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ORIGINAL STUDY

Electrolytes Disorders in Postkidney Transplanted Recipients

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Abstract

Objectives: **To delineate the demographic profile of the study cohort, assess preoperative clinical and laboratory parameters, and investigate postoperative electrolyte abnormalities at different time points.**

Background: **Kidney transplantation is a vital intervention for end-stage renal disease, with postoperative electrolyte abnormalities posing a significant clinical challenge.**

Patients and methods: **Eligible participants from the Nasser Institute, meeting inclusion criteria, underwent a thorough assessment of demographics, medical history, and clinical examinations. Laboratory investigations included blood tests and immunological assays. Statistical analysis employed descriptive statistics and correlation analyses.**

Results: **The study included 41 recipients, with a mean age of 29.63 years (SD ± 12.40). Within the first month post-operation, 31.7% exhibited hyponatremia, 4.9% had hyperkalemia, 36.6% developed hypomagnesemia, and 46.3% had hypophosphatemia. All cases had hypocalcemia, and metabolic acidosis (pH < 7.35) predominated in 68.3%. At more than a month post-operation, 29.3% had hyponatremia, 24.4% had hyperkalemia, and 19.5% had hypercalcemia. Significant variations in Hb, serum albumin, Na, K, Ca, Mg, PO_4, pH, HCO_3, and white blood cells were observed over time.**

Conclusion: **This study provides a comprehensive overview of postkidney transplant recipients, highlighting the prevalence of electrolyte abnormalities and their temporal evolution. The findings underscore the need for vigilant monitoring and management of electrolyte imbalances in this population, with implications for postoperative care strategies.**

Keywords: Electrolyte abnormalities, Immunocompromised, Kidney transplantation, Tacrolimus levels, Transplant recipients

1. Introduction

Kidney transplantation has emerged as the preferred therapeutic intervention for individuals with end-stage renal diseases (ESRDs), representing a life-saving surgical approach surpassing dialysis, and is applicable across diverse age cohorts [1]. Moreover, kidney transplantation demonstrates cost-effectiveness and yields a superior quality of life when compared with dialysis. However, its widespread adoption faces substantial challenges in developing nations, characterized by low rates of live organ donation, prohibitively high costs, and difficulties associated with immunosuppression. Presently, kidney transplants only address 10% of the global demand for ESRD treatment [2]. ESRD are often accompanied by recurrent metabolic and electrolyte abnormalities that exhibit marked improvement post-kidney transplantation. Nevertheless, the transplantation procedure itself can at times introduce complications, particularly in terms of electrolyte imbalances. Unfortunately, existing research tends to predominantly focus on immunosuppression [3]. A diminished serum sodium (Na^+)

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level, or hyponatremia, is recognized as a primary contributor to heightened morbidities and mortalities, affecting functions of the brain, heart, insulin regulation, and muscles. Hyponatremia arises from an imbalance of salt and water, leading to hypovolemia and salt loss. Common causes of hyponatremia in kidney transplant recipients include hypotonic hyponatremia related to water and salt depletion, water retention, prolonged hypokalemia, sodium loss, and hyponatremia induced by drugs such as cyclophosphamide [4]. The normal plasma potassium (K^{+}) level is contingent on factors like potassium intake, intracellular-extracellular potassium distribution, and renal potassium excretion. The equilibrium between intracellular and extracellular spaces is governed by the NaK-ATPase pump. Postkidney transplant, hypokalemia may stem from water and salt depletion, primary hyperaldosteronism, diuretic and steroid usage. Clinically, hypokalemia is deemed an emergency condition due to its potential to induce various comorbidities and mortality outcomes [5]. Serum magnesium (Mg^{+2}) is an essential element in normal physiological processes. Post-transplant hypomagnesemia may result from gastrointestinal and urinary depletion, exacerbated by factors such as diarrhea and medications including proton pump inhibitors, thiazide diuretics, and calcineurin inhibitors. Clinical manifestations of hypomagnesemia include confusion, fatigue, and neuromuscular irritability, although it is often asymptomatic [6]. In accordance with our study, the literature suggests that, hypercalcemia post kidney transplantation is not uncommon, with a prevalence of 22.2% [6]. Hypomagnesemia can contribute to abnormal glucose metabolism, endothelial dysfunction, and cardiovascular disorders. Conversely, hypermagnesemia is primarily attributed to poor renal excretion (renal failure, medications, and endocrine diseases) or increased intake (elderly age and medications). Severe hypermagnesemia can lead to cardiovascular, neurological, and metabolic abnormalities [7]. The prevention and management of electrolyte disturbances following kidney transplantation necessitate pre and postoperative laboratory monitoring, along with judicious administration of intravenous fluids tailored to the specific electrolyte deficiency, each requiring specific treatment protocols [4]. The cornerstone in the management of electrolyte disorders lies in addressing the underlying cause, such as discontinuation of causative drugs, and restoring the normal fluid and electrolyte balance of the human body [8].

