

PATIENT-RELATED FACTORS THAT INFLUENCE ADHERENCE TO POST-KIDNEY TRANSPLANT TREATMENT AMONG KIDNEY ALLOGRAFT RECIPIENTS AT A NATIONAL HOSPITAL IN KENYA

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Abstract

Introduction: The purpose of this study was to describe patient-related factors that influence adherence to post kidney transplant treatment among kidney allograft recipients at a national referral hospital in Kenya. Adherence to long term immunosuppressive medications determine the success of kidney transplantation. However, non-adherence is a global health concern among this special population.

Methods: Descriptive cross-sectional hospital-based study, census sampling method was used with a sample size of 106 kidney allograft recipients.

Findings: Almost half 49(46%) of the respondents were non adherent to medication. Majority 43(88%) pointed out that cost of the medicines was the main reason for non-adherence. Among those who adhered, 102(96%) indicated that they had adhered because the quality of their life had improved after kidney transplantation. Age was found to be a statistically significant factor in influencing outcome of adherence as indicated by body mass index (BMI) ($\chi^2(15) = 30.09, p = .012, p < .005$).

Conclusion: There exists a gap in adherence to medication among the kidney allograft recipients. Cost of medication is an important factor in non-adherence.

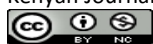
Recommendations: The health care providers should develop sustainable strategies to curb medication non-adherence. Government should consider National Hospital Insurance Fund cover to all post kidney transplant medicines. Non-governmental organizations should offer financial support to this special population by donating drugs.

Key words: *Kidney transplantation, adherence, immunosuppressive drugs.*

Introduction

Kidney transplantation is one of the best treatment modality for patients with end stage kidney disease (ESKD). The goal of kidney transplantation is to restore the initial kidney function thus prolonging life and bettering the quality of life (Vankova et al., 2018). Post kidney allograft recipients are expected to take immunosuppressant medication as long as they live or until a

complete kidney allograft rejection (Russell & Dellen, 2016). The immunosuppressant medications are aimed at weakening the patient's immune system to prevent the body from recognizing the grafted kidney. In addition, they prevent formation of de' novo antibodies which are responsible for acute graft rejection (Lorenz et al., 2018).



However, non-adherence to immunosuppressant medications has been reported as a global burden accounting for up to 30% graft failures in developed countries and more than 60% in the third world countries (Villeneuve et al., 2020) and (Hedayati et al., 2017). Patients are classified as non-adherent to medications when they give a self-report of having missed doses repeatedly within a stated period of time after kidney transplant (Villeneuve et al., 2020). Non adherence to medication has been reported to increase graft rejection by seven times; it has been ranked as the third leading cause of graft rejection (Vankova et al., 2018) and (Lorenz et al., 2018). Due to the global shortage of organs for donation, there is dire need to maintain and prolong the function of the already transplanted kidney with the aim of raising the number of potential kidney donors (Hedayati et al., 2017).

Several factors have been reported to influence adherence to medication. Among them, are patient related factors which include but not limited to age, gender, level of education, marital status, self-efficacy, beliefs and attitudes (Villeneuve et al., 2020) and (Sanders-Pinheiro et al., 2018).

Age is one of the extensively reported patient factor that influence adherence. Patients over 65 years of age often exhibit low adherence level associated to comorbidities, polypharmacy and difficulty in swallowing medication. They also have cognitive impairments which negatively affect their concentration, memory and decision making of their daily lives leading to non-adherence (Paterson et al., 2018). As reported by Tong et al (2011), sick persons above 65 years of age were found to have exaggerated drug adverse effects due to physiological changes affecting the

pharmacokinetics and pharmacodynamics of many drugs.

On the other hand, teenagers have also been reported to have lowest levels of adherence to medication related to denial of chronic illness, the need to take lifelong medications and worries about social stigma (Russell & Dellen 2016). According to Russell and Dellen (2016) teenagers were found to take drug “holidays”; they made assumptions that when symptoms improve they may discontinue the therapy.

