Pregnancy outcomes in patients with kidney transplant-A retrospective snapshot.

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Abstract:

Pregnancy in renal transplantation is a sensitive issue since fertility improves shortly after transplantation and the prevalence of pregnancy-related complications in these patients are more in comparison to non-transplanted matched cohorts. Our study aimed at assessing the outcomes of pregnancy in our transplant patients.

Methods: This study was designed as a questionnaire based retrospective cross-sectional study wherein the authors contacted all their patients who underwent kidney transplantation under our care and now being followed with us or 4 other hospitals.

Results: Total of 20 females conceived unplanned, out of 130 females of child bearing age who underwent kidney transplant. single pregnancy ended up in elective abortion at 4th month after transplant, rest of the pregnancies were successful and uneventful.

Conclusion:

Fertility related issues should be included in the counselling of kidney transplant females for planned pregnancy. Successful outcome is quite possible. There is a critical need for comprehensive support systems, including counseling, education, and resources, to empower female kidney transplant recipients in their reproductive journeys and to address the gaps in understanding family planning and contraceptive methods in the post-transplant period.

Keywords: Kidney transplantation; pregnancy outcome; healthy babies; immunosuppressive drugs; mycophenolate mofetil.

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Introduction:

Pregnancy in renal transplantation is a controversial topic. There is significant evidence to show that fertility improves shortly after transplantation and the prevalence of pregnancy-related complications in these patients are more in comparison to non-transplanted matched cohorts.[1] Areia et al. reported an 80% live birth rate which nearly comparable to normal cohorts but highlighted an elevated risk of preterm delivery, gestational hypertension, and preeclampsia. [2]

A Pakistan based study looked into the contraceptive practices of renal transplanted individuals and found that 64% of the participants (9 out of 14 female participants) were not employing any form of contraceptive method. Among these non-users, 7 patients (78%) had never received any counseling regarding contraception or pregnancy.[3]

This data highlights the significance of addressing reproductive health and pregnancy-related counseling for kidney transplant recipients, especially given the associated risks and complications that have been observed in this population. Counseling is crucial, yet nephrologists often lack confidence in discussing reproductive health, leading to infrequent and inadequate counseling sessions.[4]

Our study aims to assess the outcomes of pregnancy in our transplant patients. In addition to which we aimed to ascertain if pre-pregnancy counselling and planning was carried out appropriately. In doing so we retrospectively studied 291 female transplant recipients to identify the gaps in pregnancy counseling, planning, and the management of immunosuppressive medication among kidney transplant recipients. This study aims to highlight the importance of comprehensive reproductive health counseling, especially in light of the significant risks and complications associated with pregnancy in this population.

Methods:

This study was designed as a questionnaire based retrospective cross-sectional study wherein the authors contacted all the patients in their follow-up (which met the inclusion criteria) across 4 different hospitals in Punjab province. A total of 777 transplants had been done under their care from 2017 to 2024, out of which 291 were females. We reached out to 130 female patients who were married and were of child bearing age. Female of non-child bearing age and unmarried were not contacted.

After taking informed consent we administered the questionnaire in a private setting which included both in-person and telephonic conversation. The questions were read out individually and answered documented. At the end of the conversations, the answers were read back to ensure validity and to alleviate misunderstanding if any.

The questionnaire included basic questions only:

- Post-transplant counseling
  - Did the doctors talk about pregnancy within the first 3 months of your transplant?
- Planning of pregnancy
  - Did the doctors talk about planning the pregnancy?
  - Did you tell your doctor that you were going to plan a pregnancy?
- Switching of immunosuppressive medications
  - Did the doctors inform that certain drugs need to be modified before conception?
  - What drugs were you taking when you became pregnant?
- Live births/Miscarriages/Birth Defects
  - Did you have a live birth?
  - Were there any miscarriages?
  - Were there any birth defects?
- Renal functions
  - What there a drop in your GFR pre-pregnancy and after delivery

Results:

In our study, 291 female transplant patients met the inclusion criteria; out of which only 20 participants conceived, Table 1. This amounts amounted to a conception rate of 6.7%. The mean age of these expectant mothers was 28.