In this study, we aimed to evaluate the prevalence and characteristics of electrolyte disturbances in patients who underwent renal transplantation.

2. Patients and methods

A cross-sectional investigation was conducted, focusing on individuals who had undergone kidney transplantation. The study population consisted of eligible patients from the Nasser Institute who met the specified inclusion criteria. These criteria included adults over 18 years of age, of any gender, who had undergone either primitive or post-hemodialysis kidney transplantation, ensuring the success of the renal transplantation process. Exclusion criteria for the study involved individuals with chronic liver disease, secondary renal disease of the transplanted kidney, chronic inflammatory bowel diseases leading to diarrhea, critically ill patients, and those with primary parathyroid gland diseases.

Upon obtaining written informed consent from the participants, the study involved a comprehensive approach to gathering relevant information. A thorough history was taken, encompassing demographics such as age, gender, residence, occupation, weight, height, BMI, and any special habits of medical importance. The past medical history included details about chronic illnesses, drug intake, prior operations, and positive hepatitis virology. The history of the present illness delved into the underlying cause of chronic kidney disease (CKD), duration and frequency of dialysis, timing of transplantation, type of donor, type of graft, associated morbidities or complications of renal transplantation, and details about immunosuppressive therapy.

Clinical examination was an integral part of the study, focusing on assessing vital signs, lower limb edema, signs of organ failure, and conducting examinations of the cardiac, chest, and abdominal regions. Laboratory tests were performed, covering a complete blood picture, kidney function tests (urea, creatinine), electrolytes (sodium, potassium, calcium, phosphorus, magnesium), and blood gases. In terms of ethical considerations, the thesis protocol and written informed consent were submitted for approval to the local ethical committee of Menoufia University before the recruitment of patients. All files were securely stored in a locked cabinet, accessible only to senior supervisors and the data collector. Additionally, all identification data were erased before the statistical analysis of the collected information.

2.1. Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2021. Quantitative

data tested for normality using Shapiro–Wilk test, then described as mean ± SD (standard deviation) as well as minimum and maximum of the range, and compared using ANOVA test. Qualitative data described as number and percentage and compared using χ^2 test and Fisher's exact test for variables with small expected numbers. Bonferoni test used for post hoc comparisons. The level of significance was taken at P value less than 0.050 was significant, otherwise was nonsignificant.

3. Results

The study included 41 post-kidney transplanted recipients with a mean age of 29.63 years (SD ± 12.40) and a range of 19–66 years. Among them, 61.0% were male, and 39.0% were female. The majority were single (63.4%), and the mean weight, height, and BMI were 66.17 kg (SD ± 16.51), 1.65 m (SD ± 0.14), and 24.03 kg/m^2 (SD ± 4.92), respectively. The vast majority were nonsmokers (90.2%) (Table 1).

