Fetal Risks and Maternal Renal Complications in Pregnancy with Preexisting Chronic Glomerulonephritis

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Background: Analysis the maternal and fetal risk predictors in pregnancy in conjunction with chronic glomerulonephritis (CGN) patients are helpful to understand the influence of kidney diseases on pregnancy and the effects of pregnancy on kidney diseases. The aim of this study was to determine the predictors of adverse maternal and fetal outcomes in CGN patients.

Material/Methods: Maternal and fetal outcomes in 64 pregnancies of CGN patients were retrospectively analyzed. We randomly selected 100 low-risk-pregnancy women without chronic kidney disease (CKD) at the same time as the control group. Clinical manifestations, laboratory data, medication, and outcomes during pregnancies of these patients were analyzed by univariate and logistic regression.

Results: CGN patients were associated with higher adverse pregnancy outcomes versus general pregnancies. The gestational ages are shorter, and the incidence of preeclampsia, gestational hypertension, and abortion were increased. The rates of premature delivery, low birth weights, and intrauterine growth restriction were higher in the CGN group. Prenatal proteinuria and blood pressure were significantly increased compared with pre-pregnancy stage. Proteinuria (0.9±0.6 g/d vs. 0.5±0.3 g/d, P=0.032) and hypertension (6.9% vs. 3.4%, P=0.021) at 6 months after delivery were aggravated. Prenatal proteinuria ≥3.5 g/d (OR 12.22, 95%CI 3.16~47.32, P=0.001) was the maternal risk predictor in pregnancy. Prenatal blood pressure ≥160/110 mmHg (OR 8.97, 95%CI 1.69~47.53, P=0.010) and uric acid ≥363 μmol/L (OR 7.35, 95%CI 1.88~28.76, P=0.004) were the fetal risk predictors in pregnancy in conjunction with CGN patients.

Conclusions: Maternal-fetal risks are increased in pregnancies in conjunction with CGN patients. Prenatal proteinuria ≥3.5 g/d, BP ≥160/110 mmHg, and uric acid ≥363 μmol/L were the maternal and fetal risk predictors in pregnancy.

MeSH Keywords: Chronic Kidney Disease • Glomerulonephritis • Pregnancy Complications • Renal Insufficiency

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Background

Maternal and neonatal adverse outcomes are common in pregnant women with CKD, which increase maternal and fetal risk. The most common cause of CKD is chronic glomerulonephritis (CGN), which often occurs in young persons in China [1]. Several studies have described the relationship between glomerular disease and pregnancy outcomes; it is complicated, as pregnancy may affect maternal kidney disease activity such as worsening of urine protein or hypertension and renal insufficiency, but some studies found no significant difference in renal outcomes between pregnant women with CKD and control groups [2,3]. Otherwise, CKD patients usually have a more difficult pregnancy process, and pregnant patients with CKD have a significantly higher rate of pregnancy failure, and the odds of premature birth, cesarean section, and SGA/low birth weight were also higher in women with CKD [4–9]. The odds of preeclampsia and premature delivery were higher in women with macroproteinuria compared with those with microproteinuria [10]. Some studies found that CKD stage was significantly associated with early preterm delivery and development-doubling of proteinuria [4], but there were no statistically significant differences in outcome differences between glomerular disease subtypes [5]. The degree of renal insufficiency, uncontrolled hypertension, and severity of proteinuria are unfavorable pregnancy outcomes in some cohorts, but these were small studies on outcomes of pregnancies in CGN patients. More information is needed for informed consent in CGN women considering the risks of pregnancy. The aim of this study was to determine the potential risk predictors in pregnant women with CGN, as well as the factors affecting kidney disease deterioration, to provide pre-pregnancy counselling to CKD patients and avoid possible complications.

