Rodríguez-Medina RM, et al. https://doi.org/10.37551/S2254-28842024017

Adherence to immunotherapy and its relationship with clinical variables in young adult kidney transplant recipients

Rosa María Rodríguez-Medina[1,2], Yosileb Sinai Aranda-Hernández[2], María Beatriz Cruz-Sánchez[3], Carlos Francisco Meza- García[1,2]

[1] Department of Nursing and Obstetrics, Universidad de Guanajuato, Campus León, Mexico
[2] Nursing Management, Health services, Instituto Mexicano del Seguro Social para el Bienestar (IMSS-BIENESTAR), León, Mexico
[3] Haemodialysis Service, Clínica Médica Santa Carmen, San Miguel de Allende, Mexico

Please cite this artcle in press as:
Rodríguez-Medina RM, Aranda-Hernández YS, Cruz-Sánchez MB, Meza- García CF. Adherence to immunotherapy and its relationship with clinical variables in young adult kidney transplant recipients. Enferm Nefrol. 2024;27(3):137-42

Corresponding author:
Rosa María Rodríguez Medina
anidem_36@hotmail.com

Reception: 05-09-24
Acceptance: 04-15-24
Publication: 06-30-24

ABSTRACT

Introduction: Adherence to immunotherapy decreases rejection and graft loss, so it is necessary to identify clinical variables related to adherence in adult renal transplant recipients to optimise renal graft survival.

Objetive: To assess the prevalence of adherence to immunotherapy and its relationship with clinical variables in young adult kidney transplant recipients in a tertiary hospital.

Material and Method: Descriptive cross-sectional observational study. A non-probabilistic convenience sample was taken from 45 adult kidney transplant recipients. Sociodemographic and clinical variables, anxiety, and depression were studied. The Basel Assessment of Adherence to Immunosuppressive Medications Scale was used to assess adherence.

Results: The mean age of the participants was 33.7±9.4 years. The majority were men (66.7%). The prevalence of non-adherence was 75.5%; an association was observed between adherence and the reason for hospital admission and anxiety. Non-adherent adults showed problems such as forgetting to take the immunosuppressant and delay of at least 2 hours in taking the medication.

Conclusions: The prevalence of non-adherence to immunotherapy was higher than reported in previous studies, so continued intervention is needed to improve adherence to immunosuppressive therapy recommendations.

Keywords: compliance and adherence to treatment; anxiety; depression; transplantation; nursing.

RESUMEN

Adherencia a inmunoterapia y su relación con variables clínicas en adultos jóvenes trasplantados renales

Introducción: La adherencia a la inmunoterapia permite disminuir la incidencia de rechazo y pérdida del injerto, por lo que es necesario identificar las variables clínicas relacionadas con la adherencia de adultos trasplantados renales a fin de optimizar la supervivencia del injerto renal.

Objetivo: Evaluar la prevalencia de adherencia a la inmunoterapia y su relación con variables clínicas en adultos jóvenes trasplantados renales de un hospital de tercer nivel.

Material y Método: Estudio observacional descriptivo de corte transversal. Se ha realizado un muestreo no probabilístico por conveniencia que incluyó a 45 adultos trasplantados renales. Se estudiaron variables sociodemográficas y clínicas, ansiedad y depresión. Para evaluar adherencia se aplicó el cuestionario Basel Assessment of Adherence to Immunosuppressive Medications Scale.

Resultados: La edad media de los participantes fue de 33,7±9,4 años, la mayoría fueron hombres (66,7%). La prevalencia de no adherencia fue del 75,5%; se observó asociación

entre la adherencia con el motivo de ingreso hospitalario y la ansiedad. Los adultos no adherentes mostraron problemas como el olvido de la toma del inmunosupresor y retraso de al menos 2 horas en la ingesta del medicamento.

Conclusiones: La prevalencia de no adherencia a la inmunoterapia fue alta, superior a la reportada en estudios previos, por lo que es necesaria la intervención continua para mejorar el apego a las recomendaciones de la terapia inmunosupresora.

Palabras clave: cumplimiento y adherencia al tratamiento; ansiedad; depresión; trasplante; enfermería.