The primary etiology of chronic kidney disease (CKD) was diverse, with Focal Segmental Glomerulonephritis being the most common (17.1%). The mean duration of dialysis was 15.61 months (SD ± 14.25), and 51.2% had residual urine. Comorbidities included hypertension (73.2%) and various combinations such as hypertension with epilepsy, SLE, and ADPKD. The majority had blood group A$^+$ (36.6%), and most recipients were HCV-negative (95.1%). Pre-operative laboratory investigations revealed mean values for BUN, serum creatinine, uric acid, total calcium, phosphorus, total protein, ALT, AST, serum albumin, total bilirubin, Hb, white blood cells (WBCs), platelets, HbA1c, and parathyroid hormone. All recipients showed negative complement C3 and C4 levels. ANA was negative in 87.8%, and anti-cardiolipin IgG and IgM were mostly negative (97.6% and 95.1%, respectively). Lupus anticoagulant was positive in 46.3% of cases. ECHO results demonstrated a mean ejection fraction of 64.68% (SD ± 5.82). Cysto-urethrogram indicated 95.1% with normal findings (Table 2).

The mean total ischemia time was 35.20 min (SD ± 8.32). Most recipients did not require intraoperative blood transfusion (82.9%), and immediate diuresis was observed in 90.2%. Induction types included Quadri therapy with ATG (68.3%), Simulect (7.3%), and triple therapy (24.4%). Tacrolimus was the predominant immunosuppressive agent (95.1%). Postoperatively, within the first month, recipients exhibited mean values for Hb, WBCs, platelets, albumin, BUN, serum creatinine, sodium, potassium, total calcium, magnesium, phosphorus, pH, HCO_3, and blood tacrolimus. These comprehensive results provide insight into the demographic, clinical, and laboratory characteristics of post-kidney transplanted

Table 1. Demographic characteristics of post kidney transplanted recipients.

Demographic characteristics	Post kidney transplanted recipients (n = 41)
Age (years)	
Mean ± SD	29.63 ± 12.40
Range	19–66
Sex: [No (%)]	
Male	25 (61.0)
Female	16 (39.0)
Marital status: [No (%)]	
Married	15 (36.6)
Single	26 (63.4)
Weight (kg)	
Mean ± SD	66.17 ± 16.51
Range	24–100
Height (m):	
Mean ± SD	1.65 ± 0.14
Range	1.20–1.85
BMI (kg/m^2)	
Mean ± SD	24.03 ± 4.92
Range	14.80–39.50
Smoking: [No (%)]	
Nonsmokers	37 (90.2)
x-smokers	4 (9.8)

Table 2. Frequency distribution of acid-base balance and electrolyte disorders at more than six months after operation in post kidney transplanted recipients.

Acid-base balance and electrolyte disorders at more than six months after operation	Post kidney transplanted recipients (n = 41) No (%)
Na (mmol/l)	
Hyponatremia (<135)	12 (29.3)
Normal (135–145)	29 (70.7)
K (mmol/l)	
Hypokalemia (<3.5)	1 (2.4)
Normal (3.5–5.2)	30 (73.2)
Hyperkalemia (>5.2)	10 (24.4)
Total Ca (mg/dl)	
Hypocalcemia (<8)	2 (4.9)
Normal (8–10.2)	31 (75.6)
Hypercalcemia (<10.2)	8 (19.5)
Mg (mg/dl)	
Hypomagnesemia (<1.6)	12 (29.3)
Normal (1.6–2.8)	29 (70.7)
PO_4 (mg/dl)	
Hypophosphatemia (<2.5)	13 (31.7)
Normal (2.5–4.5)	20 (48.8)
Hyperphosphatemia (>4.5)	8 (19.5)
PH:	
Acidosis (<7.35)	6 (14.6)
Normal (7.35–7.45)	35 (85.4)
HCO_3 (mmol/l)	
Metabolic acidosis (<22)	7 (17.1)
Normal (22–28)	33 (80.5)
Metabolic alkalosis (>28)	1 (2.4)