When asked if the doctors had talked about pregnancy after transplant with the participant; all the participants i.e. 20/20 answered yes. Similarly, all the participants agreed that they were informed that they needed to plan the pregnancy and inform the doctor once they were planning the pregnancy. Surprisingly, all 20 pregnancies were unplanned.

Fourteen patients (70%) were on MMF when they became pregnant which got switched to azathioprine after seeing their nephrologist; while six patients (30%) were already taking azathioprine for other non-pregnancy related reasons Table 2.

Nineteen of the twenty (95%) pregnancies ended in a healthy, living baby with no documented birth defects or miscarriages even though most of them were taking MMF in their first trimester, One participant (5%) had an elective abortion as she got pregnant within 4 months of renal transplantation. All the remaining 19 pregnancies were timed as at least 2 year post renal transplanted pregnancies. Pre-and post-conception creatinine levels were less than 1.5 in all 20 pregnant participants Table 3. Total of 16 patients underwent cesarean section while 3 underwent spontaneous vaginal deliveries. There was no still birth, neonatal death or obvious congenital abnormalities in the babies.

Table 1: Healthy babies in pregnant females taking MMF preconception

	Non-pregnant	Pregnant	Total
Miscarriage	0	1	1
Females with healthy babies	0	19	19
Females with no babies	271	0	271
Total count Total(%)	271 93.1%	20 6.9%	291 100%

Table 2: Preconception immunosuppressive therapies since 2 years of kidney transplant:

	Non-pregnant	Pregnant	Total
MMF not stopped (preconception)	271	14	285
	95%	5%	100%
Females taking azathioprine	0	6	6
	0%	100%	100%
Total count	271	20	291
Percentage (%)	93%	7%	100%

Discussion:

In our study out of a total of 291 female transplant patients, only 20 (6.7%) successfully conceived. The relatively low conception rate among female transplant recipients, despite the high fertility potential post-transplantation, emphasizes a critical need for targeted reproductive health education and counseling. Furthermore, addressing the psychological aspects of pregnancy planning can significantly enhance patient confidence and decision-making, as many women may feel overwhelmed by the complexities surrounding their health status and medication regimens.[5] Healthcare providers should

consider implementing support groups and resources that facilitate open discussions about fertility options, potential risks, and the importance of preconception care to empower these women in their reproductive journeys.

Table 3: Level of creatinine pre conception:

		Non-pregnant	pregnant	total
Preconception creatinine	>1.5 mg/dl(count)	88	0	88
	%	100%	0%	100%
	<1.5 mg/dl(count)	183	20	203
	%	90%	10%	100%
Total		271	20	291
		93%	7%	100%

The average age of these expectant mothers was 28 years in our study which pretty comparable to the UK renal registry data.[6] None of the participants were above the age of 36 which can be a contributing factor of good pregnancy outcomes in our study.

A very interesting finding in our study was that all patients reported that they were counseled regarding pregnancy and the need to plan it yet; all the pregnancies were unplanned. This definitely raises an important question on the clarity of the information provided or on the person providing the information or both. During the writing of the manuscript that we realized that we did not ask about contraceptive counseling separately neither did we ask if the couples were using any form of contraception while they got pregnant. This information when looked into may help us in explaining our results and also look into the effectiveness of contraception counselling in this population. Despite high knowledge of modern contraceptives, many Pakistani couples do not fully understand the need for contraception, leading to low uptake and high unmet need for family planning.[7] Additionally purely from a Pakistani conservative society standpoint, maybe we need to develop an out of the box program to enhance contraceptive counseling alongside family planning as our study if anything does show that ineffective methods if any were being used.

