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Electrolytes Disorders in Kidney Transplant Recipients in Erbil City

Bland Imad Farooq[1*], Safaa Ezzuldin Nooraldin [2], Majeed Hasan Mahmood[3]

1. *M.B.Ch.B., trainee at Kurdistan Board-Nephrology-Zheen International Hospital-Erbil.*
2. *MBChB, FICMS (Internal Medicine) FICMS (Nephrology) FRCP-Zheen International Hospital-Erbil.*
3. *MBChB, FICMS (Internal Medicine) FICMS (Nephrology)- Zheen International Hospital-Erbil.*

Corresponding Author* , *contact email :* ***blndhsedoc@gmail.com*

Original Article

Summary

The kidney transplant is advancing gradually in Kurdistan region during last decades. However, the kidney transplant may be followed by frequent co-morbidities mainly graft rejection and serum electrolyte disorders. The electrolyte disturbances if not corrected, might be cause high morbidity and mortality rates. To identify the most common electrolyte abnormalities following kidney transplantation, for setting a plan for early treatment, avoiding complications, and decrease recurrent hospitalization, a retrospective cross sectional review study was carried out in Zheen International hospital at Erbil city-Kurdistan region-Iraq during the period from December 1st , 2020, to 31st of May, 2021 on 90 post-kidney transplant recipients. Serum electrolyte disorders were categorized according to level of each of them; hyponateraemia (<136 mmol/l), hypokalaemia (<3.5 mmol/l), hypochloremia (<102 mmol/l), hypomagnesaemia (<0.7 mmol/l) and hypermagneaemia (>1.0 mmol/l). Laboratory parameters were done at Hala Private Laboratory in Erbil city. Results revealed that post-transplant, 53.3% of recipients had hyponatraemia, 38.9% hypokalaemia. 61.1% hypochloremia , hypomagnesaemia in 3.3% and hypermagnesaemia in 26.7%. The means serum sodium, potassium , magnesium and serum creatinin were significantly reduced post-transplant ($p<0.001$). In conclusions the common serum electrolyte disorders among post-transplant kidney recipients were hypochloremia, hyponateraemia, hypokalaemia and hypermagnaesemia.

Keywords: *Kidney transplant, Serum electrolyte, Morbidity, Mortality*

1. INTRODUCTION

The kidney transplantation is recently the treatment of choice for end-stage renal diseases (ESRDs). It is life saving surgical method preferred on dialysis and suitable for different age groups (1). Additionally, kidney transplant is cost-saving with high quality of life in comparison to dialysis (2). However, it is faced by many obstacles in developing countries like low live donation rates, unaffordable cost and immunosuppression 3. Till now, the kidney transplant covers only 10% of ESRDs need all over the world (3). The end-stage renal diseases are accompanied with frequent metabolic and electrolyte abnormalities which resolved dramatically with kidney transplant. However, the kidney transplant is sometimes complicated by electrolyte disturbances. Unfortunately, the focus is concentrated mainly on immunosupression (4).

Low serum sodium (Na+) level or hyponatremia is regarded as main contributing factor for high morbidities and mortalities as it affects brain, heart, insulin and muscles functions. Hyponatremia is caused by salt and water imbalance that leads to hypovolemia and loss of salts (5, 6). The common reasons for hyponatremia in kidney transplant are hypotonic hyponatremia related to water and salt depletion, retention of water, long duration hypokalemia, loss of sodium and hyponatremia caused by drugs like cyclophosphamide 6. The normal level of plasma potassium (K+) is dependable on potassium intake, distribution of potassium between the intracellular and extracellular space and excretion of potassium by kidney. The hemostais intracellular and extracellular space is depending on NaK-ATPase pump (7). The hypokalemia after kidney transplant might be attributed to water and salt depletion, primary hyperaldosteronism, diuretics and steroids 7. Clinically, the hypokalaemia is regarded as an emergency condition that may cause many co-morbidities and mortality outcomes (8). The serum chloride (Cl-) is common anion in extracellular fluid and important element required for tonicity of plasma. It is regarded as essential element in maintenance of homeostasis like acid-base balance, activating muscles and in immune system activity (9). The hypochloremia is mainly reported for critically ill patients especially in intensive care units which lead to renal failure, cardiovascular complications and high death rates (10). The serum magnesium (Mg+2) is essential element in normal physiological processes. The post-transplant hypomagnesaemia might be related to gastrointestinal and urinary depletion. This depletion may be exacerbiated by diarrhea and medications such as proton pump inhibitors

