*Biomedical Research and Therapy, 8(7):4456-4460*

Open Access Full Text Article

*Case Report*

# Proteinuria in early pregnancy: Is it a reflection of chronic renal disease?

**Sonal Garg, Papa Dasari***

Use your smartphone to scan this QR code and download this article

**ABSTRACT**

Encountering pregnant women with significant proteinuria in the first trimester is rare, and it calls for investigating a renal cause. A 25-year-old primigravida was diagnosed with proteinuria during her first prenatal visit at 12 weeks. When investigated further, she was found to have bilateral renal cysts and chronic kidney disease (CKD) and, hence, was advised medical termination of pregnancy. At tertiary care Institute, her evaluation showed 22 weeks of pregnancy with live fetus and proteinuria of more than 1500 mg/day, and serum creatinine was 3.1 mg%. She was counseled and managed by a multidisciplinary team consisting of nephrologists and obstetricians. Apart from her routine hematinic, she had twice-weekly dialysis and received multiple blood transfusions, twice-weekly erythropoietin, low molecular weight heparin, and aspirin. She developed mild intrauterine growth restriction (IUGR) and had a planned vaginal delivery at 37 weeks, and delivered a neonate of 2.3 kg with an Apgar score of 9/10 at 5 min. The baby was observed in the neonatal intensive care unit (NICU) as the cord blood creatinine was high, which normalized after four days. Mother and baby were discharged after five days in good health; however, after six weeks, mother's renal function deteriorated, and she was hospitalized again for renal biopsy and further management under nephrology.

**Key words:** Chronic Kidney disease, Dialysis, Early Pregnancy, Medical Termination of Pregnancy, Proteinuria

*Department of Obstetrics and Gynaecology, Women and Children Hospital, Jawaharlal Institute of Postgraduate Education and Research, Puducherry, India*

**Correspondence**

**Papa Dasari**, Department of Obstetrics and Gynaecology, Women and Children Hospital, Jawaharlal Institute of Postgraduate Education and Research, Puducherry, India

Email: dasaripapa@gmail.com

**History**

- Received: Jun 11, 2021
- Accepted: Jul 20, 2021
- Published: Jul 31, 2021

**DOI :** 10.15419/bmrat.v8i7.684

Check for updates



## INTRODUCTION

Chronic kidney disease (CKD) is usually asymptomatic until late stages and results in premature mortality if left unrecognized and not treated timely. The incidence in the general population is reported to be 11 — 13% globally [1]. During pregnancy renal system undergoes a lot of structural and functional changes, which are physiological. In normal pregnancy, excretion of protein occurs due to hyper-filtration, and if the proteinuria exceeds more than 300 mg/dl in 24 hours, it is considered pathological. The incidence of CKD during pregnancy has been reported to be on the rise, and a recent report quotes 3% incidence [2]. Maternal and fetal morbidity and mortality increase in women with CKD. Sometimes, CKD is diagnosed during pregnancy for the first time. The following case is presented due to its diagnosis during early pregnancy and the dilemmas in continuing pregnancy.

## CASE PRESENTATION

A 25-year-old primigravida was referred to our tertiary care Institute with diagnosis of diagnose hypothyroidism, medical renal disease, and bilateral renal cyst at 21 + 6 days of gestation. She attained menarche at 12 years of age, and cycles were regular with 3/30 with average flow. She is married for one and half years and conceived spontaneously, and on antenatal check-up at nearby PHC. She was found to have proteinuria ++ at 12 weeks of pregnancy and was investigated for renal disease (CKD) at a nearby medical college. She was advised to terminate a pregnancy during the first consultation and was referred to our institute. She was not a known case of diabetes, hypertension, hypothyroidism, or renal disease; moreover, there was no family history of renal disease, hypertension or diabetes, or autoimmune disorder.

During admission, she was oriented well, and her pulse was 76 /min (regular); Pallor +; BP was 130/88 mm Hg; thyroid, breasts, and RS CVS were normal; and no pedal edema was observed. Per abdomen, the uterus was 24 weeks size. Fetal movements were felt. Urine protein was + on spot test. She was hospitalized and investigated. The investigations conducted during admission are mentioned in **Table 1**. Renal USG showed a right kidney of 9.5 cm x 4.9 cm. The left kidney measured 9.6 cm x 4.6 cm with increased echoes and multiple cysts in the upper poles. The largest cyst was on the right kidney and measured 3 cm x 3 cm. The diagnosis was bilateral medical renal disease Grade III with bilateral renal cysts. USG

BioMedPress
The Open Access Publisher

**Cite this article :** Garg S, Dasari P. **Proteinuria in early pregnancy: Is it a reflection of chronic renal disease?**. *Biomed. Res. Ther.;* 8(7):4456-4460.

of pregnant uterus showed fetal biometry corresponding to 22 weeks gestation with live fetus without gross congenital anomaly, and the placenta was anterior.

