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ORIGINAL ARTICLE

Assessment of Biochemical Parameters of Graft Survivors Post Renal Transplantation at King Faisal Hospital in Rwanda

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ABSTRACT

Background: Chronic kidney disease (CKD) remains a public health concern of 21st century. Each year, over million people die from CKD resulting from the lack of proper diagnosis and treatment of this terrible disease of the urinary system. Non-communicable diseases (NCDs) cause roughly 60% of all deaths worldwide. There is insufficient data in Rwanda for the management of kidney diseases and other NCDs for all health facilities. Renal substitution therapy appears to be the best solution for long–suffering patients with end-stage renal illness who want to survive. The study's purpose was to find out the serum creatinine and blood urea nitrogen (BUN) concentrations among kidney transplanted patients at King Faisal Hospital of Rwanda, and to show the consequences linked with the transplantation of kidney.
Methods: This was a retrospective study carried from November 2018 to December 2019. The data were collected from medical records at King Faisal Referral Hospital, and analysed with SPSS version 22.
Results: BUN and serum creatinine concentrations ranged from 77.4 to 93.5% and 67.8 to 87.1%, respectively. BUN levels that were abnormally high ranged from 3.2 to 19.4%, while creatinine levels that were abnormally high ranged from 6.5 to 29.0%. BUN and creatinine levels that were abnormally low, ranged from 0.0 to 6.5 and 3.2 to 9.7%, respectively. Diabetes mellitus affected 19.35% of the study population, hypertension affected 35.48%, and antibody-mediated rejection affected 6.45%.
Conclusion: The slight change in biochemical parameters may be a problem after kidney transplantation. There should be a monitoring of biochemical parameters tests to prevent the post kidney transplantation complications.

BACKGROUND

Worldwide, one of the vital public health issues is chronic kidney disease (CKD), whose final outcome is end-stage renal disease (ESRD). Ten percent of people worldwide are suffering from CKD. The progress of CKD toward ESRD can be prevented via early diagnosis and suitable management. The only treatments of choice available for ESRD patients are dialysis and kidney transplantation. CKD is defined as a declined working capacity of kidneys with a velocity of glomerular filtration of eGFR/1.73 m^2 < 60 ml/min. ESRD is a reduction in kidney function that is incapable of being repaired and it is mandatory to save the life of patients by renal replacement therapy (RRT). The increase of ESRD cases shows that it is a threatening health issue.[1]

Every year, more than a million people die as a result of inability to get a proper and vital CKD treatment. CKD data in countries under development are limited and mortality rates are significantly higher compared to high-income countries. In low-income and middle-income countries (LMICs), many persons are undiagnosed and a high proportion of those with CKD develop ESRD. In addition, most of them don't have accessibility to life-saving RRT.[2] In Rwanda, the prevalence of CKD varies from 4 to 24% of population-based importantly on the protein in urine as a marker.[3] Hypertension and diabetes are two important factors leading to CKD. HIV and phytodrugs were also reported to have a similar role.[3] To control and manage CKD patients and kidney transplants, follow-up is needed.[4]

Usually, serum creatinine and BUN are biological markers that are measured several times for patients who had experienced renal transplantation. Such biomarkers help to evaluate how healthy the kidneys are, after renal transplantation.[5] Urea, normally considered as BUN when it is measured in the blood is a metabolism product of protein. BUN is defined as a natural byproduct of non-protein nitrogenous waste. The protein breakdown delivers amino acids and are deaminated to produce ammonia. Through liver enzymes, ammonia is subsequently converted to urea. Consequently, the urea concentration is

dependent on protein intake, body capability for protein catabolism, and sufficient urea excretion by the renal system.[6]

Creatinine is basically a creatine phosphate metabolite. It is a composite that acts as an energy source in the muscle. It is formed at a moderately steady velocity in the body, though this does differ depending on the body mass. Due to the bigger skeletal mass, men are likely to have higher creatinine levels than women.[7-9] Creatinine is freely filtered and secreted through the glomerulus and proximal tubules. It is used in several formulas to obtain the eGFR. The decreasing kidney function can cause the increasing tubular secretion of creatinine and cause also extra renal elimination of creatinine.[10] Thus the evaluation of serum creatinine and the level of BUN is necessary for the graft survival following renal transplantation.