thiazide diuretics and by calcineurin inhibitors (11). Clinical presentations of hypomagnesemia are confusion, fatigue and neuromuscular irritability, however, it is asymptomatic in most cases. The hypomagnesemia may lead abnormal glucose metabolism, endothelial dysfunction and cardiovascular disorders (12). The hypermagnesaemia is attributed mainly to poor renal excretion (renal failure, medications and endocrine diseases) or increased intake (elderly age and medications) (13-15). Hypermagnesaemia in severe form can lead to cardiovascular, neurological and metabolic abnormalities (16).

The prevention and management of electrolyte disturbances post kidney transplant needs pre and postoperative laboratory monitoring and careful intravenous fluids administration according to type of electrolyte deficiency with specific treatment for each type 4. The cornerstone in management of electrolyte disorders is by removal of the cause (stopping drugs) and by returning back to normal fluid and electrolyte balance of human body (17).

In Iraq, incidence of ESRDs is raising during last decades and common national reasons for these diseases were glomerulonephritis and diabetic nephropathy (18). Kidney transplantation in Iraq has begun since the year of 1972 and it is mainly by live donation and after that date, national kidney transplant program is developing with better outcomes (19). This research is the first Iraqi study aimed to identify the most common electrolyte abnormalities following kidney transplantation, for setting a plan for early treatment, avoiding complications, and decrease recurrent hospitalization

2. PATIENTS and METHODS

The current study design was a retrospective cross sectional review study that carried out in Zheen International hospital at Erbil city-Kurdistan region-Iraq through duration period of six months from first of December, 2020, to 31st of May, 2021. The study population was all patients with end stage renal diseases underwent kidney transplant in Zheen International hospital during study duration. Patients with ESRDs from age group (18-70 years) underwent live donation kidney transplant with serum electrolyte disorders were the inclusion criteria. Exclusion criteria were deceased donor kidney transplantation, post kidney transplant period of more than one month and other electrolyte changes like calcium and phosphorus. The

ethical considerations were implemented according Helsinki Declaration regarding ethical approval of Health authorities; an ethical approval was taken from Kurdistan Board Ethical Committee and confidentiality of data. A convenient sample of 90 post-kidney transplant recipients was selected after eligibility to inclusion and exclusion criteria.

The data were collected by the researchers from saved records of post-kidney transplant recipients in Zheen International hospital and fulfilled in a prepared questionnaire. The questionnaire was designed by the researchers. The questionnaire included the following information: general characteristics of kidney transplant recipients (age, gender, glomerular filtration rate (GFR), post-transplant serum creatinine, post-transplant steroids use, calcineurin inhibitors use and mycophenolate mofetil use), Post-transplant electrolyte serum measures of recipients (serum sodium, serum potassium, serum chloride and serum magnesium). The diagnosis of electrolyte disturbances was done by the researchers according to the Global Observatory on Donation and Transplantation (GODT) criteria (3).

The age of kidney transplant recipients was categorized into five groups (<20 years, 30-39 years, 40-49 years. 50-59 years and ≥60 years) and ranged from 18 years to 70 years. The gender of kidney transplant recipients patients was distributed into male or female. The GFR of kidney transplant recipients was divided into (<60 mL/min/1.73 m2) and (≥60 mL/min/1.73 m2). The serum creatinine was categorized into low, normal and high taking in account normal range of serum creatinine (0.8-1,2 mg/dl). History of medications intake by recipients was taken from records of them post-transplant. The serum electrolyte disorders were categorized according to level of each of them; hyponateraemia (<136 mmol/l), hypokalaemia (<3.5 mmol/l), hypochloremia (<102 mmol/l), hypomagnesaemia (<0.7 mmol/l) and hypermagneaemia (>1.0 mmol/l). Laboratory parameters were done at Hala Private Laboratory in Erbil city.