Material and Methods

Patients

Pregnancies of 64 chronic glomerular nephritis (CGN) patients were retrospectively analyzed. All patients were between 20 and 35 years old and had been diagnosed with CGN according to the clinical feature and/or renal biopsy pathology by nephrology physicians. The key clinical feature was the presence of urinary abnormalities such as proteinuria or hematuria. Renal biopsy pathology included IgA nephropathy, mesangial proliferative glomerulonephritis, focal segmental glomerulosclerosis, membranous nephropathy, and minimal change. Renal function was measured by eGFR (estimated glomerular filtration rate calculated by the CKD-EPI equation). Secondary nephropathy patients were excluded, such as diabetic nephropathy, Henoch-Schönlein purpura nephritis, lupus nephritis, HBV/HCV related nephritis, vasculitis related renal damage, hypertensive renal damage, renal transplantation, or significant functional impairment of the brain, liver, cardiovascular, or hematopoietic systems. The clinical course of treatment for glomerulonephritis did not include RAS system inhibitors during pregnancy. We selected 100 pregnant women without CKD at the same time as the control group. The maternal and fetal characteristics were follow-up by nephrology physicians in the first 6 months after pregnancy.

Clinical characterization

Clinical manifestations, laboratory data, medication during pregnancy, and maternal and fetal outcomes were recorded. Laboratory data included hemoglobin, blood coagulation function, proteinuria, albumin, serum creatinine (CRE), immunoglobulin (IgG, IgA, and IgM), and complement C3 and C4. Clinical manifestations included blood pressure, fetal weights, and gestational weeks.

Related definitions

CGN was defined according to the Kidney Disease Outcomes Quality Initiative (K-DOQI) guidelines [11]. Proteinuria was defined by the presence of urine protein ≥0.5 g/d. Mild hypertension was defined as systolic blood pressure 140~159 mmHg or diastolic blood pressure 90~109 mmHg. Severe hypertension was defined as systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg [12]. Pregnancy-induced hypertension was diagnosed on the basis of an initial diastolic blood pressure >90 mmHg with a later increase of at least 25 mmHg, or initial diastolic blood pressure <90 mmHg with an increase of at least 15 mmHg after 20 weeks of gestation. Pre-eclampsia was diagnosed as the onset of blood pressure ≥140/90 mmHg after 20 weeks of gestation in previously normotensive patients, accompanied by new-onset proteinuria ≥300 mg/d but without proteinuria at baseline [12]. Hypoalbuminemia was defined as serum albumin lower than 35 g/L and anemia was defined as hemoglobin lower than 110 g/L.

Fetal loss referred to abortion due to the disease, spontaneous abortion, and fetal death. Small for gestational age (SGA) was defined as an estimated birth weight below the 10th percentile for the gestational age. Fetal growth restriction was defined as fetal growth impairment, based on the fetal growth curve below the 10th percentile. Low birth weight was defined as birth weights <2500 g. Premature births include scheduled earlier delivery that had to be conducted in some cases because of the disease activity; these women underwent pregnancy termination.

Statistical analysis

SPSS 10.0 software was used for statistical analysis. The technologist in our information section analyzed the charts and
controlled the database. Each pregnancy was analyzed as a separate incidence. Descriptive data are summarized as mean ±SD or frequency (percentage). Baseline data were compared between the 2 groups, including age, blood pressure, proteinuria, albumin, uric acid, gestational ages, birth weight, and low birth weights. Proteinuria, hypertension, plasma albumin, hemoglobin, creatinine, and uric acid during pre-pregnancy and prenatal period in CKD patients were compared. Univariate analysis and regression analysis were used to find which factor were associated with adverse maternal and fetal outcomes in CKD patients. Student’s t-test was used to analyze the significance of differences in mean continuous parameters between the 2 groups. Categorical variables were analyzed using χ² tests. OR and 95% CI were used to estimate the relative risk posed by an exposure variable adjusted for the effects of other covariates. Probability values less than 0.05 (p<0.05) were considered statistically significant.