INTRODUCTION

IKidney transplantation is the therapy of choice for patients with chronic kidney disease (CKD), offering them improved quality of life. However, the number of kidneys available for transplantation is limited; therefore, it is of vital importance that, once transplantation has been performed, graft survival is optimised and patients demonstrate adherence to a strict regimen of immunosuppressive drugs[1,2].

Non-adherence to immunotherapy is associated with an increased risk of acute and chronic rejection, graft loss, and higher mortality[3]. In kidney transplant recipients, the reported prevalence of non-adherence ranges from 15% to 50%[3-6]. According to the World Health Organization, five risk factors related to non-adherence have been identified: sociodemographic, psychological, kidney disease–related, immunotherapy-related, and patient-related factors[3-7].

These factors should be examined periodically to detect the risk of non-compliance early and addressed through an integrative approach that conceives adherence as a dynamic process in which the patient plays an active role[7]. Therefore, the aim of the present study was to evaluate the prevalence of adherence to immunotherapy and its relationship with clinical variables in young adult kidney transplant recipients at a tertiary-level hospital in Mexico. The findings will contribute to the development of interventions aimed at promoting adherence and self-care in young adult kidney transplant recipients.

MATERIALS AND METHODS

We conducted an observational, descriptive, cross-sectional study. Adult kidney transplant recipients who were admitted to a tertiary referral center in 2023 were included. The sample size was calculated using EPIDAT 3.1 software, based on a population of 84 patients, a precision of 10%, a 95% level of confidence, and an expected non-adherence proportion of 50%;5 a sample of 45 adults was estimated. Non-probabilistic convenience sampling was performed, including those who met the inclusion criteria: adults of both sexes aged 18–60 years; a history of kidney transplantation for more than 6 months; and agreement to participate in the study. Exclusion criteria were adults with previously diagnosed psychiatric disorders and those who declined to participate.

Sociodemographic variables (age, sex, educational level, and occupation) and laboratory parameters (creatinine, urea, blood urea nitrogen, serum tacrolimus level, and serum ciclosporin level) were collected. Clinical variables studied included the aetiology of CKD, time since transplantation, immunosuppressive treatment, anxiety, and depression, among others. Adherence to immunosuppressive therapy was also recorded. Adherence is present when a patient's behaviour matches the recommendation agreed upon by the prescriber and involves collaboration between the patient and the health care professional. Non-adherence is defined as a deviation from the prescribed medication regimen[3].

The Beck Depression Inventory, adapted for the Mexican population by Jurado et al[8], and applied in renal patients on dialysis[9], was used. Depression categories were as follows: (1) minimal depression, 0–9 points; (2) mild depression, 10–16 points; (3) moderate depression, 17–29 points; and (4) severe depression, 30–63 points[10]. The Beck Anxiety Inventory, validated in the Mexican population by Robles et al,8 was also used. Anxiety categories were as follows: 0–5 points, minimal anxiety; 6–15 points, mild anxiety; 16–30 points, moderate anxiety; and 31–63 points, severe anxiety[11]. Both questionnaires are self-administered, consist of 21 items, and use a Likert-type scale[8].

To assess adherence, the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS) was used. This self-report questionnaire consists of 5 items with a Likert-type scale (0=never, 1=once a month, 2=every 2 weeks, 3=every week, 4=more than once a week, and 5=every day). Individuals who selected "never" were considered adherent (score=4), whereas those selecting any other option were considered non-adherent (score≥5)[12,13].

Table 1. Sociodemographic characteristics of participants.

Characteristic	n	%
Sex		
Male	28	66.7
Female	14	33.3
Education		
Primary	7	16.7
Secondary	18	42.9
High school	9	21.4
University	8	19.0
Occupation		
Employed	15	35.7
Unemployed	4	9.5
Homemaker	11	26.2
Other**	12	28.6

* Presented as mean and standard deviation.
** Includes farmer and merchant.

Descriptive statistics were performed, and clinical variables were compared according to adherence using the Mann-Whitney U and chi-square tests. A p value <0.05 was considered statistically significant. SPSS version[21] was used.

