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PATTERN OF MENSTRUAL CYCLE AFTER KIDNEY TRANSPLANT IN REPRODUCTIVE WOMEN

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Background. In reproductive women, transplant disturbs the menstrual cycle pattern. The two major conditions usually encountered are amenorrhea and menorrhagia. **The objective** of the study was to assess the pattern of menstrual cycle after kidney transplant in reproductive women. **Materials and methods.** This cross-sectional study was carried out in a public sector hospital of Karachi, Pakistan. A total 69 patients of reproductive age were included who underwent living kidney donor transplant for more than a year ago. Women having genital tract infection, using hormonal treatment, organic cause of genital tract, clotting disorder and severe cardiac and/or peripheral vascular disease were excluded. Frequency and percentages were calculated for demographic characteristics. Correlation and association analysis was calculated for type of menstruation with menstrual cycle pattern. A P-value less than 0.05 was considered statistically significant. **Results.** Majority of female included in the study aged between 35–39 years (36, 52.2%). The most frequent menstrual disturbance observed was heavy menstrual bleeding (22, 31.9%) and amenorrhea (21, 30.4%). Only 2.9% cases showed normal menstrual pattern. The cross tabulation indicated that 26.1% patients had amenorrhea, 24.6% had oligomenorrhea and 31.9% had menorrhagia. The Durbin–Watson value of 0.656 indicated a strong positive relationship between menstruation cycle pattern (dependent variable) and type of menstruation, marital status, donor's age, children and living location of the patients (independent variables). **Conclusion.** From the result of the present study, it is concluded that the reproductive age women have shown a disturbed pattern of menstrual cycle after kidney transplant. The major observation was that such patients reported amenorrhea, menorrhagia, oligomenorrhea and hypomenorrhea.

Keywords: Reproductive Women, Amenorrhea, Oligomenorrhea, Menorrhagia, Renal Transplant.

ОСОБЕННОСТИ МЕНСТРУАЛЬНОГО ЦИКЛА ПОСЛЕ ТРАНСПЛАНТАЦИИ ПОЧКИ У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА

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Актуальность. У женщин репродуктивного возраста трансплантация нарушает характер менструального цикла. Обычно встречаются два основных состояния – аменорея и гиперменорея. **Цель** исследования – оценить характер менструального цикла после трансплантации почки у женщин репродуктивного возраста. **Материалы и методы.** Настоящее одномоментное исследование проводилось в государственной больнице в г. Карачи, Пакистан. Всего в исследование было включено 69 пациенток репродуктивного возраста, перенесших трансплантацию почки от живого донора более года назад. Исключались женщины с инфекцией половых путей, принимающие гормональные препараты, имеющие органические причины заболевания половых путей, нарушения свертываемости крови и тяжелые заболевания сердца и/или периферических сосудов. Для исследуемых параметров рассчитывали частоту и процентное соотношение. Проводили анализ корреляции и ассоциации типа менструации с длительностью менструального цикла. Значение $p < 0,05$ считалось статистически значимым. **Результаты.** Возраст большинства женщин, включенных

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в исследование, составлял 35–39 лет (36; 52,2%). Наиболее частыми нарушениями менструального цикла были обильные менструальные кровотечения (22; 31,9%) и аменорея (21; 30,4%). Менструации были нормальными только в 2,9% случаев. Кросс-табуляция показала, что у 26,1% развивалась аменорея, у 24,6% – олигоменорея и у 31,9% – гиперменорея. Значение коэффициента Дурбина–Уотсона (0,656) указывает на сильную положительную связь между характером менструального цикла (зависимая переменная) и типом менструации, семейным положением, возрастом донора, наличием детей и местом проживания пациенток (независимые переменные). **Выводы.** По результатам настоящего исследования можно сделать вывод, что у женщин репродуктивного возраста после трансплантации почки нарушался менструальный цикл. Основное нарушение заключалось в том, что у таких пациенток отмечались аменорея, гиперменорея, олигоменорея и гипоменорея.

Ключевые слова: женщины репродуктивного возраста, аменорея, олигоменорея, гиперменорея, трансплантация почки.

