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RENAL FUNCTION OF LIVING KIDNEY DONORS AT KENYATTA NATIONAL HOSPITAL: A CROSS-SECTIONAL DESCRIPTIVE STUDY

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STUDENT'S DECLARATION

I declare that this dissertation is my original work and does not contain without acknowledgement any material previously submitted for a diploma or a degree in any institution of higher learning. And to the best of my knowledge it does not contain any material previously published or written by another person except where due reference has been made in the text.

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LIST OF ABBREVIATIONS

BP	Blood Pressure
BMI	Body Mass Index
CKD	Chronic Kidney Disease
DNA	Deoxyribonucleic Acid
eGFR	Estimated Glomerular Filtration Rate
EGF	Epidermal Growth Factor
ESRD	End-stage Renal Disease
FSGS	Focal Segmental Glomerulosclerosis
HTN	Hypertension
KNH	Kenyatta National Hospital
KGs	Kilograms
KRA	Kenya Renal Association
M^2	Square metres
MB.ChB	Bachelor of Medicine and Bachelor of Surgery
Mmed	Master of Medicine
NHANES	National Health and Nutrition Examination Survey
NSAIDS	Non-steroidal Anti-inflammatory Drugs
OPTN	Organ Procurement and Transplantation Network
RRT	Renal Replacement Therapy
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences
TGFβ	Transforming Growth Factor Beta
TNFα	Tumor Necrosis Factor Alpha
U.O.N	University of Nairobi
µmols/l	Micromoles per litre
g/L	Grams/litre
KDOQI	Kidney Disease Outcome Quality Initiatives
mls	Millilitres
min	Minute
DTPA	Diethylene Triamine Pentaacetic Acid

ABSTRACT

Background

The outcome of live kidney donation has been of concern since the recognition of hyperfiltration injury post live kidney donation.

Studies on the topic have arrived at different conclusions regarding kidney function following live kidney donation; some suggest the possibility of renal progression while others report renal function similar to that of the general population. However, there are no studies done in a homogeneously African population to compare with.

Beginning the year 2010 at Kenyatta National Hospital, Kenya, live kidney donation happens regularly with an average of two live related kidney donation and transplantation per month.
The purpose of this study was to assess the impact of renal donation on renal function of live kidney donors at Kenyatta national hospital.

Objective

To determine serum creatinine levels, eGFR, prevalence of proteinuria, and hypertension among living kidney donors at Kenyatta National Hospital.

Study design

Cross-sectional descriptive study

Methods

Using a questionnaire, a targeted history was obtained from kidney donors. A venous blood sample was drawn for serum creatinine measurement from which an eGFR was calculated using Cockroft-Gault equation. A sample of urine was collected from which proteinuria was determined using a standard urinary dip stick. Furthermore, blood pressure, height and weight were measured followed by the determination of the body mass index of the study subjects. Patient's pre-nephrectomy records were reviewed and blood pressure, weight, height, serum creatinine levels were recorded. Their body mass index and estimated glomerular filtration rate pre-nephrectomy was then calculated. The prevalence of hypertension and proteinuria was expressed as proportions. Using a paired student's t-test, mean changes for serum creatinine, estimated glomerular filtration rate, diastolic blood pressure and systolic blood pressure were determined. Statistical significance was pegged at P-value of <0.05.

Results

A total of 52 subjects were enrolled in the study. The mean (± standard deviation) estimated glomerular filtration rate post-nephrectomy was 79.96mls/min/M^2 (± 31.95mls/min/M^2) which

transformed to 85.62% of the pre-nephrectomy estimated glomerular filtration rate. The prevalence of proteinuria, and hypertension was 21.2% and 9.6% respectively. New onset hypertension was 6%. 40% of the subjects were either overweight or obese. There was a significant mean change for serum creatinine, estimated glomerular filtration rate and diastolic blood pressure when pre-neprectomy and post-nephrectomy values were compared with p values of <0.0001, 0.002 and 0.008 respectively.