The data collected were analyzed statistically by Statistical Package of Social Sciences software version 22. Chi square and Fishers exact tests were applied for categorical variables accordingly. The paired t-test was applied for analyzing two consecutive means. Level of significance (P.value) was regarded statistically significant if it was 0.05 or less.

3. RESULTS

This study included ninety kidney transplant recipients with mean age of (37.2 years) and range of 9-66 years; 15.6% of recipients were in age group <20 years, 20% of them were in age group 20-29 years, 22.2% of them were in age group 30-39 years, 13.3% of them were in age group 40-49 years, 22.2% of them were in age group 50-59 years and 6.7% of them were in age group of 60 years and more. Male recipients were more than females with male to female ratio of 1.25:1. The glomerular filtration rate post-transplant was less than <60 mL/min/1.73 m2 in 12.2% of them, while the glomerular filtration rate was ≥60 mL/min/1.73 m2 in 87.8% of recipients. The serum creatinin post-transplant was categorized into; low (8.9%), normal (82.2%) and high (8.9%). The medications taken post-transplant by recipients were steroids (100%), Calcineurin inhibitors (100%) and Mycophenolate mofetil (100%). (Table 1). Post-transplant, the hyponatraemia was recorded among 53.3% of recipients, while the hypokalaemia was detected among 38.9% of them. Prevalence of hypochloremia in recipient post-transplant was (61.1%), while prevalence of hypomagnesaemia was (3.3%) and prevalence of hypermagnesaemia was (26.7%). (Table 2). The means of serum sodium, potassium and magnesium for recipients were significantly decreased post-transplant ($p<0.001$). The mean serum chloride of recipients was not significantly changed pre and post-kidney transplant ($p=0.1$). Mean serum creatinin of recipients was significantly decreased post-transplant of kidney ($p<0.001$). (Table 3). There was a significant association between adulthood age recipient and post-transplant hyponatraemia ($p=0.001$). No significant differences were observed between recipients with post-transplant hyponatraemia and recipients without post-transplant hyponatraemia regarding gender ($p=0.06$) and glomerular filtration rate ($p=0.2$). A significant association was observed between normal serum creatinin of recipients and post-transplant hyponatraemia ($p=0.04$). (Table 4). No significant differences were observed between recipients with post-transplant hypokalaemia and recipients without post-transplant hypokalaemia regarding age ($p=0.2$), gender ($p=0.2$) and glomerular filtration rate ($p=0.3$). A significant association was observed between low serum creatinin of recipients and post-transplant hypokalaemia ($p=0.02$). (Table 5). There was a significant association between

older age recipient and post-transplant hypochloridaemia (p=0.04). No significant differences were observed between recipients with post-transplant hypochloridaemia and recipients without post-transplant hypochloridaemia regarding gender (p=0.8) and glomerular filtration rate (p=0.8). A significant association was observed between normal serum creatinin of recipients and post-transplant hypochloridaemia (p=0.008). (Table 6). There was a highly significant association between older age recipient and post-transplant hypermagnesaemia (p<0.001). No significant differences were observed between recipients with post-transplant hypermagnesaemia and recipients without post-transplant hypermagnesaemia regarding gender (p=0.1) and serum creatinin (p=0.2). A highly significant association was observed between low glomerular filtration rate of recipients and post-transplant hypermagnesaemia (p<0.001). (Table 7).

Table 1. General characteristics of kidney transplant recipients

Variable		**No.**	**%**
Age (year)	<20	14	15.6
	20-29	18	20
	30-39	20	22.2
	40-49	12	13.3
	50-59	20	22.2
	≥60	6	6.7
Gender	Male	50	55.6
	Female	40	44.4
GFR post-transplant (mL/min/1.73 m²)	< 60	11	12.2
	≥60	79	87.8
Post-transplant-serum creatinine	Low	8	8.9
	Normal	74	82.2
	High	8	8.9
All the 90 patients received steroids, CNI and MMF			

Table 2. Post-transplant electrolyte disturbances of recipients.		
Variable	No.	%
Hyponatraemia (<136 mmol/l)	48	53.3
Hypokalaemia (<3.5 mmol/l)	35	38.9
Hypochoremia (<102 mmol/l)	55	61.1
Hypomagnesaemia (<0.7 mmol/l)	3	3.3
Hypermagneaemia (>1.0 mmol/l)	24	26.7

Table 3. Distribution of serum electrolytes and creatininee pre and post-transplant.

