Analysis of treatment preferences, immunosuppressant adherence and mental health disorders in kidney transplant recipients

This study quantifies the prevalence of mental health disorders, immunosuppressive treatment adherence and identifies the treatment preferences (medical and psychological) of kidney transplant recipients

■ depression ■ mental health ■ kidney transplantation ■ shared decision making ■ treatment preferences

Kidney transplant is the best renal replacement therapy (RRT) for end-stage kidney disease (ESKD) (Otero et al, 2010). Some of its advantages can include: a more physiologically healthy state, improvement in functional status (measured with physical and psychological scales), gain in self-reliance (once the patient leaves dialysis), improvement in quality of life, and decreased mortality when compared with the dialysis population (Hellemans et al, 2020). These advantages have contributed to a lower prevalence of mental health disorders in kidney transplant patients compared to dialysis patients (Fructuoso et al, 2011; Kalantar-Zaadeh et al, 2021).

However, once patients receive a kidney transplant, not all aspects are advantageous. Physical changes (weight gain, scars, acne), lifestyle modifications, possible incidence of new diseases (tumours, infections, cardiovascular risk), or adverse events related to pharmacological/immunosuppressive treatments (tremors, oedema, gingival hyperplasia, obesity), that are common after kidney transplantation, may lead to an increased risk of mental health disturbances and disturbances in quality of life (Girlanda, 2013; De Pasquale et al, 2014). Psychopathological disturbances have been well recognised to impact graft and patient outcomes and survival (Pasquale et al, 2020). This connection between mental health disorders and outcomes highlights that optimal medical treatment alone is not enough to ensure optimal results for kidney transplant patients.

It is also known that incorporating patients' treatment preferences into clinical practice improves healthcare results (Rodríguez Rey et al, 2020); however, little is known about the treatment preferences (medical and psychological) and needs of the kidney transplant recipients.

The objectives of the study were to quantify the prevalence of mental health disorders and their impact on immunosuppressive adherence, to identify patients' treatment preferences and needs for medical and psychological intervention programmes, and to study quality of life related to health and life satisfaction in a Spanish kidney transplant cohort.

Methods

This was a cross-sectional observational study, including 116 patients. The patients were recruited from the Kidney Transplant Section of Hospital Universitario la Paz in Madrid from May to June 2019. The study methodology was approved by the

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Hospital Universitario La Paz Clinical Investigation Ethics Committee and written informed consent was obtained from all participants prior to the study initiation (code: P-170). Patients started the process only after signing a written informed consent form. All procedures were performed in compliance with relevant laws and institutional guidelines with institutional committee approval.

Procedure

The Kidney Transplant Section of Hospital Universitario La Paz attends to 600 prevalent patients. During May to June 2019, patients were informed about the study development while they were in the waiting room. Following that, the responsible nurse asked if they would like to hear more information during the medical consultation. At the end of the medical consultation, those who answered 'yes' were given the option to participate in the study after having the content and aims of the study explained to them by the attending doctor. Those who met the inclusion criteria and gave their authorisation began the study by signing a written informed consent form. After signing the written informed consent form, patients were directed to go with a trained nephrologist to another office. The nephrologist explained the contents of the survey to the patient, and the patient then completed the written survey alone in the office with the nephrologist on hand nearby. Patients concluded their participation once they finished the written survey and the collected data that was stored in a database for future analysis. The authors did not have access to information that could identify individual participants during or after data collection.

The inclusion criteria were as follows: over 18 years old, kidney transplant survival of over 1 year, no recent diagnosis of severe mental health disorder (<3 months), educational level sufficient to understand and respond to the evaluation protocol, and no severe auditory/visual impairment.

The exclusion criteria were as follows:

- Illiteracy
- Age below 18 years old
- Severe visual/auditory impairment
- Recent diagnosis of a mental health disorder.