The couple was counseled regarding disease progression, pregnancy outcome, and future fertility issues. After three counseling sessions, they agreed to continue the pregnancy and co-operate with the treatment of undergoing dialysis. She had a lot of fears about undergoing dialysis and needed special counseling by a medical social worker. She was managed with a renal diet consisting of low salt (< 6 gm/day and K+ < 2.5 gm/day) and protein (80 gm/day), and fluid was restricted to 1.5 l/day. She was being given the following tablets: Aspirin 75 mg; Folic acid 5 mg/day, and Eltroxin 100 mcg /day. She was also given subcutaneous injections of enoxaparin 40 mg daily, erythropoietin 4000 IU twice-weekly, and Vit D3 60,000 IU once a week. She underwent hemodialysis under Nephrology Unit twice weekly, and her management was discussed often with the nephrology team. Her renal parameters are shown in **Table 1**.

## COURSE DURING PREGNANCY

Her pregnancy was managed with hematinics, and correction of anemia was undertaken by multiple packed cell transfusions, intravenous iron, methylcobalamin injection, and tablets of folic acid. Antioxidants (tablets of Vit E, C, and Arginine) were added from 29 weeks when fetal growth lag and Pulsatility Index (PI) of more than one were observed. Fetal growth and fetal well-being were monitored by USG and NST. Antenatal corticosteroids were given for fetal lung maturity after 28 weeks. The plan was to induce labor at 37 weeks with the available neonatal intensive care unit (NICU) facilities. Fetal growth and surveillance are presented in **Table 2**.

At 32 weeks, she developed earache and sinusitis, which were promptly treated with antibiotics, and later her audiogram revealed a profound hearing loss in the right ear and severe mixed hearing loss in the left ear. She had gone into labor after membrane stripping at 37 + 3 weeks and needed augmentation of labor for hypotonic uterine inertia. Oxytocin augmentation was started, and controlled ARM was done. Continuous CTG monitoring was done, and she delivered an alive male neonate of 2.3 kg with an Apgar score of 9/10, who was transferred to NICU. Cord blood was collected for urea and creatinine. The third stage of labor was actively managed, and there was no PPH. She was given one packed cell transfusion soon after delivery as her Hb was 7 gm% at the beginning of labor. The baby's urea creatinine was high, and it was normalized spontaneously after five days. She was discharged after counseling for contraception and advised to follow up with the nephrologist. During follow-up after six weeks (June 2019), her renal parameters worsened, and she was hospitalized under nephrology, and there was a plan for renal biopsy and further management.

## DISCUSSION

Proteinuria normally does not occur during early pregnancy. Proteinuria is said to be significant when the 24-hour value is $\geq$ 300 mg/dl or when it is 2+ or more on the dipstick. Proteinuria during pregnancy is classified into four main categories:

1. transient proteinuria due to urinary tract infection;
2. isolated de novo proteinuria;
3. proteinuria secondary to CKD; and
4. proteinuria due to pre-eclampsia.

If proteinuria occurs after 20 weeks of pregnancy, it is usually attributed to hypertensive disorders of pregnancy. If it occurs before 20 weeks, primary or secondary kidney disease is to be ruled out. Proteinuria > 3 gm per 24 hours is a sign of glomerular injury [3,4]. The woman under concern was rightly investigated for renal disease, and a referral was made to a tertiary care Institute.

It is a known fact that women with CKD have the risk of suffering adverse pregnancy outcomes like pre-term labor, pre-eclampsia, and IUGR. Following are the recommendations for antenatal care: starting on pre-eclampsia prophylaxis with aspirin and maintaining the diastolic BP at 85 mm Hg. Communication and discussions regarding adverse pregnancy outcomes and accelerated maternal renal loss with the patient and multidisciplinary team (MDT) are important [5]. In the woman under concern, these took place appropriately, and considerable support was provided by ancillary health care workers. The evidence for early CKD accelerated by pregnancy is limited [6]. Although impaired renal function (serum creatinine of > 1.25 mg/dL) is considered an indication for the first-trimester termination of pregnancy, the pros and cons of continuing the pregnancy and the fulfillment of patients' desire to have a child should be taken into account while counseling the patient and her family [7].