In LMICs, lifestyle is changing, plus rapid urbanization, then NCDs impacts becoming more and more recognized. After all, only some epidemiological studies have been done on the prevalence, incidence, and the cause of these diseases. Between 1990 and 2010, CKD was almost twice a cause of death internationally and it was ranked the 18th highest death cause globally in 2010.[11] Estimations show that in 2030, patients with ESRD greater than 70% globally will be in LMICs unless key problems and concerns are solved.[12]

More than half of all patients necessitating RRT worldwide die resulting from the lack of access to dialysis or kidney transplantation. In Africa, predominantly in Sub-Saharan Africa, there is the biggest disparity in access to renal replacement, and among people requiring RRT only less than 3% can receive it. Consequently, the rising saddle of CKD falls on the least equipped countries and to provide the expensive but life-saving therapies of dialysis and/or transplantation is not easy. Therefore, patients with ESRD continue to die although treatment options are established. The enormous price together with giving RRT provides a forceful economic motivation for enhancing the prevention, detection, and management of CKD in LMICs.[13]

Reports show that people with HIV/AIDs have the highest risk for CKD in the world. Sub-Saharan Africa is the region with the highest number of HIV-positive people. Kidney can change its function during antiretroviral (ARV) treatment. Previous studies did not give confirmation of the high risk of CKD on Africans with HIV and close renal function control and surveillance in patients with high blood pressure and other risk factors.[14] Besides, most studies that were conducted in East Africa about BUN and serum creatinine concentrations were based on patients with CKD only.[3,10,15,16]

This study was conducted on kidney transplant patients. It was aimed to quantify the BUN and serum creatinine levels during the period of follow-up, and to investigate the associated consequences (diabetes mellitus, hypertension, and antibody-mediated rejection) with kidney transplantation. Therefore, two research questions of the present study are "What are BUN and serum creatinine levels among kidney transplanted patients during follow-up period? and "What are the risk factors associated with renal transplantation?

METHODS

Study Area

This study was conducted in renal unit department at King Faisal Hospital, Kigali City (Rwanda). The renal unit provides close attention to patients with kidney failure and other renal-related complications. The department has a haemodialysis unit that deals with the elimination of waste products like urea and creatinine as well as water from the blood of patients when the kidneys fail to do their functions. They thus do follow-up of kidney transplant patients.

Study Design and Period

This was a retrospective study. BUN and serum creatinine levels at the beginning after transplantation, and at every appointment (15 days, 1st month, 3rd, 6th, 9th and 12th months) post-transplantation were considered. The study was conducted from November 2018 to December 2019.

Study Population

The study population was 31 patients with kidney transplants at King Faisal Hospital that had completed at least 12 months of follow-up, post-renal transplantation. Only 31 patients were available during the study period.

Inclusion and Exclusion Criteria

The present investigation included kidney transplanted patients at King Faisal Hospital for follow-up. It excluded CKD patients that had no renal transplant, and patients who did not complete at least 12 months of follow-up. Patients with pre-existing diabetes and hypertension before receiving renal transplants were also excluded.

Ethical Consideration

This study was checked and approved by the ethical review committees of INES Ruhengeri and King Faisal hospital. The approval letter from INES-Ruhengeri was presented to King Faisal hospital administration, and the hospital granted the authorization to collect data. The information of the patients and data were collected anonymously and kept confidential.

Data Collection

Data were collected using paper forms. Urea and creatinine data were collected from the data record system of the hospital in the department of biochemistry and in medical records unit. Information was recorded starting from the first day until 12 months of follow-up. The information regarding NCDs especially diabetes mellitus and high blood pressure were recorded indicating if the patients had been affected before or after kidney transplantation.