The study protocol was approved by the center Research and Ethics Committees. According to the Regulations of the General Health Law on Health Research, Article 17, it was considered a study with minimal risk[14].

RESULTS

A total of 45 young adult kidney transplant recipients participated, with a mean age of 33.7±9.4 years; most were men (66.7%). Sociodemographic characteristics are shown in **table 1**.

According to BAASIS results, the prevalence of non-adherence was 75.5%. No relationship was observed between the analytical parameters studied and adherence to immunotherapy **(table 2)**.

Table 3. Association between adherence to immunotherapy and clinical variables of participants.

Parameter	Adherence (n=11) mean±SD	Non-adherence (n=34) mean±SD	P Value
Time since diagnosis (y)*	9.1±4.3	8.6±3.0	0.764
Time since transplantation (y)*	6.3±4.2	4.5±2.9	0.257
Aetiology of kidney disease			
Unknown	8 (72.7)	27 (79.4)	0.887
Diabetes mellitus	1 (9.1)	2 (5.9)	
Other**	2 (18.2)	5 (14.7)	
Comorbidities			
Diabetes mellitus	2 (18.2)	5 (14.7)	0.896
Systemic arterial hypertension	5 (45.5)	14 (41.2)	
None	4 (36.4)	15 (44.1)	
Type of kidney donor			
Living related	4 (36.4)	10 (29.4)	0.790
Living unrelated	0 (0.0)	1 (3.0)	
Deceased	7 (63.6)	23 (67.6)	
Immunosuppressive treatment			
Tacrolimus–mycophenolate mofetil–prednisone	5 (45.5)	16 (47.1)	0.203
Cyclosporine–mycophenolate mofetil–prednisone	5 (45.5)	18 (52.9)	
Cyclosporine–azathioprine –prednisone	1 (9.1)	0 (0.0)	
Reason for admission			
• Biopsy	8 (72.7)	10 (29.4)	0.027
• Graft dysfunction/rejection	3 (27.3)	16 (47.1)	
• Other***	0 (0.0)	8 (23.5)	

Table 3, illustrates the association between adherence to immunotherapy and clinical variables. Adherence was associated with the reason for admission, as most non-adherent adults were admitted for graft dysfunction or rejection (47.1%). Adherence was also associated with anxiety: most non-adherent adults exhibited minimal (53%) or mild (44.1%) anxiety **(figure 1)**. No association was found between adherence and depression **(figure 2)**.

Regarding BAASIS responses **(table 4)**, in the non-adherent group, most adults reported forgetting to take their medication at least once per month (p=0.003). For the item concerning delaying intake of immunosuppressants by at least 2 hours, all participants in the adherent group reported never delaying, whereas most in the non-adherent group reported delaying at least once per month (p=0.002). In the final self-evaluation item regarding performance in taking immunosuppressants, the adherent group reported higher scores compared with the non-adherent group (p<0.001).

DISCUSSION

In our study, kidney transplant recipients were young adults, mostly men, with an unknown aetiology of kidney disease and grafts from deceased donors, consistent with profiles described nationally[15,16] and internationally[17].

Table 2. Association between adherence to immunotherapy and analytical parameters.

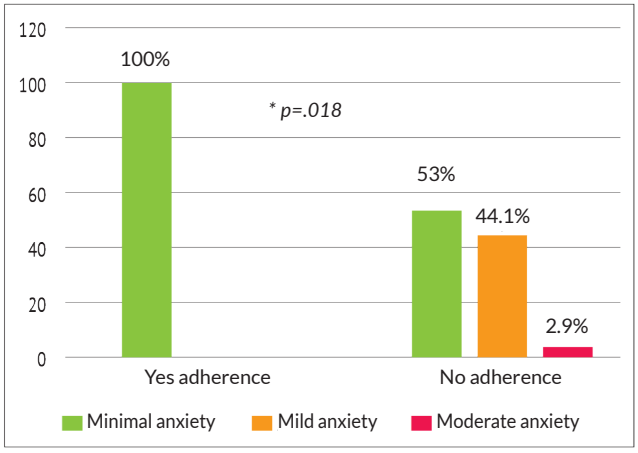
Parameter	Adherence (n=11) mean±SD	Non-adherence (n=34) mean±SD	P Value
Creatinine (mg/dL)	1.9±0.4	2.1±0.8	0.363
Urea (mg/dL)	62.7±21.1	67.0±25.1	0.629
Blood urea nitrogen (BUN, mg/dL)	29.4±9.8	30.9±10.8	0.687
Serum tacrolimus level (ng/mL)	7.3±1.3	7.9±2.1	0.551
Serum cyclosporine level (ng/mL)	142.2±41.5	195.6±70.5	0.254