The management of pregnant women with CKD includes more frequent antenatal check-ups; prevention of anemia, hypertension, IUGR, and pre-term labor; dialysis to keep the serum creatinine below 2 mg/dl; and supplementation with Vit D. Labetalol, nifedipine, and methyldopa are the drugs of choice if hypertension develops. Anemia refractory to iron needs erythropoietin [5]. Pregnancy complications increase in women on dialysis, but renal disease as such is not

**Table 1: Investigations during the course of hospitalisation**

| Investigation | Results at Feb 2019 | March 2019 | April 2019 | May 2019 | June 2019 |
|---|---|---|---|---|---|
| Hb | 8.7 | 6.3 | 8.2 | 8.0 | 8.6 |
| WBC | 7900 | 9790 | 11300 | 9630 | 7300 |
| N/L/E | 77/19/4 | 75/16/1 | 74/17/0.2 | 75/16/0.8 | 60/28/3 |
| RBC | 1.3 | 2.4 | 2.94 | 2.68 | 2.91 |
| MCV | 93.3 | 101.3 | 98.6 | 93.3 | 96.7 |
| MCH | 31.7 pg | 32.4 | 31.3 | 29.9 | 29.6 |
| MCHC | 33.9 | 32 | 31.7 | 32 | 30.6 |
| RDW | 14.2 | | | | |
| Platelets | 2.4 | 1.67 | 1.93 | 2.3 | 2.17 |
| Urine Alb | + | + | + | + | + |
| Urine Sugar | nil | Nil | - | - | - |
| 24 hr urine Protein | 1592 | - | 1800 | - | 1700 |
| Bl Urea | 64 | 59 | 54 | 39 | 82 |
| S. Creatinine | 3.1 | 3.74 | 5.01 | 2.78 | 8.09 |
| S. Cholesterol | 223 | 285 | 376 | - | - |
| Triglycerides | 184 | 349 | - | - | - |
| S.Bilirubin | 0.6 mg | 0.26 | 0.28 | 0.32 | 0.42 |
| Protein | 6 gm | 7.2 | 5.9 | 6.8 | 6.9 |
| Albumin | 2.2 gm | 3.5 | 3.0 | 3.3 | 3.8 |
| TSH | 13.88 | 1.76 | | | 0.20 |
| FT3 | 2.29 | | 2.6 | | 3.16 |
| FT4 | 1.48 | | | | |
| Procalcitonin | | 12.39 ng/ml | | | |
| 25 OH Vit D | | 18.41 ng/ml | | | |
| PTH | | | 61 ng/ml | | |
| Blood culture | | Citobacter species Sensitive to amikacin | sterile | | |

an indication for medical termination of pregnancy (MTP) if the couple does not have a live baby. It is best to optimize the renal function before conception and attempt pregnancy after renal transplantation [5,6].

Dialyzed women during pregnancy have been reported to have increased incidence of IUGR, abruption, intrauterine death, and need for blood transfusion [8]. The woman under concern developed IUGR and required multiple transfusions to keep her hemoglobin at a minimum of 8 gm%. Hemodialysis is the standard of care, and intensive dialysis has resulted in better pregnancy outcomes in recent times [6,9].

Renal biopsy can be undertaken during the first or second trimester if it is expected to make a difference in management [5,6]. It is the degree of renal insufficiency rather than the underlying renal diagnosis that determines the outcome of pregnancy [10]. In a

**Table 2: Fetal growth on USG and fetal surveillance**

| Date | BPD | HC | AC | FL | EFW | Liquor | Doppler (PI) | NST | |
|---|---|---|---|---|---|---|---|---|---|
| 5.3.19 | 26 + 2 | 25 | 26 + 2 | 25 + 6 | 902 gms | average | 1.5 | - | - |
| 23.3.19 | 29 + 3 | 28 + 2 | 28 + 2 | 28 | 1200 | AFI - 20 | 1.1 | - | - |
| 26.4.19 | 33 | 32 + 5 | 32 + 4 | 33 + 3 | 1900 | AFI - 14.2 | 1.1 | - | - |
| 1.5.19 | 34 | 33 | 33 + 3 | 34 | 2200 | AFI - 16 | 1.2 | R | 8/10 |
| 8.5.19 | 34 | 34 + 4 | 34 | 34 | 2300 | AFI - 18 | 1.2 | R | 8/10 |
| 20.5.19 | 37 + 3 | 34 + 3 | 35 + 5 | 36 + 6 | 2500 | AFI - 20 | 1.4 | R | 8/10 |

prospective longitudinal study involving 49 pregnant women with CKD of Stages 3 to 5, Imbasciati *et al.* found that the rate of decline in GFR after delivery was not statistically significantly different when compared to pre-conception when serum creatinine was more than 1.5 mg/dl. However, they reported that the rate of renal loss and pregnancy complications were high when GFR was less than 40 ml/min per 1.73 $m^2$ and proteinuria was > 1 g/d before pregnancy [11].