recipients, establishing a foundation for further analysis and discussion in the context of post-operative outcomes and complications. Within the 1st month after operation, 31.7% of the studied cases had hyponatremia, only 4.9% had hyperkalemia, More than one-third of cases (36.6%) developed hypomagnesemia and 46.3% had hypophosphatemia. All cases had hypocalcemia. PH less than 7.35 was present in 31.7% of cases. Metabolic acidosis as revealed by HCO_3 less than 22 was predominated in 68.3% of them. At more than month after operation, 29.3% of the studied cases had hyponatremia, 24.4% had hyperkalemia and 19.5% of them had hypercalcemia. More than one fourth of cases (29.3%) developed hypomagnesemia and 31.7% had hypophosphatemia. PH less than 7.35 was present in 14.6% of cases. Metabolic acidosis as revealed by HCO_3 less than 22 occurred in 17.1% of patients. There were significantly higher levels of Hb, serum albumin, Na, K, Ca, Mg, PO_4, PH, and HCO_3 at 6 months after operation than within 1st month in postkidney transplanted recipients. There was a significantly lower level of WBCs at 6 months after operation than within 1st month in post kidney transplanted recipients. There was a significantly higher prevalence of hyperkalemia and hypercalcemia at more than six months after operation than within the 1st month after operation in post kidney transplanted recipients. On the other hand, there was a significant lower prevalence of metabolic acidosis (HCO_3<22) at more than six months after operation than within the 1st month after operation in post kidney transplanted recipients (Table 3).

There were no significant correlations between blood tacrolimus level with electrolytes' levels at more than six months after operation in post kidney transplanted recipients. There were significantly higher blood tacrolimus levels in patients with abnormal HCO_3 levels than normal HCO_3 levels' patients ($P = 0.011$). There were no significant relations between blood tacrolimus level with electrolyte disorders at more than six months after operation in post kidney transplanted recipients (Table 4).

Table 3. Correlation between blood tacrolimus level with electrolytes' levels at more than six months after operation in postkidney transplanted recipients treated with tacrolimus.

Electrolytes' levels at more than 6 months after operation	Blood tacrolimus (fk506) (ng/ml) at more than six months after operation in patients ($n = 39$)	
	r	*P* value
Na (mmol/L)	−0.13	0.418
K (mmol/L)	0.02	0.916
Total Ca (mg/dl)	−0.05	0.756
Mg (mg/dl):	−0.17	0.298
PO_4 (mg/dl)	−0.16	0.317
PH	−0.18	0.266
HCO_3 (mmol/l)	−0.15	0.360

r: Pearson correlation's coefficient.

4. Discussion

The demographic and clinical characteristics of the post-kidney transplanted recipients in this study reveal a diverse and representative sample. With a mean age of 29.63 years and a majority being single non-smokers, the cohort aligns with typical trends observed in kidney transplant populations. The prevalence of hypertension and various comorbidities, including combinations such as hypertension with epilepsy, SLE, and ADPKD, underscores the complexity of health conditions in these patients. The primary etiology of chronic kidney disease (CKD) exhibited diversity, with Focal Segmental Glomerulonephritis being the most common.

The preoperative laboratory investigations offer a comprehensive overview of the recipients' health status prior to transplantation. Notably, the negative complement C3 and C4 levels, along with the low prevalence of positive autoantibodies such as ANA and anti-cardiolipin antibodies, suggest a lower incidence of autoimmune disorders in this cohort compared with some other kidney transplant populations. Based on 30 years of data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, A study by Allen *et al.*, investigated the incidence, risk factors, and outcomes of recurrent glomerulonephritis after kidney transplantation. Analyzing 6597 recipients with biopsy-proven glomerulonephritis as the primary cause of ESRD, the research identifies IgA nephropathy, focal segmental glomerulosclerosis, membranous nephropathy, and membranoproliferative nephropathy (MPGN) as the most common types. Recurrence was observed in 479 of 4637 patients, leading to allograft loss in 212 cases. Older age at transplantation was associated with a lower risk of recurrence. Notably, 5-year graft survival rates varied, with MPGN recurrence showing 30% survival, while focal segmental glomerulosclerosis, IgA, and membranous nephropathy exhibited 57–59% survival [1].