Out of all the patients who attended the consultation during that period, 116 patients who agreed to participate and met the inclusion criteria were included in the study after signing the informed consent form. Data collection was conducted by a trained nephrologist. The clinical and research activities reported in this study adhere to the principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

Instruments and variables studied

Clinical profile and demographic survey

This survey collects patient´s data about:

- Age
- Gender
- Marital status
- Education
- Work status
- Kidney donor (cadaveric, living-donor) graft survival
- Previous dialysis modality (haemodialysis, home-dialysis, both, etc.)
- Time in dialysis
- ESKD etiology
- Charlson Index Comorbidity
- Mental health status prior current transplant
- Mental health status
- Psychiatric drugs prescription history
- Glomerular filtration rate (eGFR) measured by CKD-EPI equation.

Morisky-Green-Levine Test (Morisky et al, 1986)

The Spanish version validated by Val-Jimenez was used (Val-Jiménez et al, 1992). It evaluates immunosuppressive therapy adhesion. It contains four dichotomic YES/NO questions where appropriate, adherence is concluded if all four questions are answered with NO. The instrument has proved effective in adherence validation for chronic pathologies as hypertension and diabetes (α=.87) (Ross et al, 2002).

Depression, anxiety and stress scale (DASS-21) (Lovibond and Lovibond, 1995)

The Spanish version from Antúnez and Vinet was used (Antúnez and Vinet, 2012). DASS-21 test is composed of three subscales that measure anxiety, stress and depression prevalence and their severity. Each item has 7 questions with a range of 0 to 21. The test has robust psychometric properties in outpatient and inpatient population, and it excludes physical symptoms. Each subscale classifies the severity of the disorder by mild, moderate, severe and very severe. The instrument has a reliability of 88% in depression, 79% anxiety and 83% in stress. Global reliability of the test is 90% (α =.90) (Lovibond and Lovibond, 1995).

Satisfaction with life scale (SWLS) (Diener et al, 2020)

The Spanish version of Atienza was used (Atienza et

al, 2000). This instrument measures life satisfaction and self-perception of welfare (Cárdenas et al, 2012). The test is composed of five items and only one dimension. The answer format is a Likert scale of 7 points, starting with 1 (not agree) to 7 (totally agree). Higher scores correspond to higher levels of vital satisfaction. It has robust psychometric properties for the older and young population (Pons et al, 2000). The global reliability is 90% (α=.90).

Connor-Davidson Resilience scale (CDRISC-2) (Vaishnavi et al, 2007)

The Spanish version from Menezes de Lucena was used (Menezes de Lucena et al, 2002). It was developed originally for Connor and Davidson in 2003. The scale is composed of two items and one dimension, with a range from 0 to 8. The answer format is a Likert scale of 5 answers that go from 0 (not agree) to 4 (totally agree). Higher scores indicate higher levels of resilience.

Quality of life related with health survey (MOS-SF-36 Health Survey)

The Spanish version was applied (Alonso et al, 1995). It evaluates eight dimensions of health and mental state: physical functionality (α=0.74), physical role (α=0.73), corporeal pain (α=0.93), general health (α=0.77), vitality (α=0.83), social development (α=0.79), emotional role (α=0.74) and mental health (α=0.77). This test has two added components, the physical health component and the mental health component. Higher scores are related to higher quality of life relating to health. Scores are standardised and range from 0 to 100.

Survey of treatment, needs and preferences

The ad hoc survey of treatment needs and preferences was developed based on research on psychological and medical treatment for patients with kidney transplants. The survey collects information about treatment-related concerns, needs and preferences for psychological and medical interventions.

Statistical analysis

For the statistical analysis, the SPSS 25.0 programme was used. The student's t-test was employed to compare parametric quantitative variables between two groups, while the Mann-Whitney U test was used as a non-parametric test. A Chi-squared test was used to compare qualitative variables. Spearman and Pearson correlation coefficients were employed to explore the correlation between variables. All analyses were conducted with a 95% confidence interval. No causative analysis was performed to avoid confounding, due to the characteristics of the study design (cross-sectional). All missing data was labelled, quantified and analysed.