Electrolyte	**Pre-transplant**	**Post-transplant**	**P**
Serum Sodium (mmol/l)	136.6±3.6	133.5±5.4	**<0.001**
Serum Potassium (mmol/l)	4.5±0.8	3.5±0.5	**<0.001**
Serum Magnesium (mmol/l)	1.5±0.6	1.3±0.5	**<0.001**
Serum Chloride (mmol/l)	103.5±3.5	102.5±5.3	0.100
Serum creatinine (mg/dl)	7.4±2.9	0.9±0.2	**<0.001**
Values are Mean ± SD,			

Table 4. Distribution of recipients' general characteristics according to hyponatraemia .

Variable	**Hyponatraemia**				**P**
	Yes		**No**		
	No.	**%**	**No.**	**%**	
Age (year)					
<20	5	10.4	9	21.4	
20-29	9	18.8	9	21.4	
30-39	17	35.4	3	7.1	**0.02**
40-49	6	12.5	6	14.3	
50-59	10	20.8	10	23.8	
≥60	1	2.1	5	11.9	
Gender					
Male	31	64.6	19	45.2	0.06
Female	17	35.4	23	54.8	
Glomerular infiltration rate					
< 60 mL/min/1.73 m^2	4	8.3	7	16.7	0.20
≥ 60 mL/min/1.73 m^2	44	91.7	35	83.3	
Serum creatinine					
Low	1	2.1	7	16.7	**0.04**
Normal	43	89.6	31	73.8	
High	4	8.3	4	9.5	

Table 5. Distribution of recipients' general characteristics according to hypokalaemia

Variable	Hypokalaemia				P
	Yes		No		
	No.	%	No.	%	
Age (year)					0.2 NS
<20	7	20	7	12.7	
20-29	6	17.1	12	21.8	
30-39	11	31.4	9	16.4	
40-49	2	5.7	10	18.2	
50-59	6	17.1	14	25.5	
≥60	3	8.6	3	5.5	
Gender					0.2 NS
Male	17	48.6	33	60	
Female	18	51.4	22	40	
Glomerular infiltration rate					0.3 NS
<60 mL/min/1.73 m^2	3	8.6	8	14.5	
≥ 60 mL/min/1.73 m^2	32	91.4	47	85.5	
Serum creatinine					**0.02** S
Low	5	14.3	3	5.5	
Normal	30	85.7	44	80	
High	0	-	8	14.5	

Table 6. Distribution of recipients' general characteristics according to hypochloridaemia.

Variable	Hypochloridaemia				P
	Yes		No		
	No.	%	No.	%	
Age (year)					**0.041**
<20	5	9.1	9	25.7	
20-29	11	20	7	20	
30-39	17	30.9	3	8.6	
40-49	5	9.1	7	20	
50-59	14	25.5	6	17.1	
≥60	3	5.5	3	8.6	
Gender					0.980
Male	30	54.5	20	57.1	
Female	25	45.5	15	42.9	
Glomerular infiltration rate					0.883
<60 mL/min/1.73 m^2	7	12.7	4	11.4	
>=60 mL/min/1.73 m^2	48	87.3	31	88.6	
Serum creatinine					**0.008**
Low	1	1.8	7	20	
Normal	50	90.9	24	68.6	
High	4	7.3	4	11.4	

Table 7. Distribution of recipients' general characteristics according to hypermagnesaemia.

Variable	Hypermagnesaemia				P
	Yes		No		
	No.	%	No.	%	
Age (year)					**<0.001** S
<20	0	-	14	21.2	
20-29	0	-	18	27.3	
30-39	2	8.3	18	27.3	
40-49	10	41.7	2	3	
50-59	10	41.7	10	15.2	
≥60	2	8.3	4	6.1	
Gender					0.1 NS
Male	10	41.7	40	60.6	
Female	14	58.3	26	39.4	
Glomerular infiltration rate					**<0.001** S
<60 mL/min/1.73 m^2	8	33.3	3	4.5	
>=60 mL/min/1.73 m^2	16	66.7	63	95.5	
Serum creatinine					0.2 NS
Low	1	4.2	7	10.6	
Normal	19	79.2	55	83.3	
High	4	16.7	4	6.1	