Conclusion

At the mean duration of follow up of 15.9 months, the kidney donors studied regained their renal function with a tendency towards hyperfiltration. The prevalence of proteinuria and hypertension was low. The results of the study compared well with those obtained from other studies.

1.0 LITERATURE REVIEW

1.1 INTRODUCTION

Chronic kidney disease (CKD) is a public health problem of increasing significance, consuming a growing proportion of healthcare resources (1).
The prevalence of end stage renal disease (ESRD) in developing countries is on the increase. This could be attributed to the growing incidence of risk factors for CKD namely diabetes mellitus, hypertension, HIV and chronic glomerulonephritis among others (2; 3)

Following ESRD, renal replacement therapy (RRT) becomes necessary for survival of patients. The available forms of RRT are hemodialysis, peritoneal dialysis and renal transplantation. Transplantation is the best mode of RRT as it is cost effective overall and is associated with less morbidity and mortality compared to dialysis; as a result it accords ESRD patients the best quality of life (4).

Sources of renal allograft include; cadaveric, living non-related and living related donors (5). The later is the most preferred since it is not associated with delayed graft function and minimal immunosuppression is required to stem off rejection and maintain graft function.

In Kenya with a population of approximately 40 million, according to Kenya Renal Association (KRA), an estimated 6000 patients suffer kidney failure annually. Renal transplantation services are offered at Kenyatta National hospital (KNH); a public referral hospital and a few private hospitals. The first renal transplant was performed in 1978 following erroneous nephrectomy of a pelvic horse shoe kidney in a young man (6). Since then kidney transplants were sporadic and expensive with modest results. More recently, from the year 2010 an average of 2 live kidney donations occurs per month reflecting the life of the **Interlife project**; a public private partnership between KNH and Norvatis whose main goal is the development of a centre of excellence in kidney transplantation through training of health care professionals by recognized kidney transplant specialists from Spain with a focus on enhancing surgical techniques as well as increasing efficiency and reducing cost of transplants and access to drugs.

At KNH, potential kidney donors are screened for compatibility with the recipient, occult kidney disease, co-morbidities commonly associated with kidney disease such as hypertension and diabetes and for suitability to undergo anesthesia as indicated in the recipient/ donor evaluation form (appendix3).Thus, live kidney donors are highly selected and healthy individuals.

With the increasing burden of ESRD, many patients will require renal replacement therapy in the form of renal transplantation. There is therefore need for a corresponding increase in the number of living kidney donation to meet shortage of organs.

Data regarding kidney function in living donors is limited. This is because following renal donation, there are no standard guidelines for follow up of living related donors in most kidney transplantation centres. As a result, there is no universally accepted duration for follow up of kidney donors. In spite of this, most studies done so far suggest need for regular follow up.

In Africa, data regarding renal function in living renal donors is scanty. Two studies in S. Africa (7, 8) with predominantly white subjects have suggested stability of kidney function following live kidney donation. There are no studies in Kenya and the rest Africa regarding living kidney donors.

Recently, a prospective study done in United Kingdom (9), demonstrated a decline in renal function of donors and an increase in the incidence of new onset hypertension hence rekindling the debate on the safety of kidney donors.

1.2 RENAL ADAPTATION FOLLOWING UNILATERAL NEPHRECTOMY

Following unilateral nephrectomy, the remaining kidney undergoes both structural and functional changes in order to cater for the lost function of the donated kidney:
Renal hypertrophy occurs with very little cellular proliferation; this is accomplished by the increase in the size of each cell along the nephron. Signals for this may be explained by the local expression of angiotensin II, transforming growth factor beta (TGFβ) and epidermal growth factor (EGF) which promote growth. However expression of $P27^{kip\ 1}$, a cell cycle

protein produced locally prevents cells exposed to angiotensin II from proliferation. Renal hypertrophy is complete by one week.(5, 10, 11)In an originally normal kidney, GFR returns to70- 80% of the 2 kidneys. (5, 10)This is due to the adjustments in the tubulo-glomerular and glomerulo-tubular balance resulting from increased renal blood flow with resultant increase in angiotensin II and endothelin levels in the efferent arterioles; these cause vasoconstriction which results in increased intraglomerular filtration pressure and hypertension.