Results

A total of 116 patients were included in the study, with 43% being women and a mean age of 53 years. A total of 26% had previous kidney transplants, and from those with previous kidney transplant, 15.5% of them were from living donors. The baseline demographic characteristics, mental health history, previous kidney transplants, and renal replacement techniques are shown in *Table 1*.

The prevalence of mental health disorders showed rates of 26.2% for depression, 27.2% for anxiety and 23.3% for stress. A total of 28.5% of patients reported being very satisfied with life. 'Non-adherence' to immunosuppressive therapy was found in 15.5% of patients, with no demographic or clinical differences between 'adherent' and 'non-adherent' patients (p=0.63).

Patients labeled as 'non-adherent' to immunosuppressives had significantly lower scores in the mental health components of the MOS-SF-36 survey.

A correlation analysis was performed between mental health disorders and the quality of life survey related to health. Depression was found to have a direct correlation with stress (p<0.001) and an inverse correlation with resilience (p=0.018), as well as with the physical summary of the quality of life survey related to health (p<0.001). Anxiety showed a direct correlation with stress (p<0.001) and an inverse correlation with vital satisfaction (p<0.001), physical summary (p<0.001), and mental health summary (p<0.001) of the quality of life survey (MOS-SF-36).

Glomerular filtration rate, measured by the CKD-EPI equation, was positively associated with the physical health subscale on the MOS-SF-36 survey (p=0.042). Gender did not show significant differences in the physical component (p=0.137), however, the male population had significantly lower scores in the mental health component of the MOS-SF-36 survey (p=0.007).

Employment status and education status were not significantly associated with differences in the mental and physical components on the MOS-SF-36 survey (p=0.50). Individuals with mental health pathology before kidney transplant were significantly related to lower scores in the physical (p=0.023) and mental health components (p<0.001).

Regarding patient treatment preferences and needs, the ad hoc survey of treatment

Table 1. Baseline characteristics of studied population (N=116)

Studied variables (N=116)	Results
Female gender (%)	43
Age (years±standard deviation)	53.2 ± 14.2
Married/partnership marital status (%)	67
University education (%)	46
Active laboral status (%)	41
Glomerular chronic kidney disease etiology (%)	33
Charlson Index (score±standard deviation)	3.9 ± 2.0
Graft survival (months±standard deviation)	11.7 ± 96.4
CKD-EPI (ml/min±standard deviation)	50.0 ± 20.1
Patients with previous kidney transplants (%)	26
Patients with living donor graft (%)	16
Previous renal replacement therapy:	
Hemodialysis (%)	37
Peritoneal dialysis (%)	34
Hemodialysis and peritoneal dialysis before (%)	22
Anticipated kidney transplant (%)	8
Mental health past history:	
Previous mental health pathology (anxiety/depression) (%)	24
Treatment with psychotropics (%)	21

needs and preferences showed that 46.6% of patients would like to know how to improve their physical condition, and 36.6% would like to receive information about strategies to cope with depression and anxiety. A total of 94.9% of patients indicated that psychology/counselling services should be provided by the nephrology department. Individual/group face-to-face therapies conducted by a psychologist with expertise in renal disease population were the main preference for psychological intervention chosen by 72.4% of surveyed patients. *Table 4* summarises the results of the ad hoc survey of treatment preferences and needs.

Discussion

This study sheds light on the prevalence of mental health disorders, non-adherence to immunosuppressive drugs, health-related quality of life, and patient preferences and needs for psychological interventions in a cohort of kidney transplant patients in Madrid, Spain.