Gender is an important factor in influencing adherence. In a study done in India to assess the level of adherence to post kidney recipients, female patients were found to have higher levels of adherence to medication as compared to male patients (Adhikari et al., 2018).

Family cohesion offers emotional bonding to family members. Patients who were married and lived with their spouses were found to greatly adhere to medication in comparison to the ones who were single and lived a solitary life. The spouses were found to offer emotional and financial support which promoted adherence (Russell & Dellen, 2016) and (Adhikari et al., 2018)

Adequate knowledge is the key to the success of any health program. Patients with post primary education were found to have satisfactory recognition of medication, their indications, doses, adverse effects and duration of therapy. They were found to have higher level of adherence as compared to those with low level of education (Nielsen et al., 2018) and (Oberlin et al., 2016).

On the other hand, low level of education was found to highly influence non adherence. This group of patients was found to have low self-confidence, less autonomy to their



health and poor understanding of their treatment plan which made it difficult to follow their treatment plan (Russell & Dellen, 2016). In addition, low education is an important determinant of unemployment which leads to a heavy financial burden to the patient and their family posing a challenge to health needs (Hedayati et al., 2017).

In the national referral hospital, where this study was carried out, medical records revealed 50% failure rate in patients who had undergone kidney transplantation. Of these patients, 27.5% were on management of acute graft rejection, 3.75% had been re-transplanted, 15% had reverted to dialysis, and 50% had succumbed to complications related to non-adherence while 2.5% were lost to follow up (KNH Renal unit health records 2019).

It was not known whether these patients adhered to treatment and lifestyle changes or not. The study therefore aimed at describing the patient-related factors that influenced adherence to post kidney transplant treatment regimen and lifestyle changes, among the kidney allograft recipients at a National Referral Hospital in Kenya.

Methods

This was a descriptive cross-sectional hospital-based study. The study population was all kidney allograft recipients transplanted between January 2010 and December 2017 at the Renal Unit. This period was chosen because kidney transplants were carried out consistently and records were available. This study adopted census sampling method.

Sample size was calculated from the accessible population of 143 patients. For

statistical purposes, Yamane (1967) formula for finite population was adopted in calculation of the minimum sample size. The formula has a margin error of 0.05. By substitution of the formula, a minimum of 106 study participants were required for this study.

All kidney allograft recipients transplanted between January 2010 and December 2017 attending transplant clinic, over 18 years of age and those who consented to the study were included.

The study excluded allograft recipients who had experienced kidney allograft failure and were back to dialysis, critically ill patients, those who could neither speak English nor Swahili and non-consenting kidney recipients.

A researcher developed self-administered and interviewer administered questionnaire was used to collect data.

Pre testing of the Study Instrument was done at a similar referral hospital in Kenya. A test re-test was done with an interval of two weeks in order to ensure reliability of the tool. Content validity was done by the two supervisors and a practicing nephrologist.

The researcher was the principal investigator aided by two research assistants. Data was collected in the transplant clinic over a period of ten weeks between June and August 2020. All the 106 allograft recipients' medical records were reviewed for that day's serum creatinine level, cyclosporine or tacrolimus depending on which drug the patient was taking.

Data Analysis was done using Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics were used to describe patients' demographic data; chi square was used to test the association between the variables while logistic



regression was performed to determine the predictors of adherence. A p value of less than 0.05 was considered statistically significant at 95% confidence.

The study was approved by the ethical review committees at Kenyatta University, National Commission for Science, Technology and Innovation (NACOSTI), Moi Teaching and Referral Hospital and Kenyatta National Hospital- University of Nairobi ethics and research committee. All the participants provided a written informed consent for the study.

Findings

Respondents' Demographic Characteristics

A total of 106 post kidney allograft recipients participated in the study with a mean age of 43.73 ± 12 years. Majority 70 (66%) of the respondents were female and 64(60%) were married. More than half 54(51%) of respondents had tertiary level of education as the highest level obtained. Nearly half of the respondents 52(49%) were self-employed with a greater number 62(64%) of them earning more than Kshs 20,000 monthly. In addition, 19(18%) of the respondents underwent kidney transplant in the year 2010.