Table 1. Maternal and fetal outcomes of pregnancies in chronic kidney disease (CKD) patients and the control group (general pregnancy women).

| Characteristics                  | CKD patients (N=64) | Control group (N=50) | χ² or t | P-value |
|----------------------------------|---------------------|----------------------|---------|---------|
| Age (years)                      | 30.2±3.9            | 29.5±2.5             | 1.15    | 0.252   |
| Blood pressure (mmHg)            | 123.5±6.0           | 106.2±3.0            | 5.31    | 0.003   |
| Proteinuria (g/d)                | 0.5±0.8             | 0.00±0.00            | 4.51    | 0.001   |
| Albumin (g/l)                    | 36.5±4.0            | 40.0±4.1             | 4.17    | 0.002   |
| Creatine (μmol/l)                | 67.0±7.5            | 45.8±9.3             | 2.81    | 0.006   |
| Uric acid (μmol/l)               | 313.0±103.6         | 212.5±51.2           | 6.09    | 0.001   |
| Prenatal proteinuria (g/d)       | 2.3±3.4             | 0.00±0.01            | 5.11    | 0.001   |
| Prenatal albumin (g/l)           | 35.1±5.3            | 39.9±4.2             | 5.04    | 0.001   |
| Prenatal creatine (μmol/l)       | 81.3±8.0            | 48.5±10.6            | 2.35    | 0.021   |
| Prenatal uric acid (μmol/l)      | 325.6±120.8         | 206.3±58.5           | 6.32    | 0.001   |
| Gestational ages (weeks)         | 37.3±0.4            | 39.1±0.1             | 3.51    | 0.005   |
| Gestational hypertension (%)     | 2 (3.13)            | 1 (2.0)              | 0.14    | 0.710   |
| Preeclampsia (%)                 | 19 (29.7)           | 1 (2.0)              | 14.88   | <0.001  |
| Birth weights (g)                | 3161.2±626.9        | 3427.9±370.4         | 8.32    | 0.009   |
| Premature (%)                    | 15 (23.4)           | 1 (2.0)              | 10.70   | 0.001   |
| Low birth weights (%)            | 10 (15.6)           | 0.0                  | 6.722   | 0.010   |
| Intrauterine growth restriction (%)| 8 (12.5)          | 0.0                  | 4.94    | 0.026   |
| Fetal distress (%)               | 10 (15.6)           | 6 (12.0)             | 0.31    | 0.580   |
| Fetal malformation or mortality (%)| 3 (4.7)            | 0.0                  | 0.925   | 0.336   |

Compared with the control group, P<0.05 was considered statistically significant.

Results

Maternal and fetal outcomes of pregnancies in CGN patients and low-risk-pregnancy women

The clinical characteristics of the CGN patients are summarized in Table 1. All of the 64 patients were single-pregnancy, 62 patients were primipara, 2 cases were pluripara, and 4 cases had abnormal pregnancy history. The average age of the 64 patients was 30.2±3.9 years (21~40 years old), and 7 were over 35 years old. The mean number of pregnancies was 1.3±0.6. The gestational ages were 37.3±0.4 weeks (22.4~41.4 weeks). The histories of CGN prior to the current pregnancy were 3.2±1.8 years (1~13 years). We found that 42 (65.6%) patients were diagnosed by renal biopsy, including of 21 (32.8%) IgA nephropathy (14 cases were mild mesangial proliferative and 7 cases were focal proliferative), 8 mild mesangial proliferative glomerulonephritis, 3 focal segmental glomerulosclerosis, 6 membranous nephropathy, and 4 were minimal change. Six patients had history of hypertension; 21 patients had received
Table 2. Characteristics of pre-pregnancy and prenatal in CKD patients.