4. DISCUSSION

Serum electrolyte level disturbances are common among patients with ESRDs and after kidney transplant. In addition to cardiovascular and neurological complications, the abnormalities in serum electrolytes post-kidney transplant is regarded as risk factor for graft dysfunction (4). Present study showed that (53.3%) of recipients had hyponatraemia after kidney transplant. This finding is higher than results of Han et al (5) study in South Korea on 2885 patients underwent kidney transplant which found that (4%) of kidney recipients had hyponatraemia and those recipients were at high risk of graft rejection. The high prevalence of hyponatraemia in our study might be attributed to different reasons such as single center study, small sample size and fact that all patients in included in current study had electrolyte disturbances and received calcineurin inhibitors, mycophenolate mofetil and steroids which all reported as inducers for hyponatraemia (20). Musso et al (6) documented

that kidney transplant KTPs are predisposed to develop hyponatraemia since they are exposed to immunologic, infectious, pharmacologic and oncologic disorders, the combination of which alters their salt and water homeostatic capacity. Our study revealed a significant decline in mean serum sodium of recipients post-transplant ($p<0.001$). This finding is similar to results of Higgins et al 21 study in UK. The hyponatraemia in present study was significantly related to adulthood age and normal serum creatinine. These findings revealed the major role of immunosuppressive medications in development of hyponatraemia (5).

The current study found that prevalence of hypokalaemia among post-kidney transplant recipients with electrolyte disorders was (38.9%). This finding is higher than results of Choi et al (20) study in South Korea which found that (11.8%) of kidney transplant recipients on calcineurin inhibitors had hypokalaemia. Our study also revealed a significant decline in mean serum potassium level of recipients post-transplant ($p<0.001$). Low serum potassium level among recipients might also attributed to same reasons of hyponateraemia. However, adverse effects of hypokalemia like arrhythmia and mortality are more risky than hyperkalemia 22. Our study showed a significant association between low serum creatinin of recipients and post-transplant hypokalaemia ($p=0.02$). This finding is similar to results of Tintillier et al (23) study in Belgium.

The present study found that (61.1%) of post-kidney transplant recipients with electrolyte disorders had hypochloremia. This finding is higher than results of previous literatures (17,24). The low serum chloride level in our study might be due to other electrolyte disturbances and also to effect of medications. Li et al (25) study in China stated that hypochloremia is associated with higher mortality risk. The hypochloremia in current study was significantly related to elderly age patients. This finding coincides with results of Schlanger et al (26) study in USA.

This study found that prevalence of hypomagnesaemia among post-kidney transplant recipients with electrolyte disorders was (3.3%). This finding is better than results of Odler et al et al (27) study in Australia which found (60.9%) of post-kidney transplant had hypomagnesaemia. This low prevalence of hypomagnesaemia might be due to magnesium intake of recipients, pre and post-transplant. Garnier et al (28) study in France reported that hypomagnesaemia is associated with multiple clinical co-morbidities like diabetes mellitus.

However, our study revealed a significant decline in magnesium level post-transplant ($p<0.001$). On other hand, present study showed that prevalence of hypermagnesaemia among recipients with electrolyte disorders was (26.7%). The high prevalence of hypermagnesaemia might be attribute to laxatives use by recipients especially elderly age patients (29). Our study showed a highly significant association was observed between low glomerular filtration rate of recipients and post-transplant hypermagnesaemia ($p<0.001$). This finding is consistent with results of Hod et al (30) study in USA which reported that increase in magnesium level lead to decline in glomerular filtration rate and the hypomagnesaemia within one year after transplant is considered as good prognostic marker for kidney transplant.

5. CONCLUSIONS

The common serum electrolyte disorders among post-transplant kidney recipients were hypochloremia, hyponateraemia, hypokalaemia and hypermagnaesemia. The immunosuppressive drugs, age and serum creatinine level are the common risk factors affecting serum electrolyte levels post-kidney transplant. This study recommended the continuous electrolyte monitoring pre and post-kidney transplants for both donors and recipients

Ethical Clearance: Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical issues of researches involving humans, informed consent obtained from all patients. Data and privacy of patients were kept confidentially.

Conflict of interest: Authors declared none

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