The number of nephrons in the remaining kidney determines the kidneys' adaptation to the physiologic demands of blood pressure, body size and environmental stressors (5, 10).

1.3 MECHANISMS FOR GLOMERULAR INJURY

Various mechanisms have been hypothesized trying to explain glomerular injury following nephrectomy as a step by step process.

Increased glomerular blood flow and intra-glomerular filtration pressure cause persistent intraglomerular hypertension resulting in injury to the glomeruli which engenders protein leak into the tubular fluid. Significant glomerular proteinuria is associated with accumulation of mononuclear cells, T-lymphocytes and monocytes in the interstitium. The resulting nephritogenic immune response produces interstitial nephritis. Some tubular epithelia respond by disaggregating from their tubular basement membrane and the adjacent sister cells undergo epithelial-mesenchymal transitions forming interstitial fibroblasts. Finally, fibroblasts lay down collagenous matrix that disrupts adjacent capillaries and nephron tubules resulting in scar formation (5).

Increased levels of angiotensin II has been noted in the efferent arterial and the ultra filtrate. This stimulates cellular growth via G-protein phosphorylation which activates DNA transcription of several cytokines and growth mediators such as TGFβ and TNFα that cause extracellular matrix accumulation and fibrosis (5, 11)

Hyperfiltration results in increased GFR which may cause nephrons to lose the ability to auto regulate. as a result systemic hypertension is transmitted to the glomeruli. This may result in glomerulosclerosis and reduced renal mass (5, 11)

1.4 POTENTIAL RISKS AND COMPLICATIONS IN LIVING KIDNEY DONORS

Fourcade J. *et al* (12) noted compensatory renal hyperfunction in a prospective study of 99 donors at Hospitalier de Chancery, Lyon. Measurement of serum creatinine and microalbuminuria was done; a lasting increase in GFR of 40% and renal plasma flow of 33% was noted. Microalbuminuria was noted in a few patients. They suggested the need for long term follow up.

Wan *et al* (13), noted reduced kidney function in renal donors. He analyzed 72 consecutive donors between the year 2000 and 2005, who had isotopically measured GFR >80mls/min/1.73m^2 predonation (mean103.4mls, sd 15.6mls); mean creatinine was 90.2 umols/l, sd 15.1umols/l. One year after donation mean serum creatinine was 118.6umols/l, sd 19.9umols/l consistent with studies in other metanalysis. However, this equated to a mean eGFR of 54.7±9.26mls /min/1.73m^2; resulting in 73.6% of donors with eGFR of <60mls/min/1.73m^2, equivalent to stage 3 CKD.

Sagev D. L. *et al* (14), examined perioperative mortality and long-term survival following live kidney donation. He analyzed data recorded between 1994 and 2009 by Organ Procurement and Transplantation Network from 80,347 live kidney donors, 21,603 were non white and compared the mortality rates of live kidney donors with those of healthy participants of National Health and Nutrition Examination Survey (NHANES) III after statistically sampling and matching the socio-economic and demographic factors. He concluded that, live donor nephrectomy was one of the safest operations and did not increase mortality during the study period (15, 16), however subtle physiological changes after kidney donation and their consequences needed to be investigated.

Michael Siebels *et al* (10) studied 166 living kidney donors between 1994 and 2001. Mean follow up time was 38 months. He assessed for new onset hypertension, proteinuria and

serum creatinine levels. He established that one kidney function returned to 73% of the initial value of two kidneys. The incidence of proteinuria was low and mainly occurred in the elderly. He concluded that living donor nephrectomy carried a minimal risk of progressive renal dysfunction.

