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EFFECTS OF RENAL TRANSPLANTATION ON FERTILITY IN FEMALES –EXPERIENCE FROM A TERTIARY CARE CENTRE IN SOUTH INDIA

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ABSTRACT

Background: Females with Chronic Kidney Disease (CKD) are prone to reduced fertility due to uremia. Renal transplantation corrects the metabolic changes and hormonal imbalance, which lead to menstrual regularity and ability to conceive. Our study analyzes the predictors of successful pregnancy with live birth while presenting an overview of the 13 years of experience from a tertiary care centre in South India.

Methods: This retrospective cohort study includes 200 women of reproductive age group (18 to 40 years) who underwent renal transplantation at Government Stanley Medical College and Hospital Chennai, India between 1- January - 2010 to 30 – June - 2023. We assessed them in 2 groups: Patients who conceived and those who did not.A total of 50 patients fulfilled the inclusion criteria.

Results: 50 patients wished to conceive. 18 patients conceived spontaneously, 32 patients failed to conceive. Out of the 18 patients who conceived spontaneously, 14 patients completed 36 weeks of gestation and delivered a term baby.In 1 patient pregnancy was terminated at 33 weeks of gestation and she delivered a premature baby.3 out of 18 patients who conceived, had miscarriage in the 1st trimester. The mean age of patients in the conceived group and the non-conceived group were 26.16 ± 2.92 years and 31.65 ± 2.17 years respectively with a p-value of 0.0003. We found an increase in regularity of menstrual cycle after renal transplantation from 26% before RT to 46% after RT. Age at the time of transplantation was less in the conceived group [22.16 (±2.608) years] when compared to the non-conceived group [27.84 (±1.41)years]. The mean duration of HD before RT was 11months in the conceived group and 19.5 months in the non-conceived group with a p- value of

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0.017. Regular menstrual cycles after renal transplantation, duration of HD before RT and age at transplantation were found to be favorable predictors of spontaneous pregnancy after renal transplantation.

Conclusion: CKD has negative impacts on fertility due to the menstrual abnormalities and hormonal imbalances which it causes. These can be reversed by a successful renal transplantation. Minimizing the duration of HD, particularly in patients who desire future conception, may be accepted as a logical management strategy.

KEY WORD :-

1. RT – renal transplantation
2. CKD -chronic kidney disease
3. RRT- renal replacement therapy
4. HD- hemodialysis
5. PD – peritoneal dialysis

INTRODUCTION:

Chronic kidney disease (CKD) alters the functioning of the hypothalamic-pituitary axis resulting in many hormonal disorders responsible for the deterioration of sexual functions and also fertility in both men and women.Renal transplantation (RT) allows for the normalization of hormonal balance and this quickly, ranging from a few weeks to 6 months after kidney transplantation, will therefore be associated with a return of the sexuality level as that of before the onset chronic kidney disease and an improvement in fertility that may be accompanied by a desire for pregnancy or paternity[1].

In patients with CKD, uremia,other comorbidities, hormonal imbalance, autonomic neuropathy, side effects of immunosuppressants and psycho-social factors contribute to sexual dysfunction which lead to reduction in fertility, which gradually deteriorates with time. RT reverses the metabolic and hormonal imbalances which corrects most of the issues and leads to improved fertility outcomes[2].

[1]

[2] Josephson and McKay, “Pregnancy and Kidney Transplantation.”

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Child bearing in women with CKD remains high risk with an increased prevalence of hypertension and pre-eclampsia.Therefore, pregnancy rates appear to be reduced in transplant recipients than general population[3].

Since 1958, women post RT have become pregnant. Although most pregnancies in kidney transplant recipients are successful, they are high-risk pregnancies. This seems to be more of a function of the associated issues, comorbidities that often affect individuals with kidney transplants (like hypertension) and side effects of immunosuppression rather than the kidney transplant per se. Regardless of the underlying cause, these pregnancies have high rates of preeclampsia, preterm baby and Cesarean sections.

The improvement of sexuality in both men and women after kidney transplantation can lead to a pregnancy. Adaptation of immunosuppression may be necessary to avoid any risk of teratogenicity in the fetus[4].

This study analyzes the predictors of successful pregnancy with live birth as the primary outcome. Considering the diverse clinical factors that may confound the overall pregnancy outcome in RT patients, this study is going to determine:

- Pretransplant obstetric status and menstrual regularity
- Obstetric and gynecologic outcomes after RT
- History and duration of dialysis and its effect on fertility
- Etiology of renal failure
- Donor type (live or cadaveric)
- Fetal outcomes and incidence of any congenital anomalies

INCLUSION CRITERIA

1. Females in the age group of 18 – 40 years who wish child bearing post transplantation
2. Hemodynamically stable
3. Functioning graft kidney

EXCLUSION CRITERIA:

[3] Josephson and McKay, “Women and Transplantation.”

[4] Kleinclauss, Timsit, and Thuret, “Sexualité, Fertilité et Grossesse Après Transplantation Rénale.”