Among these expectant mothers, a significant majority—14 patients, or 70%—were on MycophenolateMofetil (MMF) at the time of conception. Following the confirmation of their pregnancies, they met their respective nephrologist these women discontinued the medication, which is critical given the known risks associated with MMF during pregnancy. Conversely, 6 patients (30%) were on Azathioprine (AZA), a medication that had been modified for other health considerations rather than as part of a pre-pregnancy strategy. This information raises important questions about the preconception planning practices for female transplant patients and the need for more tailored reproductive health guidance. Remarkably, 19 out of the 20 pregnancies (95%) resulted in healthy, live births, with no recorded instances of birth defects, premature births, or miscarriages, despite the fact that most of these women were taking MMF during their first trimester. Only one pregnancy (5%) ended in an elective abortion at six weeks of gestation, prior to the detection of fetal cardiac activity. This

outcome poses a scope for further study to understand the safety and effects of MMF on fetal wellbeing, As suggested in another study, healthy babies were observed in patients on mycophenolate mofetil (MMF),with no malformations in live births despite embryonic exposure during pregnancy.[8]

It is noteworthy that in all 19 successful pregnancies, the interval between the transplant and conception exceeded two years, suggesting that a longer post-transplant period may contribute positively to pregnancy outcomes.[9] Additionally throughout the pregnancies, the pre- and post-conception creatinine levels for all 20 women remained below 1.5, suggesting stable kidney function, which is essential for both maternal well-being and fetal growth. Both these factors are known positive contributors to a healthy outcome in the pregnant transplant population.[10]

In terms of delivery methods, 16 patients underwent cesarean sections, while 3 experienced spontaneous vaginal deliveries (SVD) which may be attributable to a multitude of factors, including the preferences of the patient, the ease of the surgeon, or other considerations.[11] This of course is something that needs to be looked into with more depth and perhaps multiple separate studies.

The main point of contention with our results and the majority of the evidence available is that our cohort shows no reports of stillbirths, neonatal deaths or congenital abnormalities despite the majority of the participants getting some exposure to MMF in the first trimester.[12]We have been very careful in reporting these results and are under no false pretense that suddenly MMF has become safe in the transplant & pregnancy setting. However we do note our participants were of a young age, had excellent kidney functions both pre and post pregnancy and 95% of them became pregnant after 2 years of renal transplantation. These could all be reasonable explanation for the good outcomes seen. Of course the small number of participants in our cohort needs to be taken into account too.

Frustratingly, data on this aspect of transplantation is sparse and few in Pakistan. In our review of the literature we could only find a few studies from SIUT. One study observed 47 pregnancies in 31 patients, among which only one was taking MMF. Albuminuria was noted in 13 and new onset HTN occurred in 2. Only one patient developed graft dysfunction leading to dialysis dependency. Among these 47 pregnancies 6 resulted in premature deliveries, 9 abortions and no congenital abnormalities were observed.[13] While in our study none of such complications have occurred.

Another study from AKUH showed 8 pregnancies in 7 female transplant recipients. None of them were taking MMF. 7 babies were pre-term but no congenital anomaly or abortions were observed. No graft loss was observed in any patient after pregnancy.[14]

Future studies and collaborations need to develop to take this aspect of nephrology forward and to help our patients.

Conclusion:

In conclusion, the findings from the study reveal a complex interplay between reproductive counseling and successful conception outcomes. Despite a relatively low conception rate of 6.7% among the cohort, the majority of pregnancies resulted in healthy live births, indicating positive outcomes when

pregnancies occur after a stable post-transplant period. However, the unintended nature of these pregnancies raises concerns about the effectiveness of contraceptive counseling and the need for enhanced reproductive health education. The predominance of patients on Mycophenolate Mofetil during early pregnancy underscores the importance of tailored preconception planning and careful medication management to ensure maternal and fetal safety. Overall, there is a critical need for comprehensive support systems, including counseling, education, and resources, to empower female transplant recipients in their reproductive journeys and to address the gaps in understanding family planning and contraceptive methods.

Conflict of Interest: The authors report no conflicts of interest in this article.

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