Massimo Gai *et al* (17), in their review of the potential risks of kidney donation found that hypertension, protenuria and decline in GFR were potential long term complications related to kidney donation. They also noted that donors with GFR of <80 mls/min were at increased risk of developing renal impairment. In addition, the prevalence of proteinuria and albuminuria was found to be 20% and 30-40% respectively with more males being affected than women and this was attributed to hyperfiltration damage and Focal Segmental Glomerulosclerosis (FSGS). No significant difference with the general population was noted for hypertension. They therefore concluded that living kidney donation was a safe and low-risk procedure, but careful selection of donors and long-term follow up was necessary. Similar findings have been noted by other studies: (18-21)

Nilay S. Patel *et al* (9) recently noted at one year post live kidney donation an increase in mean serum creatinine level from 83 to 112umol/L. This translated into a mean eGFR from 100-59mL/min/1.73m^2. At one year 53% of patients could be classified as having CKD stage 3-4. However mean GFR did not change significantly between 1 and 5 years.
New onset hypertension was diagnosed in 10% of subjects

1.5 RACIAL VARIATION IN MEDICAL OUTCOMES AMONG KIDNEY DONORS

Lentine K.L.*et al* (22), analyzed data from Organ Procurement and Transplantation Network (OPTN) registry and a private health insurance provider to obtain information on long-term outcome of individuals after donation independent of their interactions with transplant centre beyond OPTN 2 year follow up. Median follow up time was 7.7 years. Of the population studied, 73.6% were white, 13.1% black, 8.2% Hispanic, 2.4% other races. He found increased risk of CKD and hypertension in blacks and Hispanics irrespective of their social status. He concluded that lifetime co-morbidities, CKD and ESRD were increased in blacks and Hispanics in general and seamed to include non white people who had donated kidneys. He advocated for longer and more reliable follow up for renal donors.

In North America, the incidence of ESRD is 4-6 times in African Americans compared to whites (23). Various theories have been advanced to try and explain the disparities in the prevalence and rate of renal progression among different races: To start with, low socioeconomic status is thought to be a cause of poor access to health care and increased prevalence of co-morbidities (25). Furthermore, race may be associated with genetic differences in: inflammatory and fibrotic pathways, renal response to injury, sensitivity to salt, toxins, medications and to hemodynamic auto regulation (1). In addition, it has been postulated that blacks have fewer nephron numbers; some of the reasons advanced for these are low birth weight, maternal hypertension and smoking among others. All this factors are thought to result in nephromegaly which predisposes them hyperfiltration with resultant accelerated renal progression when compared to the whites (21, 25-28).

1.6 RENAL DONORS LIVE NORMAL LIVES

Fehrman-Ekholm *et al* (16) examined survival and causes of death among kidney donors. He also assessed renal function in those who had donated a kidney 20 years prior. He found mortality that was similar to that of the general population. After 20 years follow up, 85% of live donors were alive whereas the expected survival rate was 66%. Deterioration in renal function was similar to that seen among normal subjects. Better survival among donors was thought to be probably due to selection bias of only healthy individuals as donors.
Similar results were arrived at by Goldfarb *et al* (15) who noted overall well preserved renal function 25 years after donor nephrectomy.

In South Africa, Cassidy and Beck (7) studied renal function of 12 live kidney donors who had donated a kidney 3-10 years previously. They observed no clinically significant impairment in renal function.

2.0 STUDY JUSTIFICATION

The burden of CKD and ESRD is on the rise and it is associated with increased consumption of public health resources. Living kidney donation and transplantation is the best form of renal replacement therapy available since compared with dialysis it is associated with low incidence of complications and is cost effective overall.

The little data available regarding renal function of kidney donors post nephrectomy is from Europe, North America and Asia Pacific and seems to suggest that the course of renal function decline may be accelerated in blacks compared to whites. The studies available are inconclusive and suggest the need for more studies on the subject.

Kenya is among a few African countries that perform kidney transplantation in tropical sub-Saharan Africa with predominantly African race. Others include Nigeria and Cameroon albeit on low scales yet none of these countries have shown renal function status of their living kidney donors. In the rest of Africa kidney transplantation services are offered in South Africa, Egypt, Morocco, Algeria, Tunisia, Sudan, Mauritius and Libya (2). In spite of this, there is limited data regarding kidney function post live kidney donation.