INTRODUCTION

Chronic kidney disease (CKD) is a major global health problem in about 11–17% [1]. Globally, about 37% of the CKD patients get kidney transplantation [2]. In CKD, other organ functions are also highly affected. In females, irregular pattern of menstruation has been reported in 66% to 80% of the women, leading to either amenorrhea, polyomenorrhea, oligomenorrhea or heavy menstrual bleeding [3–6]. In the end stage renal disease (ESRD), the pulsatile secretion of gonadotropin releasing hormone (GnRH) is affected, eventually results in loss of release of luteinizing hormone (LH) and causing anovulation [7–9]. After kidney transplant, immunosuppressive therapy resumes ovarian function in approximately 73.9% in about one year time [10, 11]. There is little information in the literature about changing menstrual patterns after kidney transplantation. The aim of this study was to observe the post-transplant menstrual pattern in women in our local population.

MATERIALS AND METHODS

This cross-sectional study was carried out in a public sector hospital of Karachi, Pakistan during January 2018 to April 2021. Ethical considerations were followed according to Helsinki Declaration. Patients were enrolled using convenient sampling after their written informed consent. They were properly briefed about the study and were assured that their identity will remain confidential to all other than the researchers themselves. A total 69 patients of reproductive age were included who underwent living kidney donor transplant for more than a year ago. Women having genital tract infection, using hormonal treatment, organic cause of genital tract, clotting disorder and severe cardiac and/or peripheral vascular disease were excluded. A standardized proforma for data collection was developed. Data including age, marital status, number of children, living location of the patients and types of menstruation and menstruation cycle pattern were recorded via face to face interview by a research personnel. Types of menstruation was set as independent variables, while menstruation cycle pattern was defined

as dependent variable. Menstrual pattern were classified into polyomenorrhea <21 days, normal (22–35 days) and oligomenorrhea >35 days. Data was entered and analyzed using Statistical Package for Social Sciences (SPSS) version 20. Frequency and percentages were calculated for demographic characteristics. Correlation and association analysis was calculated for type of menstruation with menstrual cycle pattern. A *P*-value less than 0.05 was considered statistically significant.

RESULT

The demographic characteristics of study participants are shown in Table 1. Majority of female included in the study aged between 35–39 years (36, 52.2%). The menstrual cycle pattern is shown in Table 2. The most frequent menstrual disturbance observed was heavy menstrual bleeding (22, 31.9%) and amenorrhea (21, 30.4%). Only 2.9% cases showed normal menstrual pattern. The cross tabulation indicated that 26.1% patients had amenorrhea, 24.6% had oligomenorrhea and 31.9% had menorrhagia. The Durbin–Watson value of 0.656 indicated a strong positive relationship between menstruation cycle pattern (dependent variable) and type of menstruation, marital status, donor's age, children and living location of the patients (independent variables).

DISCUSSION

Kidney transplant is the best kidney replacement treatment for ESRD and poor quality of life. Usually, kidney transplant is recommended when the glomerular filtration rate (GFR) is less than 15 ml/min/1.73 cm². Furthermore, in other words, the kidney transplant is needed when kidney's functional ability is lost about 90%. At this stage, the body's response to medicines is nearly 10% along with further emergence of other diseases. The liver and the reproductive organ are significantly damaged by kidney failure due to high imbalance of electrolytes, fluid retention, occasional urinary output and edema. Edema occurs due to high sodium in circulation with high fluid retention, less vessel filtration leading to development of pressure on heart and brain as well [12].

The peered articles documented that in kidney transplant recipients' anovulation can be completely reversed through a series of medications and the patients can conceive and give birth in a healthy and normal manner. Moreover, start of menstruation cycle is considered as one of the major advantages of kidney transplant women of reproductive age. Patients with stable creatinine level are even more likely to attain normal menstruation cycle within six months [6].

Table 1

Demographic Characteristics of Study Subjects

S. No	Variables	Frequency (n)	Percentage (%)
1.	Age (Years)		
	20–24	01	1.4
	25–29	05	7.2
	30–34	24	34.8
	35–39	36	52.2
	40 years and above	03	4.3
2.	Marital Status		
	Unmarried	02	2.9
	Married	57	82.6
	Separated / Divorced	10	14.5
3.	Parity		
	Nulliparous	09	13.0
	1–2	39	56.5
	3–4	18	26.1
	>4	03	4.3
4.	Residence		
	Karachi	27	39.1
	Sindh	21	30.4
	Punjab	07	10.1
	KPK	12	17.4
	Baluchistan	02	2.9
5.	Duration of Menses		
	>21 days	03	4.3
	21–45 days	48	69.6
	<45 days	18	26.1
6.	Menstrual Pattern		
	Normal	02	2.9
	Amenorrhea	21	30.4
	Oligomenorrhea	17	24.6
	Hypomenorrhea	07	10.1
	Menorrhagia	22	31.9

On the other hand, high creatinine level takes time, either a year or two to restore normal ovulation. Furthermore, in women of reproductive age, the kidney disease primarily cause abnormal ovarian function. The level of irregularity of normal hypothalamus pituitary gonadal axis is dependent on the magnitude of kidney disorder [13].

