR 5.71,95%CI 1.75-18.5) were significant predictors of induced preterm delivery in CKD patients. On multivariate analysis, hypertension and stage of CKD were significant risk factors for induced preterm delivery.

Table 6 :Univariate analysis of induced preterm delivery in CKD patients

Characteristic	Odds Ratio	95% Confidence Interval	P value
Stage of disease (stage ≥ 3)	15.0	1.8-127.4	0.013
Haemoglobin (First trimester)	0.68	0.47-0.99	0.046
Serum urea levels (First trimester)	1.08	1.02-1.14	0.003
Serum creatinine levels (First trimester)	2.4	1.96-5.03	0.014
Serum uric acid levels	1.7	1.15-2.44	0.007
Anaemia	10.50	1.2-88.5	0.03
Hypertension	5.71	1.75-18.5	0.004

DISCUSSION

Over the years, with better health care more pregnancy in CKD patients are being reported^{4,5}. Our data also depicted an increase in number of pregnant patients with CKD as 28.07% (n=16) cases were found from 2004-2010 and 42.10% (n=24) cases from 2011-2017. Pregnancy with CKD is considered as high risk pregnancy and it is associated with an increased risk of adverse maternal and fetal outcomes which worsen as the stage of disease advances^{3,4}. So, the present study was conducted to study the characteristics and various pregnancy-related adverse outcomes in women with different CKD stages. As preterm births contribute to significant perinatal morbidity in these patients, we further analysed risk factors for preterm delivery in pregnancy with CKD.

In present study, 57 pregnant patients with CKD were analyzed. The mean age of our study population was 27.09 ± 3.95 years which is comparable to other Indian studies^{8,9}. While the mean age in studies by Braham et al and Piccoli et al was 33.1 ± 4.7 yrs and 31 ± 5 yrs respectively^{3,10}. This difference in the mean age may be attributed to sociocultural differences in terms of early marriage and child bearing in the Indian population.

Out of 57 patients, 19.29% were diagnosed de novo during pregnancy which is comparable to other studies in literature^{3,9}. We classified CKD stages based on eGFR in accordance with KDOQI guidelines¹. This provided us with advantage of picking women even in very early stages of disease when renal parameters like blood urea and serum creatinine are not much deranged. Several studies in literature have mentioned that despite being an important predictor of pregnancy outcomes in CKD,

serum creatinine is relatively insensitive to mild and moderate renal impairment^{3,11,12}. Alsuwaida et al has also demonstrated that eGFR is more sensitive in detecting subclinical renal disease as compared to serum creatinine alone¹³. In our analysis, most (70.17%) of the patients belonged to early CKD stage which may indicate early childbearing in our population and at that age patient may be in earlier stages of disease. This suggests that pregnancy also provide an opportunity to screen for renal disease and diagnosis early in the course of CKD.

Our study depicted a gradual increase in pregnancy related risk from early (stage 1,2) to late stage (3-5) disease. The same has been reported in literature¹⁴⁻¹⁶. This increase in risk particularly included development of hypertension, anaemia and risk of prematurity. Hypertensive disorders of pregnancy was found to be most common complication observed in 46.4% of CKD patients followed by anaemia in 21.1% of study population. Preeclampsia was more in late stage CKD as compared to early stage (76.47% vs 45.0%). Overall, two third of patients (57.89%) received antihypertensives. Monotherapy for treatment of hypertension was used in 46.1% (12) women while 53.84% (14) needed two or more drugs. Several studies have mentioned increased incidence of hypertension in patients with kidney disease^{4,8,9}. Piccoli et al also found new onset hypertension to be more in CKD patients as compared to controls (12% vs 5.5%)¹⁴. We found anaemia was significantly more in advanced stage disease (47.1% vs 10.0%). The response to traditional oral and injectable iron therapy was less in anaemia of advanced CKD and it got improved with simultaneous use of erythropoietin therapy. Erythropoietin was needed in 87.5% (7 out of 8) women belonging to stage 3-5. Among late stage CKD, all the 7 patients who received erythropoietin had primary glomerulonephritis as underlying cause with median duration of disease of 2 years. We should consider early use of erythropoietin therapy if there is no improvement in haemoglobin levels with oral and injectable iron therapy. Consistent with other reported data, our study also had a high caesarean rate which was comparable in early (52.5%) and late stages (64.70%)^{9,14,17}.