Statistical Analysis

The data were presented in tables. The SPSS version 22 was used for data analysis. Descriptive analysis was calculated in terms of mean ± SD and some using frequencies and percentages. Additionally, the significance was considered based on *p-value* of < 0.05.

RESULTS

Levels of BUN among Kidney Transplanted Patients

In the present study, serum creatinine and BUN at King Faisal hospital were assessed, post-transplantation of the kidney. The normal range of BUN varies between 2.50 and 7.50 mmol/l. Table 1 shows that patients with normal ranges were more than those with abnormal levels. Within abnormal values, the ones with upper limits were more than those with lower limits. The mean BUN in the first 3 months was lower than in the subsequent months with a significant increase starting from the 6th to 12th month.

Levels of Serum Creatinine among Kidney Transplanted Patients

Serum creatinine levels were determined among kidney transplanted patients. Data were stratified into 6 groups according to days and months. The normal range of serum creatinine in King Faisal hospital in Kigali was between 60 and 130 µmol/l. Patients with normal creatinine levels were more than those with abnormal levels. Patients with high creatinine levels were more than those with low creatinine. The levels of creatinine were raised progressively for some patients. This was noticed from the 3rd to the 9th month (Table 2).

Consequences Associated with Kidney Transplantation

Kidney transplantation may be associated with some adverse effects. The results in Table 3 show that the study population had hypertension more than diabetes mellitus. Few were with antibody mediated rejection. All these risk factors were statistically significant.

TABLE 1: BUN Within First Year post Kidney Transplantation Follow-up

Period (post transplantation)	Normal (7-30 mg/dl)	High	Low	Mean	Std. Deviation
15 days	24 (77.4%) 29 (93.5%)	5 (16.1%) 2 (6.5%)	2 (6.5%) 0	4.87 4.63	2.76 2.18
1 month	28 (90.3%) 26 (83.9%)	2 (6.5%) 5 (16.1%)	1 (3.2%) 0	4.70 4.92	1.75 2.54
3 months	28 (90.3%) 29 (93.5%)	2 (6.5%) 1 (3.2%)	1 (3.2%) 1 (3.2%)	4.69 4.62	1.66 1.52
6 months	27 (87.1%) 27 (87.1%)	4 (12.9%) 3 (9.7%)	0 1 (3.2%)	5.22 5.10	2.05 2.59
9 months	26 (83.9%) 26 (83.9%)	5 (16.1%) 5 (16.1%)	0 0	5.42 5.42	3.30 3.34
12 months	24 (77.4%) 25 (80.6%)	6 (19.4%) 6 (19.4%)	1 (3.2%) 0	5.59 5.27	3.76 2.95

TABLE 2: Levels of Serum Creatinine Within First Year post Renal Transplantation

Period (post transplantation)	Normal (0.7-1.2 mg/dl)	High	Low	Mean	Std. Deviation
15 days	26 (83.9%) 27 (87.1%)	2 (6.5%) 3 (9.75)	3 (9.7%) 1 (3.2%)	98.77 97.72	32.68 29.79
1 month	26 (83.9%) 23 (74.2%)	4 (12.9%) 5 (16.1%)	1 (3.2%) 3 (9.7%)	97.79 96.52	33.11 33.37
3 months	27 (87.1%) 23 (74.2%)	2 (6.5%) 6 (19.4%)	2 (6.5%) 2 (6.5%)	97.87 98.97	25.91 30.85
6 months	26 (83.9%) 27 (87.1%)	4 (12.9%) 3 (9.7%)	1 (3.2%) 1 (3.2%)	101.06 100.37	30.77 31.52
9 months	25 (80.6%) 23 (74.2%)	5 (16.1%) 7 (22.6%)	1 (3.2%) 1 (3.2%)	105.18 108.94	42.26 47.45
12 months	21 (67.7%) 21 (67.7%)	9 (29.0%) 9 (29.0%)	1 (3.2%) 1 (3.2%)	127.93 117.21	104.79 51.89