In normal health condition, the LH and follicle stimulating hormone (FSH) are metabolized by liver and kidneys. But, in case of renal disease, primarily at last stage, these hormones get raised in the bloodstream. The kidney transplantation improves metabolism of LH and FSH. Furthermore, at post kidney transplantation, usually Rapamycin inhibitors are given that assist in normalizing these reproductive hormones to restore the ovulation cycle [14].

The most frequent menstrual disturbance observed in present study was oligomenorrhea and amenorrhea. It could be due to hormonal imbalance in pre-kidney transplant phase in reproductive women. This elevated hormone prolactin occurs due to incrimination of urine wastes in blood. The kidney transplantation improves the GFR, restoring prolactin metabolism and safely eliminating the end product through urine. It has also been found that prolactin secretion is highly sensitive and is largely affected by the daily life stresses. Besides, the restoration of prolactin and testosterone level also gets normal in post-transplant phase [15].

Though menstruation is a part of normal reproductive cycle of female, it plays a significant role in women's health and easily disturbed by disease processes. It can affect both physical and psychological health. Menstrual pattern variation is frequently observed among female with CKD and after kidney transplant. The pattern of menstrual periods after kidney transplant is irregular and women experience bleeding mostly after 16 days with more than 20 ml of bleeding. Due to decreased progesterone level with high level of FSH, LH and estrogen, this condition is usually experienced by women mostly after 16 days. Our study results correlates with this finding. The hormonal irregularities shortens the luteal phase. The cycle is continued for more than 7 days. The overall prevalence of menstrual disturbances in reproductive women in CKD is reportedly 64.2% [16]. In our study, overall menstrual disturbances was found to be 69.6%.

Table 2

Association between Menstrual Pattern and Type of Menstruation (P-value <0.0001)

S. No	Menstrual Pattern	Amenorrhea	Hypomenorrhea	Normal	Oligomenorrhea	Menorrhagia
1.	Normal (21–35 days)	3 (4.3%)	0	0	0	0
2.	Short cycle (>21 days)	18 (26.1%)	7 (10.1%)	2 (2.9%)	17 (24.6%)	4 (5.8%)
3.	Longer (<35 days)	0	0	0	0	18 (26.1%)
Total		21 (30.4%)	7 (10.1%)	2 (2.9%)	17 (24.6%)	22 (31.9%)

Our findings are different from others. One study showed no difference between bleeding pattern before and after transplantation [17]. Another case-control study showed regular menstrual cycle in 72.7%. This result did not correlate with our findings and this might be due to data collection which was done after 1–5 years post-transplantation. Thus, the duration was long as compared to our study [18].

Usually, after six months of kidney transplantation, the normal ovarian cycle restoration occurs. The hormonal therapy reduces the thickness of endometrium with ameliorating the FSH, LH, estrogen and progesterone. The inhibin hormone causes to stop the cycle with 7 days of bleeding of less than 10 ml. Furthermore, it also improves the ovulatory phase that assists in normal formation of endometrium [19]. The cycle is repeated after 24 to 31 days with normal releasing and inhibin pattern. The 5 days of menstruation is with 5 ml to 8 ml blood [20]. The result on cycle length shows 69.6% of the females reported menstrual cycle shorter than 21 days and 26.1% had menstrual cycle longer than 35 days. Earlier studies did show variable results regarding cycle length. The result of the present study showed a significant association between menstrual pattern and type of menstruation (P -value <0.0001).

The findings of our study showed higher incidence of menstrual pattern disturbance. However, our study findings are limited by studying of only clinical symptoms and their relations. Further exploratory research in this regard is needed.

CONCLUSION

From the result of the present study, it is concluded that the reproductive age women have shown a disturbed pattern of menstrual cycle after kidney transplant. The major observation was that such patients reported amenorrhea, menorrhagia, oligomenorrhea and hypomenorrhea. Adopting healthy life style is of utmost importance and can significantly reduce the number of affected individuals and burden of this underestimated disease.

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The authors declare no conflict of interest.

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