This study aims to evaluate the renal function status of the kidney donors at Kenyatta National Hospital and also generate local African based data. The study will determine if there are any detrimental short term changes in renal function of live kidney donors. Data generated from this study will form a bench mark for future studies on the same topic. It is also hoped that the results may be used to help formulate policy guidelines on kidney donation and follow up at Kenyatta National Hospital.

3.0 RESEARCH QUESTION

What is the renal function of living kidney donors at Kenyatta National Hospital?

4.0 OBJECTIVES

4.1 Broad objective

- To asses renal function of living kidney donors at Kenyatta National Hospital.

4.2 Specific objectives

1. To determine serum creatinine levels and eGFR of living kidney donors at KNH
2. To compare renal function pre and post-kidney donation using eGFR at KNH.
3. To determine the prevalence of proteinuria among living kidney donors at KNH.
4. To determine the prevalence of hypertension in living kidney donors at KNH

5.0 MATERIALS AND METHODS

5.1 Study design

Cross sectional descriptive study.

5.2 Study site

The study was conducted at Kenyatta National Hospital renal unit.
KNH is the principal public treatment centre for ESRD and the main national teaching and referral hospital.

5.3 Study population

All individuals who had had live donor nephrectomy at Kenyatta National Hospital in the period starting one week and beyond post nephrectomy

5.4 Eligibility criteria

5.4.1 Inclusion criteria

1. All persons who had had donor nephrectomy at Kenyatta National Hospital one week and beyond from time of study
2. Those who gave written informed consent.

5.4.2 Exclusion criteria

1. Persons who had had donor nephrectomy less than one week from the time of study
2. Persons who refused consent

5.5 Recruitment

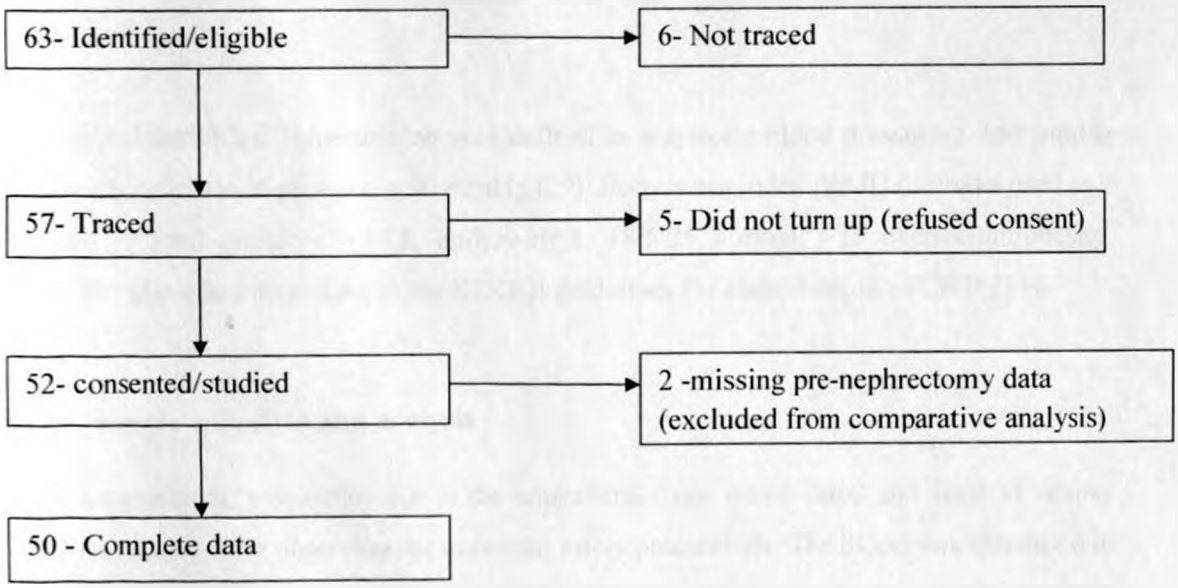

Figure 1: Recruitment flow chart

The study was carried out after approval from the University of Nairobi Department of Medicine and Therapeutics and KNH/UON Research and Ethics Committee. Persons who met the inclusion criteria were contacted through their mobile phone numbers available in their files or where this was not available, through their respective renal allograft recipients

who are followed up regularly at the renal clinic. The reason for their being contacted was explained and those who agreed were given an appointment to come to KNH renal unit for review and possible recruitment. From the records available, 63 persons were eligible for recruitment. 57 persons were traced. 52 of those traced were included in the study. A total of 11 eligible persons who did not participate in the study were 4 males and 7 females. This was a population study hence all persons who met the inclusion criteria were recruited and studied.