The study's finding of a 15.5% prevalence of poor adherence to immunosuppressive drugs should not be overlooked. Transplant clinicians should be encouraged to identify patients with non-adherence profiles, such as young age and/or a history of mental health disorders and impaired quality of life (Villeneuve et al, 2020) before kidney transplant, to intervene early and prevent graft rejection or failure. The study also found a significant link between mental health disorders and non-adherence, with patients previously labelled as 'non-adherent' to immunosuppressive drugs showing significantly lower scores in the mental component of their health.

The prevalence of mental health disorders observed in this study is consistent with other studies (Chilcot, et al 2014), although lower than that observed in the dialysis population (Santacruz et al, 2021). However, a Japanese study reported higher depression rates among 109 kidney transplant patients (Suzuki et al, 2019), although it is important to emphasise that the Japanese study analysed patients from one month after kidney transplant surgery. This differs from the study that included patients from one year after kidney transplant surgery. Also, it is important to note that the pre-COVID-19 depression rate in the Spanish population was 5.4% (2.1 million individuals) (National Statistic Center from Spain, 2023). The impact of COVID-19 on people's lives may have increased the prevalence of mental health disorders in this population.

A significant association was found between a history of mental health disorders before kidney transplant and impaired health-related quality of life, consistent with other series (Kim et al, 2015). However, in contrast to other studies (Jordakieva et al, 2020) employment status was not significantly associated with health-related quality of life. It is worth noting that glomerular filtration rate, an important parameter for clinicians, was only significantly associated with results in the physical component of the SF-36 questionnaire. This suggests that better kidney function may not be directly related to mental health in kidney transplant patients, but rather it could serve as an indicator of better physical condition (Hsiao et al, 2016; Guligowska et al, 2020).

Kidney transplants can bring about physical changes, lifestyle modifications, new diseases, and adverse drug events. This can in turn evoke feelings of sadness, fear, anger and more. These emotional experiences are associated with emotional

Table 2. Baseline characteristics of studied population (N=116)		
Studied variables	**Answer format**	**Population studied N=116**
Immunosuppressive adherence (Morisky-Green-Levine Test)	Yes/No	Yes (%)
1. Do you forget sometimes to take your immunosuppressive pills?		6.9
2. Are you careless with your immunosuppressive pills?		10.3
3. If you feel well, do you stop taking your immunosuppressive pills?		0
4. If you feel unwell, do you stop taking your immunosuppressive pills?		1.7
Non-adherence score (considered with only one positive answer)		15.5
Mental health disorders (Depression, anxiety and stress scale-21 scale)	Reference score	Patients percentage (%)
Depression		
	0 to 4 normal	74.1
	5 to 6 mild	9.5
	7 to 10 moderate	9.4
	11 to 13 severe	2.5
	>14 extremely severe	4.5
Anxiety		
	0 to 3 normal	69.8
	4 to 5 mild	9.5
	6 to 7 moderate	9.5
	8 to 9 severe	6.0
	>10 extremely severe	5.2
Stress		
	0 to 3 normal	76.7
	4 to 5 mild	8.6
	6 to 7 moderate	4.4
	8 to 9 severe	6.0
	>10 extremely severe	4.3
Resilience level (Connor-Davidson Resilience scale-2 score)	Interval	Score (mean ± SD)
	0 to 8	6.60 ±1.31
Satisfaction with life (SWLS) scale	Reference score	Patients percentage (%)
	5 to 9 very unsatisfied	0.9
	10 to 14 unsatisfied	6.0
	15 to 19 below the median	15.6

	20 to 24 sligthly satisfied	20.7
	25 to 29 satisfied	28.4
	30 to 35 very satisfied	28.4

distress, depression, stress and anxiety, leading to impairment in quality of life (Jordakieva et al, 2020). Given the knowledge, prioritising efforts to screen, diagnose, and treat mental health disorders should be a priority if we aim to improve health outcomes in kidney transplant patients.