| Characteristics | Pre-pregnancy | Prenatal | $\chi^2$ or $t$ | P-value |
|-----------------|---------------|----------|----------------|---------|
| Hematuria (%)    | 4 (6.25)      | 15 (23.4)| 7.48           | 0.011   |
| Hypertension (%) | 2 (3.13)      | 17 (26.6)| 19.1           | 0.001   |
| Proteinuria (g/d)| 0.5±0.8       | 2.3±3.4  | 3.78           | 0.001   |
| Plasma albumin (g/L)| 36.5±4.0     | 35.1±5.3 | 1.52           | 0.131   |
| Hemoglobin (g/L) | 112.8±13.6    | 109.4±18.1| 1.21           | 0.229   |
| Creatinine (μmol/L)| 67.0±7.5     | 81.3±8.0 | 1.05           | 0.296   |
| Uric acid (μmol/L)| 313.0±103.6  | 325.6±120.8| 0.58          | 0.565   |

Data are expressed as means ±SD or percentage, P<0.05 was considered statistically significant.

In the low-risk group (100 pregnant women), the average age was 29.5±2.5 years. None had history of chronic renal disease, diabetes, hypertension, or cardiovascular disease, all women were proteinuria-negative, and serum creatinine was 45.8±9.3 μmol/L. The pregnancy ages and plasma albumin of CGN patients were lower than in the low-risk group, and the urine protein, serum creatinine, and uric acid were significantly higher than in the low-risk group (P<0.05).

Compared with the low-risk-pregnancy women, the CGN pregnancy patients had higher morbidity of preeclampsia and shorter gestational ages, and the incidences of prematurity, low birth weights, and intrauterine growth restriction were significantly higher. Risk factors included urinary proteinuria, renal function, uric acid, and blood pressure (Table 1).

Characteristics of pre-pregnancy and prenatal periods in CGN patients

The incidence of proteinuria, hematuria, and hypertension in the prenatal period were significantly increased compared with pre-pregnancy in CGN patients, but serum creatinine, albumin, hemoglobin, and uric acid were not different (Table 2).

Risk factors for adverse maternal outcomes in CGN patients

The adverse maternal outcomes included gestational hypertension, preterm, early and extreme preterm delivery and abortion. In the 64 cases, 22 (34.4%) had adverse maternal outcomes, which was higher than in the low-risk group (1.2%). By univariate analysis, pre-pregnancy or prenatal proteinuria, and prenatal blood pressure were factors associated with adverse maternal outcomes (Table 3). Logistic regression analysis demonstrated that prenatal urinary protein ≥3.5 g/d was an independent risk factor for adverse maternal outcomes (Table 4).

Risk factors of adverse fetal outcomes in CGN patients

The fetal adverse outcomes were prematurity, intrauterine growth restriction, small for gestational age (SGA), and fetal death, and 17 (26.6%) patients had fetal adverse outcomes, which was higher than in the low-risk group (1.2%). Univariate analysis showed that pre-pregnancy or prenatal proteinuria or serum creatinine, prenatal blood pressure, and prenatal uric acid were associated with adverse fetal outcomes (Table 5). Logistic regression analysis indicated that prenatal blood pressure ≥160/110 mmHg and prenatal uric acid ≥363 μmol/L were independent risk factors for adverse fetal outcomes (Table 6).

Follow-up study of CGN patients at 6 months after delivery

To clarify the influence of pregnancy on renal damage, our analyzing laboratory performed a follow-up study of 29 cases of CGN diagnosed by renal biopsy in pregnant women. The renal function in 29 CGN patients at 6 months after delivery remained stable compared with the baseline of pre-pregnancy, although the proteinuria was elevated 6 months after delivery (Table 7).