The prevalence of non-adherence to immunotherapy in our sample was higher than in former studies. Massey et al. reported a prevalence of 65% in young adult kidney transplant recipients[18], whereas other studies reported prevalences of 5.9%[17] and 23.3% in older recipients. This is consistent with the literature describing age as one of the factors associated with non-adherence[9].

Table 4. Frequency of Responses to BAASIS Questionnaire Items.

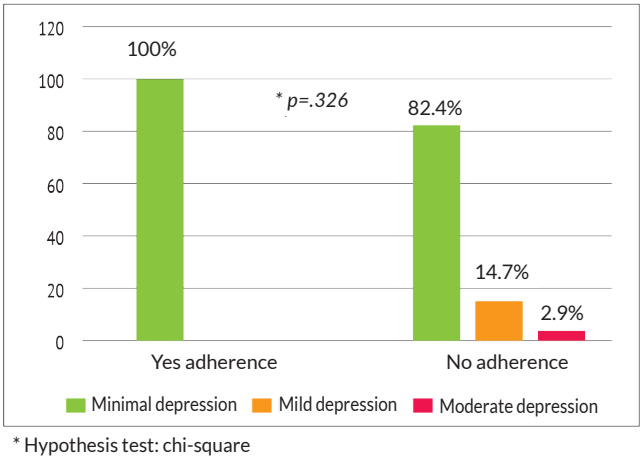
BAASIS Items	Adherence (n=11) mean±SD	Non-adherence (n=34) mean±SD	P Value
a. How often did you forget to take your immunosuppressive drugs?			0.003
Never	11 (100.0)	12 (35.3)	
Once a month	0 (0.0)	18 (52.9)	
Every 2 weeks	0 (0.0)	3 (8.8)	
Every week	0 (0.0)	1 (2.9)	
More than once a week	0 (0.0)	0 (0.0)	
Every day	0 (0.0)	0 (0.0)	
b. How often did you forget several consecutive doses of your immunosuppressive drugs?			
Never	11 (100.0)	26 (76.5)	0.207
Once a month	0 (0.0)	7 (20.6)	
Every 2 weeks	0 (0.0)	0 (0.0)	
Every week	0 (0.0)	1 (2.9)	
More than once a week	0 (0.0)	0 (0.0)	
Every day	0 (0.0)	0 (0.0)	
c. How often did you delay taking your immunosuppressive medications by at least 2 hours?			
Never	11 (100.0)	13 (38.2)	0.002
Once a month	0 (0.0)	14 (41.2)	
Every 2 weeks	0 (0.0)	0 (0.0)	
Every week	0 (0.0)	7 (20.6)	
More than once a week	0 (0.0)	0 (0.0)	
Every day	0 (0.0)	0 (0.0)	
d. Have you reduced the dose of your immunosuppressive drugs?			
• Never	11 (100.0)	34 (100.0)	Not calculated
• Once a month	0 (0.0)	0 (0.0)	
• Every 2 weeks	0 (0.0)	0 (0.0)	
• Every week	0 (0.0)	0 (0.0)	
• More than once a week	0 (0.0)	0 (0.0)	
• Every day	0 (0.0)	0 (0.0)	
e. How well have you managed taking your anti-rejection drus? (minimum: 0, maximum: 100)*	95.8±6.6	86.5±5.9	<0.001

* Data expressed as mean ± standard deviation.



* Hypothesis test: chi-square

Figure 1. Association between adherence to immunotherapy and the presence of anxiety.