We found that even stage 1 CKD is associated with risk of adverse pregnancy outcomes. In our study, 57.9% of the women belonged to stage 1 CKD based on eGFR. Their renal parameters were in normal range. The association of stage 1 disease with adverse outcome suggests that presence of kidney disease per se affects pregnancy and eGFR is more sensitive than serum creatinine values for pick up of kidney disease patients in early stages. In our analysis, 42.42% of the stage 1 CKD women developed preeclampsia, 15.2% had intrauterine growth restriction, 48.5% had preterm delivery with mean POG of 35.4 weeks and birth weight of 2.1 kg respectively and caesarean rate of 57.58%. Literature has enough evidence that even early stage CKD is associated with adverse pregnancy outcomes^{14,18-19}. Alsuwaida et al also reported that early stage CKD have significantly increased risk of preeclampsia (20.8%), intrauterine growth restriction (38.5%), preterm birth (31.2%) and caesarean delivery (39.8%)¹³. Considering the high incidence of preeclampsia (42.42%) even in early stage CKD in, it is advisable to screen patients with preeclampsia for CKD especially in the absence

of other high risk factors . Every CKD patient even with conserved renal function should be closely monitored and treated with combined efforts of obstetrician ,neonatologist and nephrologist at tertiary care centre.

Our result specifically focused on preterm delivery as a complication in CKD patients and analysed risk factors for the same. Preterm delivery occurred in 60% of our CKD patients irrespective of the stage of the disease. As the stage of disease advanced , risk increased significantly to 90.90% in stage 3 and 100% of women in stage 4,5. Recently Piccoli et al also confirmed that CKD patients are at higher risk than a low risk population for preterm delivery ¹⁹. Kendrick et al reported 52% increased odds of preterm delivery in women with kidney disease as compared to women without kidney disease ¹⁷. We found that the patients with preterm delivery had significantly higher SBP in each trimester as compared to patients with term delivery. Our analysis highlighted that the presence of hypertension and anaemia ,more commonly found in advanced CKD stages(3-5) increases the risk for preterm delivery with odd's ratio of 10.50 and 5.71 respectively (Table 6).This relationship is further confirmed by multivariate analysis in our study and underlines the importance of CKD stages for preterm delivery. This finding may thus suggest focusing special attention on hypertension and anaemiapreconceptionlly and in first trimester . Piccoli et al 2017 concluded that development of proteinuria as a risk factor for preterm delivery but not the presence of hypertension .Although they does mentioned importance of CKD stage for early preterm delivery ¹⁹.

Our study has several limitations. It was an observational study with relatively small sample size and absence of control population. Casual relationship between kidney disease and adverse outcome could not be established. Due to lack of data on kidney function in postpartum period we were unable to find out the impact of pregnancy on kidney function.

We conclude that every pregnancy with CKD is at increased risk of adverse fetomaternal outcome and should be managed with combined efforts of obstetrician ,neonatologist and nephrologist at tertiary care health centre. In CKD patients even with conserved renal function , development of hypertension and anaemia is an alarming sign and need close monitoring and prompt action for improved maternal and fetal outcomes.