Preoperative laboratory values for various parameters such as BUN, serum creatinine, and parathyroid hormone offer insights into the severity of kidney disease before transplantation. Understanding these preoperative values is crucial for evaluating the success of the transplant procedure and predicting potential postoperative complications.

Table 4. Blood tacrolimus level acid-base balance and electrolyte disorders at more than six months after operation in post kidney transplanted recipients treated with tacrolimus.

Acid-base balance and electrolyte disorders at more than six months after operation	N	blood tacrolimus level (ng/ml) at sex months after operation in patients (n = 39) Mean ± SD	Test of significance	*P* value
Na (mmol/l)				
Hyponatremia (<135)	12	7.48 ± 1.79	T = 0.37	0.711
Normal (135−145)	27	7.71 ± 1.79		
K (mmol/l)				
Hypokalemia (<3.5)	0	7.76 ± 1.97	T = 0.72	0.474
Normal (3.5−5.2)	29	7.28 ± 0.98		
Hyperkalemia (>5.2)	10			
Total Ca (mg/dl)				
Hypocalcemia (<8)	2	8.75 ± 1.48	F = 0.683	0.512
Normal (8−10.2)	29	7.46 ± 1.80		
Hypercalcemia (<10.2)	8	7.99 ± 1.75		
Mg (mg/dl):				
Hypomagnesemia (<1.6)	12	7.79 ± 1.50	T = 0.37	0.718
Normal (1.6−2.8)	27	7.57 ± 1.90		
PO_4 (mg/dl)				
Hypophosphatemia (<2.5)	13	8.35 ± 2.31	F = 1.67	0.203
Normal (2.5−4.5)	18	7.32 ± 1.45		
Hyperphosphatemia (>4.5)	8	7.19 ± 1.11		
PH:				
Acidosis (<7.35)	6	8.87 ± 1.86	T = 1.92	0.063
Normal (7.35−7.45)	33	7.41 ± 1.68		
HCO_3 (mmol/l)				
Metabolic acidosis (<22)	7	8.80 ± 1.70	T = 5.17	**0.011**[a]
Normal (22−28)	31	7.26 ± 1.58		
Metabolic alkalosis (>28)	1	11.18		

Relationship between tacrolimus level after renal transplantation and electrolytes as small part of our study received neural. But result show that different levels of tacrulimus didn't affect electrolytes balance there is significant correlation p value > 0.011.

[a] Significant.

Operative details, including induction types and immunosuppressive agents, shed light on the procedural aspects of kidney transplantation. The mean total ischemia time of 35.20 min and the high percentage of cases not requiring intra-operative blood transfusion (82.9%) suggest efficient surgical procedures and favorable intraoperative conditions. Results from a cohort of 7542 recipients over a median follow-up of 5.3 years revealed recipients with a total ischemic time of 14 h or longer had an increased odds of DGF compared with those with less than 14 h, particularly pronounced among those with older donors. A significant interaction was observed between total ischemic time, donor age, and graft loss. On average, there was a 9% increase in the overall risk of graft loss per hour increase in total ischemic time (adjusted hazard ratio, 1.09; 95% confidence interval (CI), 1.01−1.18) for recipients with older donation after circulatory death grafts [2]. Multivariable models revealed that longer Cold Ischemia Time was associated with an increased rate of Delayed Graft Function (odds ratio [OR], 1.41; 95% CI, 1.38−1.44) and extended Length of Stay (OR, 1.04; 95% CI, 1.02−1.05). Recipients at the institution experiencing DGF had a prolonged LOS (OR, 1.71; 95% CI, 1.50−1.95), suggesting that the impact of CIT on LOS is partially mediated by DGF [3]. These findings underscore the importance of considering total ischemic time and donor factors in assessing graft outcomes in deceased donor kidney transplantation.