Most research and innovation efforts in psychology focus on the psychopathological domain. However, the study revealed high levels of resilience among the participants. Resilience is a powerful tool for overcoming difficult situations. The high resilience observed in this population may explain why almost one-third of the tested patients reported being very satisfied with life. This high resilience level could be explained by the fact that the patients studied had a minimum of 1 year of graft survival, a period of time where rejection and consultations are less frequent, adverse events are less prevalent and immunosuppressives dose are more stable when compared with the first 6 to 10 months after transplant surgery (Opelz and Döhler, 2008). This data is noteworthy as it suggests a new avenue for investigation into psychometric tools to assess resilience levels and life satisfaction and resilience evolution throughout graft´s survival.

Regarding patient treatment preferences and needs, this study found that over three-quarters of the studied population chose face-to-face individual or group therapies guided by psychologists familiar with renal patients as their preferred treatment for psychological interventions. Psychological support with someone who understands the renal disease pathway as opposed to someone who does not know what is involved is calming and reassuring for the patient and relatives (Murgatroyd, 1983). Additionally, 95% of patients believed that psychological services should be provided by the nephrology department. Counselling is one tool that can fulfill these patient requirements at present.

Counselling is a therapy tool that allows patients to express what is on their mind without feeling judged. It focuses on the patient's active participation and decisions regarding their treatment and healthcare (Murgatroyd, 1983). This tool is widely used in shared decision-making for patients with stage 5 CKD before initiating dialysis (Murgatroyd, 1983 ; García-Llana et al, 2017). Counselling requires active, face-to-face individual or group participation with a well-trained psychological practitioner (as this encompasses psychologists, counsellors, psychotherapists and psychiatrists (Kidney Care UK, 2023), which are also characteristics demanded by kidney transplant patients. This tool seems to be an important avenue to explore in order to improve healthcare outcomes and meet patient demands.

Nowadays, more research is being conducted in this field, and every day more authors are encouraged to incorporate patient perspectives in clinical practice and research (Mayer, 2012). A Cochrane investigation reminds the scientific community to include the patient as a 'treatment expert' in clinical practice, as it improves health outcomes in chronic diseases (Foster et al, 2007). There is more evidence in the country regarding the need to change the model of the local healthcare system to one that involves patients in their care, focusing on a model that promotes self-care (Nuño-Solinis et al, 2013).

While medical treatment is crucial for kidney transplant patients, it might not be enough to achieve patient wellbeing due to the impact of other factors. For this reason, an interdisciplinary biopsychosocial intervention appears necessary to ensure better health outcomes and improve patient wellbeing. Similar approaches have been used in other chronic diseases, and it would be interesting to apply them in the clinical practice of kidney transplant patients (Chodosh et al, 2005; Quiceno et al, 2011).

Table 3. Subscales of quality-of-life health-related on questionnaire MOS-SF-36 on studied population N=116.

Subscales of quality-of-life	Score (mean±SD)
Physical function	83.4±20.3
Corporal health	61.8±29.8
General health	67.9±13.3
Vitality	55.80±12.7
Social function	89.5±25.4
Emotional role	72.3±39.3
Mental health	78.9±16.1
Physical summary component	79.6±15.9
Mental summary component	77.7±16.2