TABLE 3: Consequences Within First Year Post Kidney Transplantation

Consequences	Number of subjects	Positive cases(%)	P-value	Degree of freedom	X2
Diabetes mellitus	31	6 (19. 35)	.0006	1	11.64
Hypertension	31	11 (35.48)	.001	1	2.61
Antibody mediated	31	2 (6.45)	.000	1	23.51

DISCUSSION

Serum creatinine and BUN of graft survivors post the transplantation of kidney were analysed at King Faisal hospital. It is more helpful to evaluate the function of kidneys by using a biomarker which is BUN which it must be measured several times for patients who were renal transplanted.[17] The change rate of BUN concentrations was recorded recurrently over time following renal transplantation. Patients with normal ranges were higher than those with abnormal levels. The patients with high levels of BUN increased gradually as days post renal transplantation increased. The longitudinal study done by Jaffa *et al.*[5] on renal outcome analysis, following transplantation and demographic factors, demonstrated that the BUN levels change was only influenced by the donor's vital status. The advantage was to put together recipient patients from living donors (as opposed to deceased donors). Urea levels can be changed by many factors including diet but the main cause can be the degree of damage to kidneys which have the role of urea excretion.

Renal allograft dysfunction occurs most commonly after one year following renal transplantation. It is often asymptomatic, and is typically detected by an increase in serum creatinine level.[18] Patients with normal creatinine were more than those with those with abnormal values. Creatinine levels increased progressively, with an important increase between 3rd and 6th month. Similar to investigations conducted by Donald *et al.*[19] and Hariharan *et al.*[20], serum creatinine concentrations increased at one year post-transplantation. Those studies evaluated the effect of a number of variables on graft survival and it was confirmed that there is an important independent relationship between serum creatinine concentrations and kidney graft loss. The impaired kidneys and use of high doses of anti-rejection drugs can cause a rise in serum creatinine. They can cause nephrotoxicity and kidney damage. Generally, there is an agreement among the investigations in nephrology domains concerning the importance of BUN and serum creatinine levels in influencing graft non-success following kidney transplantation.

Many nephrons can be damaged by high blood sugar levels leading to the incapacity of kidneys to maintain fluids and electrolytes homeostasis.[21] The study population had hypertension more than diabetes mellitus. In the report of Alalawi *et al.*[22], diabetic kidney disease (57%) and high blood pressure (12.4%) were rising as the most usual causes of ESRD. In that study, 10.9% of patients had undetermined causes and f4.6% had transplant rejection reactions. Similar to the present study, patients with diabetes were 19.35% and those with hypertension were 35.48% one year post renal transplantation, while 6.45% had antibody-mediated rejection. Furthermore, Donald *et al.*[19] indicated that for at least 6 months, the majority of patients with kidney transplants had hypertension regardless of their degree of renal function. In one year after transplantation, 75% had systolic blood pressure (SBP) greater than 130 mmHg. The increased SBP was independently and importantly related to chronic graft non-success within seven years of monitoring. There was significant link of SBP in the absence or presence of acute rejection with the loss of long-term graft. One of the main causes of renal transplant to be vulnerable to developing hypertension and diabetes is the use of anti-rejection drugs that can damage organs in the body.

Limitations of the Study

This was a retrospective investigation conducted at one referral hospital in Rwanda (Kind Faisal hospital) from November 2018 to December 2019. As it was retrospective, laboratory data records were gathered from the department of biochemistry and in the medical records unit and missing data from the records could not be recovered. As the results are from one hospital, they cannot be generalised to the entire country.

CONCLUSION

The first years post renal transplant follow-up are of great importance for improving graft survival. It is essential to use a combination of serum creatinine and BUN as makers, and it is very important to take care of the consequences associated with kidney transplantation. This provides an opportunity to carry out secondary interventional assessment early to delay graft failure in this population. Creatinine and urea were found to be vital indicators of normal kidney function. It is recommended to King Faisal hospital to advise all renal transplantation patients to attend follow up monthly, inorder to be evaluated, and access services for the control renal failure risk factors to ensure that their renal grafts are working properly.

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