Discussion

CKD may lead to maternal and neonatal adverse outcomes in pregnant women, but there are few relevant studies and their conclusion are conflicting. CKD is made up of several diseases, the progression of CKD differs from patient to patient, and the
Table 3. Univariate analysis of adverse maternal outcomes in CKD patients.

| Characteristics                        | Non-adverse outcomes cases (%) | Adverse outcomes cases (%) | Chi² | P-value |
|----------------------------------------|--------------------------------|---------------------------|------|---------|
| Proteinuria before pregnancy (g/d)     |                                |                           |      |         |
| <0.5                                   | (78.6)                         | (45.5)                    | 8.043| 0.027   |
| 0.5~1                                  | (11.9)                         | (3.1)                     | 7.182| 0.007   |
| ≥3.5                                   | (9.5)                          | (4.5)                     | 0.110| N/A     |
| Serum creatinine before pregnancy (umol/l) |                                |                           |      |         |
| <71                                    | (78.6)                         | (54.5)                    | 3.993| 0.046   |
| 71~132                                 | (19.0)                         | (31.8)                    | 1.496| 0.221   |
| 132~265                                | (2.4)                          | (4.5)                     | N/A  | 0.115   |
| Blood pressure before pregnancy (mmHg) |                                |                           |      |         |
| <140/90                                | (95.2)                         | (100)                     | N/A  | 0.542   |
| 140~159/90~109                         | (47.6)                         | (0)                       | N/A  | N/A     |
| ≥160/110                               | (0)                            | (0)                       | N/A  |         |
| Albumin before pregnancy (g/l)         |                                |                           |      |         |
| <30                                    | (100)                          | (95.5)                    | N/A  | 0.344   |
| ≥30                                    | (1)                            | (4.5)                     |      |         |
| Uric acid before pregnancy (umol/l)    |                                |                           |      |         |
| <363                                   | (95.2)                         | (81.8)                    | 1.685| 0.194   |
| ≥363                                   | (4.8)                          | (18.2)                    |      |         |
| Prenatal proteinuria (g/d)             |                                |                           |      |         |
| <0.5                                   | (52.4)                         | (22.7)                    | 14.176| 0.003   |
| 0.5~1                                  | (11.9)                         | (13.6)                    | 1.133| 0.287   |
| ≥3.5                                   | (2.4)                          | (18.2)                    | 13.181| <0.001  |
| ≥3.5                                   | (0)                            | (0)                       |      |         |
| Prenatal serum creatine (umol/l)       |                                |                           |      |         |
| <71                                    | (81.0)                         | (59.1)                    | 7.214| 0.037   |
| 71~132                                 | (16.7)                         | (27.3)                    | 1.954| 0.16    |
| 132~265                                | (2.4)                          | (13.6)                    | 3.344| 0.067   |
| ≥265                                   | (0)                            | (0)                       |      |         |
| Prenatal blood pressure (mmHg)         |                                |                           |      |         |
| <140/90                                | (95.2)                         | (22.7)                    | 36.806| <0.001  |
| 140~159/90~109                         | (4.8)                          | (31.8)                    | 19.310| <0.001  |
| ≥160/110                               | (0)                            | (45.5)                    |      |         |
| Prenatal serum albumin (g/l)           |                                |                           |      |         |
| <30                                    | (4.8)                          | (18.2)                    | 6.334| 0.042   |
| ≥30                                    | (0)                            | (0)                       |      |         |

Data are expressed as percentage, P<0.05 was considered statistically significant.

Table 4. Predictors of adverse maternal outcomes in CKD patients by logistic regression analysis.

| Predictors                  | OR    | 95%CI       | P-value |
|-----------------------------|-------|-------------|---------|
| Prenatal proteinuria ≥3.5 g/d| 12.22 | 3.16~47.32  | 0.001   |

P<0.05 was considered statistically significant.
Table 5. Univariate analysis of adverse fetal outcomes in CKD patients.