5.6 Data collection/procedures

All persons studied signed a written informed consent form upon agreeing to participate in the study (see appendix 1). The principal investigator then administered the study questionnaire by way of direct questioning (see appendix 2). The BP, weight and height were measured in the standard way using standardized measuring instruments. The BMI was then calculated, using the formula: BMI=weight (KGs)/height (M^2). All data collected was entered in the questionnaire.

The clinical variables: Hypertension was defined as a systolic blood pressure $\geq$ 140 mmHg and /or diastolic blood pressure $\geq$ 90 mmHg (29). Body mass index (BMI) (30) was used as a measure of total obesity : <18.5, underweight: 18.5-25 normal: >25 overweight/obesity. eGFR was classified according to the KDOQI guidelines for classification of CKD (31).

5.6.1 Sample collection and analysis

Using a tourniquet, a suitable vein in the antecubital fossa was located and 2mls of venous blood was drawn after observing the universal safety precautions. The blood was dispensed in a clean labeled cuvette. A clean labeled poly pot was given to the participants to collect 5mls of midstream spot urine specimen. The samples were submitted to KNH renal laboratory for analysis.

Proteinuria was measured using a standard urine dip stick and the result was noted.
Analysis for serum creatinine was done by direct calorimetric method using Technicon RA-1000 analyzer.

Pre-nephrectomy records were reviewed and documented pre-nephrectomy data was extracted with the most recent result/ value of the study variables recorded.

eGFR was calculated using Cockroft-Gault equation:

eGFR=(140-age in years)weight(KGs) x a constant/serum creatinine: where the constant value for males and females is 1.23 and 1.04 respectively

5.6.2 Quality assurance

All measurements and specimens collected were undertaken using standard instruments and techniques. In addition, standard operating procedures were followed in carrying out of laboratory investigations.

5.6.3 Data storage

All the raw data in this study was filed and stored in a lockable drawer accessible only to the principal investigator. In addition, all the sheets were checked to confirm completeness before being filed. Furthermore, the data was entered by the principal investigator into a pass word protected ms-excel data base.

5.6.4 Data presentation and analysis

Analysis was undertaken using the SPSS version 17.0 statistical software with the input of a statistician who was involved since the beginning of this study. Descriptive statistical analyses such as means, medians and standard deviations were generated for continuous variables and frequency tables were produced for categorical variables. Prevalence conditions were calculated as percentages within 95% confidence intervals. Associations between pre and post live kidney donation BP, eGFR and serum creatinine was made using paired student t-test. Statistical significance was defined as p-value of ≤ 0.05.

6.0 ETHICAL CONSIDERATIONS

Measures were undertaken to safeguard the interests of all persons who participated in this study. The study was carried out following approval and written permission from UON/KNH research and ethics committee. The benefits of the study and the expected risk were fully explained to the participants. Informed consent was sought in writing and those who did not

consent were not discriminated against. All patients' data were treated with utmost confidentiality at all stages of the study by the principal investigator. Only samples intended for the study were drawn. Results relevant to the management of the donors were promptly relayed to the renal team to help in the management and follow up. Furthermore, patients were educated on lifestyle and behavior that leads to the preservation of function in the remaining kidney like maintenance of healthy weight, nutrition, exercise and avoidance of indiscriminate use of non prescription medication.