On the relationship between recipients and donors, siblings were the majority constituting for 72 (68%). A total of 68(64%) of the respondents had been treated with

hemodialysis 3-4 years prior to transplantation. This is shown in table 1:

Table 1: Demographic Characteristics of the Respondents

Characteristic	n(%)
Age : mean(SD)	42.73±12
Monthly income in Kshs	
≤ 10,000	20(20.6)
10,001- 20,000	15(15.5)
≥20,001	62(63.9)
Duration of dialysis	
≤2 years	2(1.9)
3-4 years	68(64.2)
≥5 years	36(34)
Year of transplantation	
2010	19(17.9)
2011	14(13.2)
2012	13(12.3)
2013	16(15.1)
2014	17(16)
2015	12(11.3)
2016	6(5.7)
2017	9(8.5)
Gender	
Male	36(34)
Female	70(66)
Marital status	
Single	37(34.9)
Married	64(60.4)
Divorced/separated /widowed	5(4.7)
Level of education	
Primary	12(11.3)
Secondary	40(37.7)
Tertiary	54(50.9)
Occupation	
Self-employment	52(49.1)
Formal employment	43(40.6)
Unemployed	11(10.4)
Recipient-donor relationship	
Parent	15(14.2)
Sibling	72(67.9)
Extended family member	12(11.3)
Offspring	7(6.6)



Table 2: Adherence to Medication

<i>Characteristic</i>	<i>Statistic n(%)</i>
<i>No. of patients who missed medication in the last one month</i>	<i>49(46)</i>
<i>No. doses missed in the last one month(N=49)</i>	<i>One</i> <i>16(33)</i>
	<i>Two</i> <i>19(38)</i>
	<i>Three</i> <i>5(10)</i>
	<i>More than three</i> <i>9(19)</i>

Adherence to medication

To assess adherence to medication, the respondents were asked to indicate whether they ever missed medication in the last one month and if so, to indicate the number of times they did. Forty-nine (46%) indicated missed medication in the last one month with majority having missed twice accounting for 19 (38%). This is shown in table 2.

Reasons Given by Patients for Taking Medication

The entire sample 106 (n=100%), indicated that they adhered to medication in order to prevent graft rejection. Majority 102 (96%)

of the respondents indicated that they adhered to medication because the quality of their life improved after kidney transplant while 84

Eighty-one percent adhered to medication as an appreciation of the donors and health care providers. In addition, 75(71%) of the respondents adhered to medication since they scheduled them at meal times while 74(70%) of the respondents adhered to medications because family members offered financial support. More than half of the respondents 56 (53%) indicated that their family members reminded them to take medications. This is as shown in table 3.

Table 3: Reasons given by patients for taking medication

<i>Description</i>	<i>Statistic n(%)</i>
<i>“I adhered to medication to prevent rejection”</i>	106(100)
<i>“I adhered in appreciation to donor & health-care provider”</i>	84(81)
<i>“Quality of my life improved after kidney-transplant”</i>	102(96)
<i>“My family members offer financial support”</i>	74(70)
<i>“My Family members remind me to take pills”</i>	56(53)
<i>“I use an alarm as a reminder to take medication”</i>	40(38)
<i>“I use a medication pill box to organize my medicine”</i>	30(29)
<i>“I scheduled my medications on mealtimes”</i>	75(71)

Reasons given by Patients for Missed Medication Doses

Forty-nine patients who missed medications were further probed to evaluate the reasons that led to this. Majority 43(88%) of the respondents pointed out that the cost of the medicines was the main reason for missed

doses since they could not manage to stock the medicines at all times. More than half 26(54%) of the respondents indicated that they forgot to take their medicines. This is as shown in table 4.