| Characteristics                      | Non-adverse outcomes cases (%) | Adverse outcomes cases (%) | χ²  | P-value |
|--------------------------------------|-------------------------------|---------------------------|-----|---------|
| Proteinuria before pregnancy (g/d)  |                               |                           |     |         |
| <0.5                                 | 35 (74.5)                     | 8 (47.1)                  | 4.254 | 0.039   |
| 0.5–1                                | 8 (17.0)                      | 4 (23.5)                  | 2.949 | 0.086   |
| 1–3.5                                | 3 (6.4)                       | 5 (29.4)                  | 5    | 1.000   |
| ≥3.5                                 | 1 (2.1)                       | 0                         |     |         |
| Serum creatinine before pregnancy (umol/l) |                     |                           | 16.003 | <0.001 |
| <71                                  | 39 (83.0)                     | 6 (35.2)                  | 13.599 | <0.001  |
| 71–132                               | 8 (17.0)                      | 7 (41.2)                  | 8.122 | 0.004   |
| 132–265                               | 0                             | 2 (11.8)                  | N/A  | 0.067   |
| Blood pressure before pregnancy (mmHg) |                             |                           |     |         |
| <140/90                               | 46 (97.9)                     | 16 (94.1)                 | 0.000 | 1.000   |
| 140–159/90–109                        | 1 (21)                        | 1 (5)                     | N/A  | N/A     |
| ≥160/110                              | 0                             | 0                         |     |         |
| Albumin before pregnancy (g/l)       |                               |                           |     |         |
| <30                                  | 0                             | 1 (5.9)                   |     | 0.266   |
| ≥30                                  | 47 (100)                      | 16 (94.1)                 |     |         |
| Uric acid before pregnancy (umol/l)  |                               |                           |     |         |
| <363                                  | 45 (97.7)                     | 13 (76.5)                 |     |         |
| ≥363                                  | 2 (4.3)                       | 4 (23.5)                  |     |         |
| Prenatal proteinuria (g/d)           |                               |                           |     |         |
| <0.5                                 | 25 (51.2)                     | 2 (11.8)                  | 8.785 | 0.003   |
| 0.5–1                                 | 6 (12.8)                      | 2 (11.8)                  | 9.069 | 0.003   |
| 1–3.5                                 | 9 (19.1)                      | 5 (29.3)                  | 5.517 | 0.019   |
| ≥3.5                                  | 7 (14.3)                      | 8 (47.1)                  |     |         |
| Prenatal serum creatine (umol/l)     |                               |                           |     |         |
| <71                                  | 40 (85.1)                     | 7 (41.2)                  | 10.202 | 0.001   |
| 71–132                                | 7 (14.9)                      | 6 (35.3)                  | 8.122 | 0.004   |
| 132–265                               | 0                             | 1 (5.9)                   | N/A  | 0.016   |
| ≥265                                  | 0                             | 3 (17.6)                  |     |         |
| Prenatal blood pressure (mmHg)       |                               |                           |     |         |
| <140/90                               | 38 (80.8)                     | 7 (41.2)                  | 9.414 | 0.002   |
| 140–159/90–109                        | 6 (12.8)                      | 3 (17.6)                  | 8.977 | 0.003   |
| ≥160/110                              | 7 (14.9)                      | 7 (41.2)                  |     |         |
| Prenatal serum albumin (g/l)         |                               |                           |     |         |
| <30                                  | 3 (6.4)                       | 3 (17.6)                  |     | 0.774   |
| ≥30                                  | 44 (91.6)                     | 14 (82.4)                 |     | 0.379   |
| Prenatal uric acid (umol/l)          |                               |                           |     |         |
| <363                                  | 40 (85.1)                     | 7 (41.2)                  | 10.202 | 0.001   |
| ≥363                                  | 7 (14.9)                      | 10 (58.8)                 |     |         |

Data are expressed as percentage, P<0.05 was considered statistically significant.
modulating role of proteinuria, hypertension, and renal function in pregnancy of CKD patients is still unknown [9]. The lack of “low-risk-pregnancy” control groups in many studies still hinders the contextualization of the results, as the baselines vary in different countries. CGN is the most common CKD disease in young women. Every pregnancy in these women remains a high-risk pregnancy even though obstetric outcomes have improved in obstetrics and neonatology in recent years [13,14]. Research on maternal and fetal outcomes in CGN patients will help determine the effects of pregnancy on kidney diseases and the effects of kidney diseases on pregnancy.