## CONCLUSION

Proteinuria during early gestation points out to renal disease, and CKD can be asymptomatic in the early stages. Multidisciplinary management can ensure safe outcome of pregnancy in women with renal disease, and MTP can be avoided, especially in primigravida.

## ABBREVIATIONS

**CKD**: Chronic kidney disease
**IUGR**: Intrauterine growth restriction
**MTP**: Medical termination of pregnancy
**MDT**: Multidisciplinary team
**NICU**: Neonatal intensive care unit
**NST**: Non-stress test
**PI**: Pulsatility Index
**Vit**: Vitamin

## ACKNOWLEDGMENTS

Department of Nephrology and Department of Immunology.

## AUTHOR'S CONTRIBUTIONS

SG: Case file retrieval and case summary preparation
PD: Case summary preparation and preparation of manuscript and editing

## FUNDING

None.

## AVAILABILITY OF DATA AND MATERIALS

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

## CONSENT FOR PUBLICATION

Not applicable.

## COMPETING INTERESTS

The authors declare that they have no competing interests.

## REFERENCES

1. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis. PLoS One. 2016;11(7):e0158765. PMID: 27383068. Available from: 10.1371/journal.pone.0158765.
2. Piccoli GB, Daidola G, Attini R, Parisi S, Fassio F, Naretto C, et al. Kidney biopsy in pregnancy: evidence for counselling? A systematic narrative review. JOG. 2013;120(4):412–427. PMID: 23320849. Available from: 10.1111/1471-0528.12111.
3. Thadhan RI, and SEM. Evaluation of Proteinuria in Pregnancy and management of Nephrotic Syndrome. https://wwwuptodatecom/contents/evaluation-of-proteinuria-in-pregnancy-and-management-of-nephrotic-syndrome;.
4. Airoldi J, Weinstein L. Clinical significance of proteinuria in pregnancy. Obstet Gynecol Surv. 2007;62(2):117–124. PMID: 17229328. Available from: 10.1097/01.ogx.0000253301.55009.ac.
5. Wiles K, Chappell L, Clark K, Elman L, Hall M, Lightstone L, et al. Clinical practice guideline on pregnancy and renal disease. BMC Nephrol. 2019;20(1):401. Available from: 10.1186/s12882-019-1560-2.
6. Fitzpatrick A, Mohammadi F, Jesudason S. Managing pregnancy in chronic kidney disease: improving outcomes for mother and baby. Int J Womens Health. 2016;8:273–285. PMID: 27471410. Available from: 10.2147/IJWH.S76819.

7. Guiahi M, Davis A. First-trimester abortion in women with medical conditions: release date October 2012 SFP guideline #20122. Contraception. 2012;86(6):622–630. PMID: 23039921. Available from: 10.1016/j.contraception.2012.09.001.
8. Saliem S, Patenaude V, Abenhaim HA. Pregnancy outcomes among renal transplant recipients and patients with end-stage renal disease on dialysis. J Perinat Med. 2016;44(3):321–327. PMID: 25719292. Available from: 10.1515/jpm-2014-0298.
9. Hladunewich MA, Hou S, Odutayo A, Cornelis T, Pierratos A, Goldstein M, et al. Intensive hemodialysis associates with improved pregnancy outcomes: a Canadian and United States cohort comparison. J Am Soc Nephrol. 2014;25(5):1103–1109. PMID: 24525032. Available from: 10.1681/ASN.2013080825.
10. Maynard SE, Thadhani R. Pregnancy and the kidney. J Am Soc Nephrol. 2009;20(1):14–22. PMID: 19118150. Available from: 10.1681/ASN.2008050493.
11. Imbasciati E, Gregorini G, Cabiddu G, Gammaro L, Ambroso G, Giudice AD, et al. Pregnancy in CKD stages 3 to 5: fetal and maternal outcomes. Am J Kidney Dis . 2007;49(6):753–762. PMID: 17533018. Available from: 10.1053/j.ajkd.2007.03.022.