Table 4: Reasons given by Patients for Missed Medication Doses

<i>Description</i>	<i>Statistic n(%)</i>
<i>“I forgot”</i>	26(54)
<i>“Medicines are too expensive to buy”</i>	43(88)
<i>“I felt worse after taking medicines ”</i>	4(8)
<i>“The doses are too frequent”</i>	1(2)
<i>“The pills are too many to take at once”</i>	4(8)

Respondents' drug trough levels

In order to measure the level of adherence to medication, medical records of all respondents were reviewed for the current cyclosporine or tacrolimus blood drug trough level. In this study, laboratory

reference range for cyclosporine and tacrolimus level was 100-400ng/ml and 5-15ng/ml respectively. Majority 88% (n=93) of the respondents' had normal drug trough level. None of the respondents had high drug trough levels. This is shown in Table 5.

Table 5: Patient-related Factors That Influence Immunosuppressive drug trough level

<i>Variable</i>		<i>Frequency</i>		<i>DF</i>	<i>Chi-square Value</i>	<i>p-value</i>
Gender		<i>Normal Levels</i>	<i>Low levels</i>			
	<i>Female</i>	31	5	1	0.328	.567
	<i>Male</i>	62	7			
Age	<i>15 – 24</i>	6	2			
	<i>25 – 34</i>	20	2			
	<i>35 – 44</i>	27	4	5	2.278	.810
	<i>45 – 54</i>	20	2			
	<i>55 – 64</i>	16	2			
	<i>65 – 74</i>	4	0			
Marital status	<i>Single</i>	31	6			
	<i>Married</i>	58	6	2	1.621	.445
	<i>Widowed/divorced/separated</i>	4	0			
Religion	<i>Muslim</i>	1	0	1	0.130	.718
	<i>Christian</i>	92	12			
Level of education	<i>Primary</i>	11	1			
	<i>Secondary</i>	35	4	2	0.292	.864
	<i>Tertiary</i>	47	7			
Occupation	<i>Self Employed</i>	47	4			
	<i>Formal Employment</i>	38	5	2	3.377	.185
	<i>Unemployed</i>	8	3			
Monthly income	<i>10000 or less</i>	18	2			
	<i>11000 – 20000</i>	13	1	2	0.098	.952
	<i>Above 20000</i>	56	6			
Relationship with the donor	<i>Parent</i>	11	4			
	<i>Sibling</i>	64	7	3	4.630	.201
	<i>Extended family member</i>	11	1			
	<i>Offspring</i>	7	0			
		<i>2010</i>	17	1		
	<i>2011</i>	13	1			
	<i>2012</i>	13	0			
Year of Transplant	<i>2013</i>	15	1			
	<i>2014</i>	13	4	7	8.598	.283
	<i>2015</i>	10	2			
	<i>2016</i>	4	2			
	<i>2017</i>	8	1			
Duration of dialysis	<i>Less than 2 years</i>	2	0			
	<i>3 to 4 years</i>	60	8	2	0.266	.876
	<i>Over 5 years</i>	31	4			



Table 6: Respondents' drug trough levels

	<i>Drug levels</i>	<i>Statistic n(%)</i>
<i>Valid</i>	<i>Normal Level</i>	93(88)
	<i>Low Levels</i>	12(11)
	<i>Total</i>	105(99)
<i>Missing</i>		1(1)
<i>Total</i>		106(100)

Patient-related Factors That Influence Immunosuppressive drug trough level

A chi square test was used to determine whether patient-related factors had a statistical significance in influencing immunosuppressive drug trough level. The test showed no statistically significant relationship between the patient factors and the levels of the immunosuppressive drugs as shown in table 6.

Patient related factors that influence Current Body Mass Index

There was found to be a statistically significant association between age and current body mass index, ($\chi^2(15) = 30.09, p = .012, p < .005$). Older people were more likely to have a higher BMI. A significant association was also found between marital status and BMI, ($\chi^2(6) = 18.00, p = .006, p < .005$). Married respondents were more likely to have a higher BMI. This is shown in table 7.