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1. Females who are not willing to participate in the study at any point of time
2. Hemodynamically unstable

METHODS

The study is a retrospective cohort study planned to conduct at a tertiary referral center – Government Stanley Medical College and Hospital, Chennai 600001, Tamil Nadu, India. Data has beeb reviewed from a prospectively maintained database of 200 women of reproductive age (18-40 years) who underwent RT between 1-January- 2010 to 30-June-2023.

The patients were evaluated in 2 groups:

1. Those who conceived spontaneously and
2. Those who failed to conceived after 1 year of having unprotected intercourse on a regular basis.

Patients who had been trying to conceive for less than 1 year and were not pregnant were excluded from the study.
The subjects were invited to take part in a survey regarding their obstetric history including regularity of menstrual cycle, presence of a documented gynecologic illness, history of pretransplant childbirth, miscarriage, or termination of a pregnancy.

In this study the following were evaluated:

1. Mean age at the time transplantation
2. Outcomes of fetuses
3. Effect of duration of dialysis on fertility
4. Effect of RT on menstrual cycle
5. Source of allograft (live v/s cadaveric)
6. Types of immunosuppression and their effect on fetal outcome

The data was statistically analysed by SPSS 25.0 version. Fisher's exact test was used to compare categorical variables and data are presented as frequencies and percentages. A multivariable linear regression analysis was conducted to figure out the predictors of a successful pregnancy. Binary logistic regression was used to examine the strength of predictors. The limit for statistical significance was accepted as $p < 0.05$.

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RESULT

A total of 200 women underwent renal transplantation between 1-January- 2010 and 30-june-2023, out of which 50 patients were included in our study who fulfilled the inclusion criteria.18 patients conceived spontaneously, 32 patients failed to conceived.Out of 18 patients, 14 patients completed 36 weeks of gestation and delivered a term baby.1 patient had a premature termination of pregnancy at 33 weeks of gestation and delivered a premature baby.3 out of 18 patients conceived but had a miscarriage in 1st trimester.

The mean age were 26.16 ±2.92 years and 31.65±2.17 years in the conceived and non-conceived groups, respectively with p-value of 0.0003. The mean age at the time of renal transplantation was 22.16±2.608 years in conceived group and 27.84±1.41years in non-conceived group with a p- value of 0.016. In our study all the patients had a history of hemodialysis. The mean duration of dialysis was 11 months in the conceived group vs 19.5 months in the non-conceived group with a p- value of 0.017.

Out of 50 patients 13 (26%) patients had regular menstrual cycle and 37 (74%) patients had irregular menstrual cycle before transplantation. After transplantation 23 (46%) patients regained regular menstrual cycle and 27(54%) patients still had irregular menstrual cycles.

In the conceived group 11(61.1%) patients had regular menstrual cycle before transplantation and 7(38.8%) patients had irregular menstrual cycle. After RT, in the conceived group all the patients achieved regular menstrual cycles.

In non-conceived group, before RT 3(9.3%) patients had regular menstrual cycle and 30(93.7%) patients had irregular menstrual cycle. After RT 7(21.8%) patients achieved regular menstrual cycle and 26(81.2%) patients still had irregular menstrual cycle.

In the conceived group, out of 15 deliveries, 8 patients underwent normal vaginal delivery and 7 patients underwent LSCS.One patient had abortion at 11th week of gestational age. All term babies were normal without any congenital anomalies.One premature baby was kept in Neonatal ICU for observation and on follow up the baby was normal.

The cause of CKD in the conceived group was unknown in 16 patients and 2 patients had IgA nephropathy. In the non- conceived group,cause of CKD was unknown in 28 patients and the cause was IgA nephropathy in 4 patients.

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In our study, a total of 41 live donor transplantations were done, 16 in the conceived group and 25 in the non-conceived group. 9 cadaveric transplantations were done, 2 in the conceived group and 7 in the non-conceived group. Out of 2 patients with cadaveric transplantation in the conceived group one achieved term delivery and another had an abortion in the 1st trimester.