* Hypothesis test: chi-square

Figure 2. Association between adherence to immunotherapy and the presence of depression.

Consequently, adolescents and young adults have the highest rate of graft rejection[20], consistent with our findings, as most non-adherent participants were admitted for graft dysfunction or rejection.

Regarding immunosuppressive therapy, monotherapy has been suggested as a strategy to improve adherence in clinical practice, given the complexity of current regimens[21]. In our study, no relationship between immunosuppressive treatment and adherence was observed. However, when BAASIS item responses were compared, most non-adherent adults reported forgetting doses and delaying intake by at least 2 hours. As a result, this group scored lower in the self-evaluation of performance, consistent with Lalic et al[19]. Notably, although non-adherence prevalence was high, self-perceived adherence was good, revealing a discrepancy already reported by other authors[18].

Although the prevalence of anxiety and depression in our study was low, these disorders have been described as possible side effects of immunosuppressants. Therefore, early detection and preventive measures are recommended to improve mental health in transplant recipients[22].

Other authors recommend assessing patients' beliefs regarding immunotherapy[23] and implementing cost-effective educational programmes[24]. For example, Kim et al. developed multimedia educational materials to increase patient interest and motivation, addressing limitations of existing programmes[25], while Predreira et al. developed a standardised care plan for clinical practice[26]. However, multidisciplinary work remains essential to achieve better outcomes[17].

A limitation of our study was its cross-sectional design, as adherence is a dynamic process and a behaviour that may change over time[4]. Furthermore, it is advisable to evaluate the various factors that may influence adherence in young adult recipients.

From our results, we observed that the prevalence of non-adherence to immunotherapy was higher than that reported in other contexts, underscoring the need for continuous interventions to improve adherence to immunosuppressive therapy. Special attention should be given not only to taking the medication but also to the timing of intake, as these were the areas with the greatest non-compliance in non-adherent adults. It is possible that these patients are unaware of the degree of precision required in immunotherapy to prevent rejection episodes.

Conflicts of interest

None declared.

Funding

None declared.

REFERENCES

1. Ali A, Al-Taee HA, Jasim MS. Adherence to Immunosuppressive Medication in Iraqi Kidney Transplant Recipients During the First Year of Transplant. A Single-Center Experience. Exp Clin Transplant. 2022;20(3):107-12.
2. Nevins TE, Nickerson PW, Dew MA. Understanding Medication Nonadherence after Kidney Transplant. J Am Soc Nephrol. 2017;28(8):2290-301.
3. Weng LC, Yang YC, Huang HL, Chiang YJ, Tsai YH. Factors that determine self-reported immunosuppressant adherence in kidney transplant recipients: a correlational study. J Adv Nurs. 2017;73(1):228-39.
4. Villeneuve C, Rousseau A, Rerolle JP, Couzi L, Kamar N, Essig M, et al. Adherence profiles in kidney transplant patients: Causes and consequences. Patient Educ Couns. 2020;103(1):189-98.
5. Doalto-Muñoz Y, Valle RC, Manrique MLC. Factores asociados a la resiliencia y adherencia terapéutica en pacientes con injerto renal funcionante. Enferm Nefrol. 2018;21(2):123-9.
6. Argüeso-Gómez L, Rodrigo-Calabia E, Pelayo-Alonso R, de Cos-Cossío MÁ. Adherencia al tratamiento en pacientes con trasplante renal y su relación con los niveles plasmáticos de inmunosupresores. Enferm Nefrol. 2023;26(4):344-50.
7. Belaiche S, Décaudin B, Dharancy S, Noel C, Odou P, Hazzan M. Factors relevant to medication non-adherence in kidney transplant: a systematic review. Int J Clin Pharm. 2017;39(3):582-93.
8. Guillén Díaz-Barriga C, González-Celis Rangel AL. Propiedades psicométricas del Inventario de Ansiedad de Beck en adultos asmáticos mexicanos. Psicología y Salud. 2018;29(1):5-16.
9. Brito DCS de, Machado EL, Reis IA, Cherchiglia LP de F do CML. Depression and anxiety among patients undergoing dialysis and kidney transplantation: A cross-sectional study. Sao Paulo Med J. 2019;137(2):137-47.
10. Sevinc M, Hasbal NB, Sakaci T, Basturk T, Ahbap E, Ortaboz M, et al. Frequency of depressive symptoms in Syrian refugees and Turkish maintenance hemodialysis patients during COVID-19 pandemic. PLoS One. 2021;16(1):0244347.
11. Baloch MH AA. Prevalence of anxiety and depression in chronic kidney disease patients according to CKD stages. Isra Med J. 2017;9(5):280–3.
12. Low JK, Manias E, Crawford K, Walker R, Mulley WR, Toussaint ND, et al. Improving medication adherence in adult kidney transplantation (IMAKT): A pilot randomised controlled trial. Sci Rep. 2019;9:7734.