7.0 RESULTS

Between October 2011 and April 2012, 52 out of the expected 63 living kidney donors were studied; 25 females and 27 males. The mean age at donation was 32.73 years, with the youngest age of 21 years and the oldest of 50 years. Of the 11 not studied, 7 were female and 4 were male. The socio-demographic characteristics of those studied are summarized in tables 1 and 2.

Table 1: socio-demographic characteristics

		n	%
Sex	Female	25	48.1
	Male	27	51.9
	Total	52	100.0
Age group at donation (years)	20-29	23	44.2
	30-39	17	32.7
	40-49	10	19.2
	50-59	32	3.9
Mean age(SD)(years)	32.73(8.64)		
Range (years)	21-50		

Table 2: socio-demographic Characteristics

Marital Status	Single	16	30.8%
	Married	35	67.3%
	Other	1	1.9%
	Total	52	100.0%
Education Level	Primary	10	19.2%
	Secondary	10	19.2%
	Tertiary	32	61.5%
	Total	52	100.0%
Employment status	Employed	33	63.5%
	Unemployed	18	34.6%
	Retired and Pensionable	1	1.9%
	Total	52	100.0%

Majority of our patients were married, had tertiary education and were in gainful employment. However, donor sources cut across all socio-demographic charecteristics.

Table 3: Medical History

History	No		Yes		Total
	N	%	N	%	N
Significant illness post kidney donation	51	98.1%	1	1.9%	52
Hospital admissions post-kidney donation	52	100.0%	0	.0%	52
Routinely uses analgesics or NSAIDS	51	98.1%	1	1.9%	52

Generally all patients enjoyed good physical health. Only one 60 year old woman used NSAIDS routinely as analgesia for the pain from osteoarthritis that had been prescribed for her in the orthopedic clinic.

Table 4: Clinical variables

Variable	n	Mean (Range)	Median	Standard Deviation
Duration post-nephrectomy (months)	52	15.90 (0.4-157)	12.50	23.90
post-nephrectomy BMI (kg/m^2)	52	24.40 (17.4-34.9)	23.65	4.13
Serum creatinine(µmols/l) : pre-nephrectomy	50	86.50 (51-123)	86.00	13.73
post-nephrectomy	52	106.15 (51-229)	106.00	29.58
eGFR (mls/min/1.73M^2) pre-nephrectomy	50	93.39 (53.2-150.4)	90.09	21.34
post-nephrectomy	52	80.25(37.1-186.5)	70.55	31.91

The duration post kidney donation ranged from a minimum of two weeks to a maximum of 15 years with a mean of 15.9 months. The mean BMI post kidney donation was 24.40, standard deviation 4.13. There was a significant rise in serum creatinine level from a mean pre-nephrectomy level of 86.50 µmol/l to106.15 µmols/l post-nephrectomy. As a result a significant drop was observed in the eGFR from a mean pre-nephrectomy level of 93µmols/l to 80.25µmols/l.

Table 5: eGFR pre -nephrectomy

eGFR(mls/min/m²)	n	%
<15	0	0%
15-29.999	0	0%
30-59.999	3	6.0%
60-89.999	21	42.0%
≥90	26	52%

Table 6: eGFR post-nephrectomy

Stage	eGFR(mls/Min/m²)	n	%
5 (ESRD)	<15	0	0%
4	15-29.999	0	0%
3	30-59.999	10	19.2%
2	60-89.999	28	53.8%
1	≥ 90	14	26.9%

Majority of the kidney donors could be classified as CKD stage 2 (54%) and stage 1 (27%) post kidney donation.

Table 7: Prevalence of Proteinuria

Degree of proteinuria	N	%
Nil	41	78.8
Trace(15-30mg/dl)	7	13.5
+ (30-100mg/dl)	3	5.8
++ (100-300mg/dl)	0	0
+++(300-1000mg/dl)	1	1.9
++++(>1000mg/dl)	0	0
Total	**52**	**100**

Majority of patients with proteinuria had mild proteinuria with either trace or +. Only 1 had +++, probably nephritic.