REFERENCES:

1. Zhang JJ, Ma XX, Hao L, et al. A systematic review and meta-analysis of outcomes of pregnancy in CKD and CKD outcomes in pregnancy. *Clin J Am Soc Nephrol*. 2015;10(11):1964-1978.
2. Piccoli GB, Attini R, Vasario E, Conijn A, Biolcati M, D'Amico F, Consiglio V, Bontempo S, Todros T: Pregnancy and chronic kidney disease: A challenge in all CKD stages. *Clin J Am Soc Nephrol* 5: 844–855, 2010

3. Bramham K, Lightstone L. Pre-pregnancy counselling for women with chronic kidney disease. *J Nephrol* 2012;25:450–9.
4. Cabiddu G, Castellino S, Gernone G et al (2016) A best practice position statement on pregnancy in chronic kidney disease: the Italian Study Group on Kidney and Pregnancy. *J Nephrol* 29(3):277–303
5. Smyth A, Radovic M, Garovic V Dv :Women,kidney disease and pregnancy.*Adv Chronic Kidney Dis*,2013;380:1662-73
6. National Kidney Foundation . K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39(2 Suppl 1):S1–266
7. Report of the National High Blood Pressure Education Program Working Group on high blood pressure in pregnancy, *Am J Obstet Gynecol* 2000;1831:S1–22.
8. Singh R, Prasad N, Banka A, et al. Pregnancy in patients with chronic kidney disease: maternal and fetal outcomes. *Indian J Nephrol* 2015;25(4):194–9.
9. Bharti J, Vatsa R, Singhal S et al. Pregnancy with chronic kidney disease: maternal and fetal outcome.*Eur J Obstet Gynecol Reprod Biol* 2016;2014:83-87
10. Bramham K, Briley AL, Seed PT, Poston L, Shennan AH, Chappell LC. Pregnancy outcome in women with chronic kidney disease: a prospective cohort study. *Reproduct Sci* 2011; 18:623.
11. Ahmed SB, Bentley – Lewis R,HollenbergNK,Graves SW ,Seely EW. A comparison of prediction equations for estimating glomerular filtration rate in pregnancy. *HypertensPregnan* 2009;28:243-255
12. Levey AS , Stevens LA , Schmid CH , Zhang YL ,Castro AF ,Feldman HI , Kusek JW ,Eggers P,Van Lente F , Greene T et al. A new equation to estimate glomerular filtration rate . *Ann Intern Med* 2009;150: 604-612
13. Alsuwaida A, Mousa D, Al-Harbi A, Alghonaim M, Ghareeb S, Alrukhaimi MN: Impact of early chronic kidney disease on maternal and fetal outcomes of pregnancy. *J Matern Fetal Neonatal Med* 24: 1432–1436, 2011
14. Piccoli GB, Cabiddu G, Attini R, et al. Risk of adverse pregnancy outcomes in women with CKD. *J Am Soc Nephrol* 2015 Aug;26(8):2011–22.
15. Imbasciati E, Gregorini G, Cabiddu G. Pregnancy in CKD stages 3 to 5: fetal and maternal outcomes. *Am J Kidney Dis* 2007;49(6):753–62.
16. Fischer MJ , Lehnerz SD ,Hebert JR, Parikh CR :Kidney disease is an independent risk factor for adverse fetal and maternal outcomes in pregnancy .*Am J Kidney Dis* 2004 ; 43: 415-423
17. Kendrick J, Sharma S, Holmen J, Palit S, Nuccio E, Chonchol M. Kidney disease and maternal and fetal outcomes in pregnancy. *Am J Kidney Dis* 2015;66 (1):55–9.

18. Nevis IF, Reitsma A, Dominic A, et al. Pregnancy outcomes in women with chronic kidney disease: a systematic review. *Clin J Am Soc Nephrol*. 2011;6(11):2587-2598.
19. Piccoli GB, Attini R, Cabiddu G, Kooij I, Fassio F, Gerbino M, Maxia S , Biolcati M , Versino E, Todros T : Maternal-foetal outcomes in pregnant women with glomerulonephritides. Are all glomerulonephritides alike in pregnancy? *Journal of Autoimmunity* 2017: 1-8

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