Pregnancy complications occurred frequently in CGN patients, such as morbidity of hypertension, gestational hypertension, and preterm, early, and extreme preterm delivery [14,15]. In the present study, prenatal urine proteinuria ≥3.5 g/d was an independent risk factor for adverse maternal outcomes. Accompanied with proteinuria, plasma albumin decreased and liquid diffused, hypertension and thrombotic states increased, and complications such as thrombus, pulmonary edema, and placental abruption were increased [15]. A rapid drop in plasma proteins may reduce utero-placental flows, resulting in placental hypoperfusion, and lower maternal plasma proteins may reduce utero-placental flows, result in placental hypoperfusion and lower maternal plasma protein levels can induce fetal growth impairment. Patients with overt proteinuria less than 3.5 g/d and blood pressure <160/110 mmHg are also at higher risk of adverse fetus outcomes. Strict blood pressure control is valuable in reducing proteinuria and slowing CKD progression, but target blood pressure values in hypertensive CKD pregnancies have not been established. Jungers et al. reported that blood pressure ≥140/90 mmHg was a significant risk [16]. This ‘ideal’ target <130/80 mmHg, acceptable <140/90 mmHg is in keeping with the most recent Control of Hypertension In Pregnancy Study (CHIPs) trial [1,16]. There are no previous reports about the safety limits of proteinuria, but results of the present study suggest that abnormal blood pressure creates more risk of adverse maternal and fetus outcomes than does proteinuria.

Renal function is one of the most important factors in adverse pregnancy outcomes. Alsuwaida [9] et al. analyzed the outcomes of 87 CKD pregnant patients who registered in 5 centers from 2002 to 2008, showing that eGFR 60–89 mL/min was a risk factor for renal function deterioration and preeclampsia. Simultaneously, the proportion of fetal growth restriction, prematurity, and fetal death was also increased. During pregnancy, renal plasma flow and tubule dilatation increase the excretion of serum creatinine and urea nitrogen, and the glomerular filtration rate increased by 50%. These changes usually occur in the first 3 months of pregnancy and last up to 3 months postpartum. As a result, estimated GFR was not accurate during pregnancy. Maynard [13] believed that serum creatinine fell by an average of 0.4 mg/dl to 0.8 mg/dl during pregnancy. Smith [16] distinguished the degree of renal dysfunction during pregnancy as follows: 71 μmol/L ≤Scr ≤132 μmol/L as mild renal injury, 132 μmol/L <Scr ≤265 μmol/L as moderate injury, and Scr ≥265 μmol/L as severe injury. This standard was

Table 6. Predictors of adverse fetal outcomes in CKD patients by logistic regression analysis.

| Characteristics                                      | Pre-pregnancy | Prenatal | 6-months after delivery | P1    | P2    |
|-------------------------------------------------------|---------------|----------|-------------------------|-------|-------|
| Hypertension (%)                                      | 2 (6.9)       | 7 (24.1) | 3 (10.3)                | 0.007 | 0.052 |
| Proteinuria (g/d)                                     | 0.5±0.3       | 1.8±2.1  | 0.9±0.6                | 0.001 | 0.032 |
| Plasma albumin (g/l)                                  | 36.8±3.5      | 35.8±3.8 | 37.0±4.2               | 0.521 | 0.531 |
| Creatine (μmol/l)                                     | 68.2±8.0      | 73.2±6.7 | 70.2±7.9               | 0.355 | 0.296 |
| Uric acid (μmol/l)                                    | 311.5±86.1    | 318.3±98.6 | 316.4±89.3             | 0.630 | 0.585 |
| Serum creatine (μmol/l)                               |               |          |                         | 0.001 | N/A   |
| <71                                                   | 26 (89.7)     | 25 (86.2) | 26 (89.7)              |       |       |
| 71–132                                                | 3 (10.3)      | 4 (13.7) | 3 (10.3)               |       |       |