13. Krause AV, Bertram A, Nöhre M, Bauer-Hohmann M, Schiffer M, De Zwaan M. Use of an electronic medication monitoring device to estimate medication adherence in kidney transplant patients. Transl Behav Med. 2021;11(3):842–51.

14. Secretaría de Gobernación de México. Reglamento de la Ley General de Salud en materia de investigación para la salud. Publicado en Diario Oficial de la Federación en 2014.

15. Martínez-Mier G, Ávila-Pardo SF, Irigoyen-Castillo A, Rodríguez-Fernández A, Jiménez-López LA, Varela-Pérez V. Análisis de la supervivencia a 10 años de trasplante renal en el Hospital de Alta Especialidad de Veracruz. Rev Mex Traspl. 2016;5(3):113–9.

16. Ayala-García MA, Díaz-Chávez E, Soel-Encalada JM, Orozco-Mosqueda A, Balandrán-Ortiz MH, Ceja-Guzmán SR, et al. Supervivencia de los pacientes receptores de trasplante renal. Gac Med Mex. 2020;156(1):34–9.

17. Taj SM, Baghaffar H, Alnajjar DK, Almashabi NK, Ismail S. Prevalence of non-adherence to immunosuppressive medications in kidney transplant recipients: Barriers and predictors. Ann Transplant. 2021;26:928356.

18. Massey EK, Meys K, Kerner R, Weimar W, Roodnat J, Cransberg K. Young adult kidney transplant recipients: Nonadherent and happy. Transplantation. 2015;99(8):89-96.

19. Lalič J, Velickovič-Radovanovič R, Mitič B, Paunovič G, Cvetkovič T. Immunosuppressive medication adherence in kidney transplant patients. Med Princ Pract. 2014;23(4):351-6.

20. Matsuda-Abedini M, Marks SD, Foster BJ. Transition of young adult kidney transplant recipients. Pediatr Nephrol. 2023;38(2):383-90.

21. Van Zanten R, de Weerd A, Betjes M, Boer-Verschragen M, Massey EK. Is simplification of immunosuppressive medication a way to promote medication adherence of kidney transplant recipients? Findings from a randomized controlled trial. Transpl Int. 2021;34(9):1703-11.

22. Uyar B. The analysis of immunosuppressant therapy adherence, depression, anxiety, and stress in kidney transplant recipients in the post-transplantation period. Transpl Immunol. 202;75:101686.

23. Rebafka A. Medication adherence after renal transplantation—a review of the literature. J Ren Care. 2016;42(4):239-56.

24. Varnell CD, Rich KL, Modi AC, Hooper DK, Eckman MH. A cost-effectiveness analysis of adherence promotion strategies to improve rejection rates in adolescent kidney transplant recipients. Am J Kidney Dis. 2022;80(3):330-40.

25. Kim S, Ju MK, Son S, Jun S, Lee SY, Han CS. Development of video-based educational materials for kidney-transplant patients. PLoS One. 2020;15(8):0236750.

26. Pedreira-Robles G, Garcimartín P, Bach-Pascual A, Giró-Formatger D, Redondo-Pachón D, Morín-Fraile V. Creating the nursing care map in the evaluation of kidney transplant candidates: A scoping review and narrative synthesis. Nursing Open 2023;10:6668–89.