Table 7: Patient Related Factors that Influence Current Body Mass Index

<i>Variable</i>	<i>Frequency</i>				<i>DF</i>	<i>Chi-square Value</i>	<i>p-value</i>	
	<i>Under weight</i>	<i>Healthy weight</i>	<i>Pre-obesity</i>	<i>Obesity class-1</i>				
<i>Gender</i>	<i>Female</i>	1	22	11	2	3	0.323	.956
	<i>Male</i>	1	43	21	5			
<i>Age</i>	<i>15 – 24</i>	1	7	0	0	15	30.088	.012
	<i>25 – 34</i>	1	18	1	2			
	<i>35 – 44</i>	0	19	11	1			
	<i>45 – 54</i>	0	12	7	3			
	<i>55 – 64</i>	0	6	12	1			
	<i>65 – 74</i>	0	3	1	0			
	<i>Single</i>	1	31	3	2			
<i>Marital status</i>	<i>Married</i>	1	33	25	5	6	17.998	.006
	<i>Widowed/divorced/separated</i>	0	1	4	0			
<i>Religion</i>	<i>Muslim</i>	0	0	1	0	3	2.335	.506
	<i>Christian</i>	2	65	32	7			
<i>Level of education</i>	<i>Primary</i>	0	7	5	0	6	5.643	.464
	<i>Secondary</i>	2	22	13	3			
	<i>Tertiary</i>	0	36	14	4			
<i>Occupation</i>	<i>Self employed</i>	0	30	19	3	6	11.075	.86
	<i>Formal employed</i>	1	25	13	4			
	<i>Unemployed</i>	1	10	0	0			
<i>Monthly income</i>	<i>10000 or less</i>	0	16	5	0	6	11.147	.084
	<i>11000 – 20000</i>	1	9	5	0			
	<i>Above 20000</i>	0	33	22	7			
<i>Year of Transplant</i>	<i>2010</i>	1	9	6	3	21	14.322	.855
	<i>2011</i>	1	8	4	1			
	<i>2012</i>	0	8	5	0			
	<i>2013</i>	0	11	3	2			
	<i>2014</i>	0	13	4	0			
	<i>2015</i>	0	7	4	1			
	<i>2016</i>	0	4	2	0			
	<i>2017</i>	0	5	4	0			
<i>Duration of dialysis</i>	<i>Less than 2 years</i>	0	1	1	0	6	3.139	.791
	<i>3 to 4 years</i>	2	41	19	6			
	<i>Over 5 years</i>	0	23	12	1			



Predictors of Adherence to Treatment Among Post Kidney Recipients

Logistic regression was used to compute the predictors of adherence to treatment on the patient factors that were statistically significant at bivariate level.

Relationship between Patient Related Factors (age and marital status) and Current BMI

An ordinal logistic regression was computed to predict the relationship between age and the current BMI; marital status and the current BMI. Age was found to be significant, $p = .013$ and an odds ratio of 1.054. Therefore, an increase in age by one year increases the odds of getting a high BMI by approximately 5%. However, marital status was found to be a predictor, $p = .383$, $p > 0.05$. This information is shown in table 8.

Table 8: Relationship between Age, Marital Status and Current BMI

	Variable	Estimate	OR	D.F	p-Value	95% Confidence Interval	
						Lower	Upper
Threshold	Underweight	-3.174	0.042	1	.031	-6.065	-0.283
	Healthy weight	1.957	7.08	1	.146	-0.684	4.599
	Pre-obesity	4.293	73.2	1	.002	1.528	7.058
Location	Age	0.053	1.054	1	.013	0.011	0.095
Marital status	Single	-1.604	0.201	1	.113	-3.587	0.379
	Married	-0.781	0.46	1	.383	-2.535	0.974
	Divorced/separated/widowed	Reference					