Data are expressed as means ±SD or percentage, P1 is Prenatal compared with pre-pregnancy, P2 is 6-months after delivery compared with pre-pregnancy, P<0.05 was considered statistically significant.
adopted in the present study to evaluate the renal function. Many studies revealed that pregnancy can aggravate renal injury in CKD patients, especially in patients with serum creatinine >2.0 mg/dL before pregnancy. Kevin [12] considered that, compared patients with renal function (eGFR >70 mL/min/1.73 m² or serum creatinine <1.4 mg/dL), the incidence of acute kidney injury increased by 30% in patients with moderate or severe renal insufficiency, and renal function may decline as a result of pregnancy among patients with renal disease [17]. Increased risks for this decline are conferred by an elevated plasma creatinine concentration (above 1.5 mg/dL or 132 μmol/L) and hypertension [18,19]. However, in our study, multivariate analysis revealed that renal function was not an independent risk factor for adverse maternal and fetal outcomes, and this may be because the renal function of most patients in this study was normal or mildly impaired. Generally, patients with severe renal dysfunction or high CKD activity are not recommended to become pregnant. If such a patient becomes pregnant accidentally, she should be monitored and treated regularly by nephrology specialists. The renal function did not change significantly in patients with CGN stage 1 or 2 at 6 months after delivery as compared with the baseline in pre-pregnancy, but the proteinuria was aggravated at 6 months after delivery.

Compared with the low-risk-pregnancy women, fetuses were more likely to suffer adverse outcomes in CGN patients, such as prematurity, small for gestational age, intrauterine growth restriction, and death. Ramin [20] investigated 53 pregnant patients with macro-albuminuria, showing that nearly 50% of fetuses were premature and 25% had growth retardation. Barcelo studied 59 pregnant patients with nephrotic syndrome and observe that fetal survival was only 72.9%, and the rate was even lower when the macro-albuminuria appeared in early and mid-pregnancy. The incidence of low birth weights, neonatal asphyxia and fetal mortality increased [21]. Jungers [22] showed that hypertension as an independent predictor was much more harmful to the fetus, and badly controlled blood pressure easily causes poor intrauterine fetal growth and deteriorates maternal renal function. Our study revealed that the incidence of preeclampsia, premature, abortion, small for gestational age, and intrauterine growth restriction was higher in CGN patients. Prenatal blood pressure ≥160/110 mmHg and prenatul uric acid ≥363 μmol/L were independent risk factors for adverse fetal outcomes; these mechanisms may be associated with systemic small artery spasm, endothelial cell dysfunction, reduced placenta blood flow, or direct toxic effects to the fetus.

In general, nephrologists and obstetricians should monitor pregnancy of patients with chronic renal disease. The main risks for the mother and fetus include worsening of renal function, hypertension, proteinuria, albumin, and serum uric acid, and these should be monitored carefully during pregnancy and delivery. The prognosis of pregnancy is the result of a combination of these elements. Multidisciplinary management and strict clinical follow-up are the basis for maternal-fetal care.

The limitations of the present study are that it was a retrospective review of data from a single center, and the number of patients in the study was small. A retrospective analysis was conducted, which may not be as informative as a forward-planned randomized comparison. Further retrospective studies need to recommend advice to prospective parents. However, the results of our study demonstrate that CGN patients with prenatal proteinuria ≥3.5 g/d, BP ≥160/110 mmHg, and UA ≥363 μmol/L should be closely monitored before and during pregnancy, and strict clinical follow-up is the basis for maternal-fetal care.

Conclusions

Maternal-fetal risks are increased in pregnancies in CGN patients. Higher risks include gestational hypertension; preterm; early and extreme preterm delivery; premature birth; intrauterine growth restriction and small for gestational age. Prenatal proteinuria ≥3.5 g/d is an independent maternal risk predictor, and prenatal BP ≥160/110 mmHg and uric acid ≥363 μmol/L are independent fetal risk predictors in pregnancy of CGN patients.

Conflict of interest

None.

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