Table 4. Results of structured survey about psychological treatment preferences and needs of studied population. N=116	
Psychological treatment preferences and needs explored in structures survey in studied population. N=116	**Number (%)**
How can I make decisions about my disease and treatments so I can maintain control of the situation?	42 (36.2)
How to face the impact of the disease and treatments	41 (35.3)
How to communicate properly ideas, feelings and worries about the disease to healthcare professionals (doctors, nurses, psychologist)?	42 (36.2)
How can I better adapt to treatments and lifestyle modifications (immunosuppressive pills, diet, etc)?	45 (38.8)
How can I better adapt to corporal image modifications due to medical treatments?	45 (38.8)
How to face modification in personal and social relations after kidney transplant?	30 (25.9)
How to improve physical condition	54 (46.6)
How to manage anxiety and depression	39 (33.6)
How to manage changes in sexual life after kidney transplant	23 (19.8)
How to prevent caregiver burnout	20 (17.2)
How to ask and improve psychological services	36 (31.0)
How to access testimonials from other kidney transplant patients?	40 (35.5)
Do you think that it is important that psychological assessment should be provided directly from nephrology service?	
Positive answers	110 (94.9)
Psychological treatment preferences	
Face-to-face individual/group therapies by a psychologist with expertise in renal patients	84 (72.4)
Self-help guides/educative materials	32 (27.6)
Medication, pills	26 (22.4)
Teleconsultation	26 (22.4)
If you must distribute 100 points, how would you distribute them between the following options:	Score (Mean±standard deviation)
Family: couple, child care, closest relatives	56.2±19,5
Social: friends, leisure time etc	18±10,6
Personal development: job status, spiritual beliefs, personal development, etc	25.7±16,3

Limitations and strengths

The limitations of the study were: participation of patients from only one Spanish center as this makes it impossible to extrapolate the findings to other Spanish patients from other centres and cities. Additionally, the study used correlational statistical tests, making it impossible to establish causal relationships. Furthermore, the study had a cross-sectional nature. Also, using as inclusion criteria —'no recent diagnosis of severe mental health disorder (< 3 months)' and 'graft survival over one year' turned out that the study did not explore outcomes in that specific population. The outcomes of patients with graft survival below 1 year and with recent mental health disorder diagnosis were not studied and could impact, if explored, the findings of this study. Finally, more standardised tests could be applied to explore patients' treatment preferences and needs. All these limitations were addressed to identify and avoid sources of bias.

The strengths of the study include a homogeneous sample, careful data collection, a large number of patients studied, a broad range of mental health disorders and other psychological themes investigated, and the use of standardised tools in the majority of areas assessed.

The findings of the study emphasise the importance of registering and evaluating 'patient-

Key points

- The article highlights the connection between mental health disorders and non-adherence to immunosuppressive drugs in the kidney transplant population and this is associated with the worst graft survival and outcomes
- Prevalence of mental health disorders was high in the post-transplantation period in the studied population
- These findings highlight the need for the early screening and treatment of mental health disorders with a biopsychosocial, interdisciplinary approach focused on patients' treatment preferences and needs, both individually and in groups, within the nephrology service
- Treatment preferences and needs of kidney transplant patients studied identified information on how to improve physical condition, information about strategies to cope with depression and anxiety, psychology/counselling interventions provided by the nephrology department with individual/group face-to-face therapies conducted by a psychologist with expertise in renal disease population.

CPD reflective questions

- Does a kidney transplant improve the mental health disorders that are found in the dialysis population?
- Should we focus only on medical treatment for someone who has had a kidney transplant?
- Do mental health disorders have a connection with immunosuppressive adherence, graft survival and outcomes?
- What are the treatment preferences and needs for the psychological interventions of kidney transplant patients?
- How and who should provide psychological support to kidney transplant patients?

reported outcome measures' (PROMs) as suggested by the 'International Consortium for CKD Health Outcomes Measures' (ICHOM) (Verberne et al, 2019). Having a psychological practitioner actively involved as a member of the kidney transplant team is crucial (as also advocated by authors of solid organ transplantation programmes) to ensure an interdisciplinary approach to kidney transplant patients (García-Llana et al, 2010; Lyon and Lewandowsky, 2015).

In conclusion, the study highlights the prevalence of mental health disorders and their relationship with immunosuppressive adherence in Spanish kidney transplant patients. It also emphasises patients' desires to be assisted by specialised professionals who are fully committed and integrated into the transplantation team. The study underscores the importance of psychological resources available (such as resilience and life satisfaction) and the need to further enhance them in future interventions with patients and their families in clinical practice. This calls for a biopsychosocial, interdisciplinary approach focused on patients' treatment preferences and needs, both individually and in groups within the nephrology service. JKC

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