Discussion

Various patient related factors are known to positively or negatively influence adherence to medication and lifestyle changes. The current study findings demonstrated that family support was an important factor in promoting adherence. The findings tie well with a study done in South Africa which pointed out that family support is vital in adherence to post kidney medication and lifestyle changes (Ndemera & Bhengu, 2017). Comparable findings were also reported in a study conducted in India where post kidney transplant patients with family support were found to be more adherent to treatment and lifestyle changes than those without family support (Adhikari et al., 2018a). The findings from this study indicate that kidney recipients adhered to medication and lifestyle changes because the quality of their life improved after kidney transplantation. According to Muduma et al., (2016) kidney transplant recipients linked adherence to post kidney transplant therapy with a better quality of life compared to dialysis life. The findings concur with a study done in South Africa where kidney recipients were seen to adhere to recommended medications and lifestyle changes in order to maintain the transplanted graft which had brought back the premorbid state of life (Ndemera & Bhengu, 2017). The findings also concur with a study done by Moreso et al (2015) which reported that patients adhered to medication because the quality of their life improved after kidney transplant as compared to dialysis period and they feared to go back to dialysis.

The study findings indicated age as a significant factor in influencing BMI. BMI was found to be increasing with every increase in age. The findings are in harmony with a study done in Germany on

obesity post kidney transplantation which revealed advanced age was directly proportional to high BMI (Nöhre et al., 2020). Similar to this finding is report of a study by Liñán González et al., (2020) on weight and BMI after graft loss conducted in Spain which pointed out that higher age positively influenced BMI.

Post kidney recipients take steroids as part of the immunosuppressive therapy. Steroids are known to increase appetite and in return increase in weight. As age advances, the individual tend to lose muscle and to gain body fat. These two factors coupled with inactivity quadruples the risk of obesity indicated by high BMI (de Souto Barreto et al., 2018). Post kidney transplant follow up is very crucial for close monitoring of obesity since increase in age is a continuous process.

From the study findings, forgetfulness had a significant negative influence on medication adherence. The findings conform with a study done in Australia on identifying the barriers to immunosuppressive therapy which reported forgetfulness as the main barrier to immunosuppressive therapy (Cossart, et al., 2017). Similar findings were reported in Spain where forgetfulness was reported to be the main psychosocial factors leading to non-adherence of medication and lifestyle changes among kidney recipients (Scheel et al., 2018).

Cognitive disability is a common challenge among kidney transplant population. This is linked to the prolonged effect of high urea levels on the brain blood vessels during the dialysis period. The high urea levels are known to damage the brain cells leading to memory impairment (David, et al., 2019). In addition, long term use of immunosuppressant is associated with



cognitive dysfunction which impairs the memory (Jurgensen, et al., 2020). These challenges could adversely affect medication and lifestyle adherence. The study also showed that the cost of drugs was a challenge to most of the patients.

Although this finding was not statistically significant in this study since most of the patients could afford to buy medicines during the period of data collection, financial burden has been reported as a major challenge in third world countries particularly where no health policies are put in place to cater for such expenses (Lagou et al., 2017). According to studies done in India and Nigeria financial constrain was reported as a significant barrier to medication adherence since the purchase of medication is recurrent and life-long (Adhikari et al., 2018); (Okafor et al, 2016). The findings in this study could be explained by the fact that patients reported missing clinic appointments in order to save money to cater for the drugs. In addition, data was collected in a short period of time which could probably not be a true picture in the long run.

Conclusions

The study concludes that there exists a gap in medication adherence among kidney allograft recipients. The study has described age as a statistically significant factor in

influencing outcome of adherence as indicated by BMI. Age was found to be directly proportion to BMI. In addition, improved quality of life and family support positively influenced adherence. After successful kidney transplantation, patients led better lives and enjoyed freedom from dialysis restriction. On the other hand, financial burden on the patients and their families was linked to non-adherence since they could run out of medications stock due to lack of finances. Forgetfulness was also described as an important patient-related factor that negatively influenced adherence to post kidney treatment among post kidney transplant recipients.

Recommendations

The study recommends that the health care providers develop achievable and affordable strategies to curb medication adherence. Family conferences should be held both in pre and post-transplant periods to emphasize on the need for family support in success of long-term outcome of kidney transplant. Government should consider universal health coverage by offering comprehensive National Hospital Insurance Fund coverage to all post kidney transplant patients. Non-governmental organization should offer financial support to this special population by donating drugs. Close monitoring of the elderly in order to continuously monitor weight gain.

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