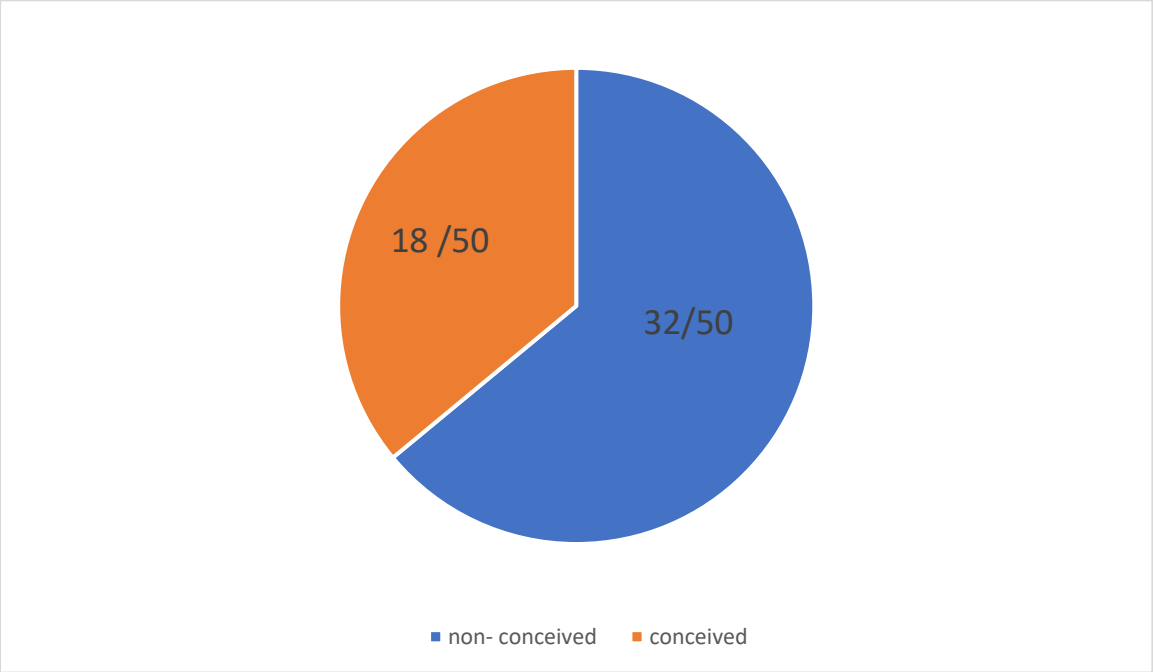

Table 1: Features of study participants

Variable		Conceived group (n = 18)	Non-conceived group (n = 32)
Age at time of study (mean)		26.16 (±2.92)	31.65 (±2.17)
Age at time of RT (mean)		22.16 (±2.608)	27.84 (±1.41)
Duration of HD mean (month)		11	19.5
Menstrual cycle before RT	Regular Irregular	11(61.1%) 7(38.8%)	3(9.3%) 30(93.7%)
Menstrual cycle after RT	Regular Irregular	18 (100%)	7(21.8%) 26(81.2%)

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Obstetric history before RT	Nulliparous Monoparous	16 (88.8%) 2 (11.2%)	27(84.3%) 5 (15.7%)
Type of graft	Live Cadaveric	16 (88.8%) 2 (11.2%)	25 (78.2) 7 (21.8%)
Co-morbidity	HTN HTN+DM	15 (83.4%) 3 16.6%)	23 (71.8%) 9 (28.2%)
Cause of CKD	Unknown IgA nephropathy	16 (88.8%) 2 (11.2%)	28 (87.5%) 4 (12.5%)

In our study we found duration of HD, age at the time of transplantation and menstrual regularity as the factors which were significantly different between conceived and non-conceived groups.

DISCUSSION

CKD is a systemic disease and it affects hormonal balance at hypothalamic pituitary gonadal axis due to uremia which can lead to decrease in estradiol level and increase in LH (luteinising hormone)level. This leads to irregularity in menstrual cycle and ovulation and thus, affects fertility in CKD patients when compared to the normal population.[5] Saglimbene et al have shown in their study that patients with CKD have low level of sexual desire and that male patients with CKD also have erectile dysfunction due to uremia and peripheral neuropathy, factors which can also lead to reduction in fertility outcomes.[6]

In the last few decades as the number of renal transplantation for CKD patients have increased, it has been found that fertility outcomes have also improved. RT improves hormonal balance and regainment of regular menstrual cycle which leads to achievement of reproductive functions.[7]It has been noticed that despite almost 50% of RT recipients being in the reproductive age group, only 2%- 5% had achieved pregnancy.[8]

[5] Holley et al., "Gynecologic and Reproductive Issues in Women on Dialysis."
[6] Saglimbene et al., "The Prevalence and Correlates of Low Sexual Functioning in Women on Hemodialysis."
[7] Kurtulus et al., "Effects of Renal Transplantation on Female Sexual Dysfunction."
[8] "Scopus Preview - Scopus - Welcome to Scopus."

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In our study group we found some predictors or factors which can lead to improvement of fertility after RT like improvement in menstrual cycle regularity, duration of HD and age at the time of transplantation.

We found an improvement in regularity of menstrual cycle from 26% before RT to 46% after RT which is comparable to study done by Yaprak et al.[9] where he found improvement in menstrual regularity from 51% befor RT to 72% after RT.

In our study, duration for HD before RT was significantly less in the conceived group. So minimizing the duration of HD in patients who want to get conceived in future, can minimize the effect of uremia on hormonal balance and early regainment of fertility.

In our study age at the time of transplantation was less in the conceived group [22.16 (±2.608) years] compared to the non-conceived group [27.84 (±1.41) years]. So early transplantation is advisable for better fertility outcomes.

The limitation of our study are that it is a retrospective study with a low sample size. In our study other factors which alters the fertility in normal women have not been studied.

CONCLUSION

The reduced fertility rates post renal transplantation can be improved by minimizing the duration of HD and by transplantation at an early age, thus by not delaying renal transplantation in patients in the reproductive age group who want to conceive.

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