The choice of immunosuppressive agents, with tacrolimus being the predominant choice (95.1%), aligns with established protocols. A meta-analysis aimed to compare the positive and negative effects of tacrolimus and ciclosporin as initial treatments for renal transplant recipients. The analysis included 123 reports from 30 trials involving 4102 patients. At six months, tacrolimus-treated recipients experienced a significantly reduced risk of graft loss (RR = 0.56, 95% CI 0.36 to 0.86), an effect sustained up to three years. The reduction in graft loss with tacrolimus was influenced by higher concentrations of the drug. However, it did not vary with ciclosporin formulation or ciclosporin concentration. At one year, tacrolimus-treated patients exhibited lower rates of acute rejection (RR = 0.69, 0.60 to 0.79) and steroid-resistant rejection (RR = 0.49, 0.37 to 0.64), but a higher incidence of diabetes mellitus requiring insulin (RR = 1.86, 1.11

to 3.09), as well as tremor, headache, diarrhea, dyspepsia, and vomiting. The excess of diabetes was more pronounced with higher tacrolimus concentrations. Ciclosporin-treated recipients had significantly more constipation and cosmetic side effects. No significant differences were observed in infection or malignancy between the two treatments [4].

The variations in induction types, including Quadri therapy with ATG, Simulect, and triple therapy, reflect the diverse approaches employed in managing post-transplant immune responses. The high incidence of immediate diuresis (90.2%) is a positive indicator of early graft function. These operative details collectively contribute to the understanding of the procedural success and immediate postoperative outcomes in this cohort.

The postoperative period is a critical phase in the care of kidney transplant recipients, and monitoring electrolyte and acid-base balance is paramount. The study's findings highlight significant variations in these parameters within the first month and beyond six months after transplantation.

In this study, within the first month, a substantial proportion of cases experienced hyponatremia (31.7%), hypomagnesemia (36.6%), and hypophosphatemia (46.3%). The prevalence of metabolic acidosis, as indicated by HCO_3 less than 22, was notable at 68.3%. These early disturbances may be attributed to factors such as changes in fluid balance, medication effects, and the adaptation of the transplanted kidney to its new environment.

A longitudinal cohort study comprising 957 renal transplant recipients transplanted utilized a real-life dataset with 28 178 phosphate measurements to investigate the impact of serum phosphate levels on outcomes. Results showed that the median intra-individual lowest phosphate level was 1.58 mg/dl, reached at a median of 33 days post-transplant, with estimated glomerular filtration rate being the main correlate. Over a follow-up period of 9 years, 181 (19%) patients experienced graft failure, and 295 (35%) patients died, including 94 (32%) deaths attributed to cardiovascular disease. In multivariable Cox regression analysis, more severe hypophosphatemia was associated with a lower risk of death-censored graft failure (fully adjusted hazard ratio, 0.61) and cardiovascular mortality (fully adjusted hazard ratio, 0.37) but not with non-cardiovascular mortality or all-cause mortality [5].

At more than six months post-transplantation, hyperkalemia (24.4%) and hypercalcemia (19.5%) became more prevalent. Conversely, there was a decrease in the prevalence of metabolic acidosis (HCO_3<22) to 17.1%. These trends suggest a dynamic process of adaptation and stabilization in the postoperative period.

A study by Emily *et al.*, showed that out of 505 renal transplant patients, 48 developed at least one episode of hyperkalemia. These episodes were not associated with metabolic acidosis, and most patients experienced persistent values in the hyperkalemic range. The majority of patients were on a combination of tacrolimus and trimethoprim-sulfamethoxazole, with approximately half on three or more medications contributing to abnormal potassium handling. Elevated tacrolimus levels were present in only 10% of hyperkalemic episodes [9].

Hyperkalemia in the early post-transplant period was primarily related to the additive effects of multiple therapeutic medications altering potassium homeostasis, rather than being associated with metabolic acidosis or as a direct effect of supra-therapeutic tacrolimus levels.

In accordance with our study, the literature suggests that, hypercalcemia post kidney transplantation is not uncommon, with a prevalence of 22.2% [6]. This is corroborated by an analysis of 104 patients, which focused on calcium levels at the 12th month after transplantation, dividing participants into two groups: hypercalcemia (Ca^{2+} >10.2) and normocalcemia (Ca^{2+} ≤10.2). Alkaline phosphatase levels (ALP) showed no significant difference at the time of transplantation. However, a notable difference emerged in ALP during the 12^{th}-month measurements. Parathormone levels exhibited significant disparities, both at the time of transplantation and in the 12^{th}-month follow-up, with higher levels observed in the hypercalcemia group. Graft functions, as assessed by estimated glomerular filtration rate levels, did not show significant differences between the hypercalcemia and normocalcemia groups during the 1st, 3rd, and 12th months [7]. These findings suggest that while hypercalcemia, accompanied by elevated ALP and parathormone levels, was prevalent in a subset of transplant recipients, it did not significantly impact graft functions within the evaluated timeframes post-transplantation.

The significantly higher levels of hemoglobin, serum albumin, sodium, potassium, calcium, magnesium, phosphate, pH, and bicarbonate at six months compared with the first month indicate an overall improvement in metabolic and electrolyte homeostasis over time. The observed decrease in WBC count at 6 months may reflect a resolution of early postoperative stress responses.

Finally, the association between blood tacrolimus levels and electrolyte disorders adds an intriguing dimension to our understanding of post-transplant

complications. While no significant correlations were found between blood tacrolimus levels and electrolyte levels at more than six months postoperation, patients with abnormal bicarbonate levels exhibited significantly higher blood tacrolimus levels.

Several studies could demonstrate an association of calcineurin inhibitors with the occurrence of chronic metabolic acidosis, with some evidence that it occurs more frequently with tacrolimus than cyclosporine A [8,10]. This effect seems to be dose dependent [11]. Human and animal studies have shown that both cyclosporine A and tacrolimus may cause functional tubular damage. The different molecular mechanisms that lead to an alteration of the tubular electrolyte transport causing RTA were characterized in animal experiments. Cyclosporine A seems to block the adaptation of type B intercalated cells in the distal tubule by inhibiting the peptidyl-prolyl cis-trans isomerase activity [12]. With intake of tacrolimus, the expression or cellular distribution of important acid-base transport proteins such as the vacuolar proton pump, the anion exchanger AE1, or the sodium bicarbonate carbonate cotransporter NBCe1 was altered [13]. In addition, the use of mycophenolate formulations, antibiotics, and other drugs may cause chronic diarrhea in some patients after transplantation and subsequently contribute to nonanion gap MA.

This suggests a potential relationship between tacrolimus dosage and acid-base balance, emphasizing the need for careful titration of immunosuppressive medications to maintain optimal graft function while minimizing metabolic disturbances. The lack of significant correlations between blood tacrolimus levels and electrolyte disorders underscores the complexity of these interactions and suggests that factors beyond tacrolimus levels alone may contribute to electrolyte imbalances in the post-transplant period.

Metabolic acidosis is defined as an excessive accumulation of non-volatile acid manifested as a primary reduction in serum bicarbonate concentration in the body associated with low plasma pH. Certain conditions may exist with other acid-base disorders such as metabolic alkalosis and respiratory acidosis/alkalosis.

4.1. Conclusions

The findings underscore the dynamic nature of postoperative electrolyte and acid-base disturbances. The observed associations between tacrolimus levels and bicarbonate abnormalities offer a compelling avenue for further research to delineate the underlying mechanisms.

Ethics information

Ethical committee code: 10/2022INTM26.

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Conflicts of interest

There are no conflicts of interest.

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