Table 8: Prevalence of hypertension

		N	%
Pre-nephrectomy HTN	No	48	96.0%
	Yes	2	4.0%
Post-nephrectomy HTN	No	47	90.4%
	Yes	5	9.6%

Hypertension was defined as systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg. Hypertension was documented in 4% of the study subjects pre-nephrectomy. Post-nephrectomy, hypertension was observed in 9.6% of the population. There were three cases of new onset hypertension making 6% of the population. All cases were stage one hypertension.

Table 9: Mean change

Variable	Mean	95% CI		P Value
		Lower	Upper	
Change in Serum creatinine (µmol/l)	19.98	11.50	28.46	<0.0001
Change in eGFR (mls/min)	-13.43	-21.58	-5.28	0.002
Change in BP Systolic (mmHg)	2.36	-1.39	6.11	0.211
Change in BP Diastolic (mmHg)	4.10	1.12	7.08	0.008

Significant mean change pre and post-nephrectomy was observed for serum creatinine, eGFR and diastolic blood pressure with p values of <0.0001, 0.002, and 0.008 respectively.

Table 10: Post-nephrectomy BMI

		n	%
Underweight	<18.5	2	3.8
Normal	18.5-24.999	29	55.8
Overweight	25-29.999	14	26.9
Obese	>=30	7	13.5
Total		**52**	**100**

40.4 % of the kidney donors were either overweight or obese post kidney donation.

7.0 DISCUSSION

In this cross-sectional descriptive study kidney donors generally did not report any ill health. None had been admitted in hospital or suffered any significant physical illness. Only one patient used non steroidal anti-inflammatory drugs regularly for osteoarthritis.

The population was composed of mainly young kidney donors with a similar sex distribution. However, a total of 11 eligible persons did not participate in the study, 4 males and 7 females. Most donors who did not honor the appointment for participation cited feeling healthy and work commitments as the reason for their non participation. The mean duration post live kidney donation was 15.9 months reflecting the life of the **Interlife project.**

Serum creatinine and eGFR

Studies have shown that following live kidney donation, renal adaptation is complete by one week (5, 10, 11) and GFR returns to 70-80% of the original.

A significant mean increase in serum creatinine with a corresponding decline in eGFR was observed. The study participants recovered 85.62% of the original 2 kidney function post kidney donation. 80.8% of the participants could be classified as CKD stage 1 and 2 with only 19.2% being classified as stage 3. It is important to note that in the initial pre-nephrectomy work up of potential kidney donors isotopically determined GFR by DTPA method was used.

Wan *et al* (13) studied 72 patients and noted that at 1 year following kidney donation in his group of patients who had had isotopically determined GFR mean of 103.4 mls/min (SD 15.1mls/min) and serum creatinine 90.2μmols/l (SD 15.1μmols/l). One year later had mean serum creatinine levels of 118.6μmols/l(SD 19.9 μmols/l) resulting in eGFR of 54.7mls/min/1.73M²(SD 9.26μmols/min/1.73M²). Thus, 73% of the donors had eGFR <60mls/min/1.73M² equivalent to CKD stage 3.

Michael Siebels *et al* (12) observed that kidney function returned to73% of the initial value of 2 kidneys after he followed up 166 patients for a mean of 38 months.

Nilay S. Patel *et al* (9) noted that at 1 year following live kidney donation, mean eGFR declined from 100mls/min/1.73M² to 59mls/min/1.73M². Thus, 53% of his patients were classified as CKD stage 3 or 4. However he noted that kidney function remained stable thereafter.

Forcade *et al* (12) noted a lasting increase in GFR of the remaining kidney of 40% following donor nephrectomy.

The results of the study compares with those from the studies mentioned above such that an elevation in serum creatinine and consequently an overall decline in eGFR was demonstrated. An increase in one Kidney eGFR was also demonstrated. It is thought that the increase in GFR post-nephrectomy is partly a consequence of hyperfiltration and intraglomerular

hypertension emanating from tubule-glomerular and glomerulo-tubular balance adjustments which results in elaboration of the vasoconstrictors, angiotensin II and endothelin in the efferent glomerular artery (5; 10). The study demonstrated a higher mean eGFR compared to other studies which may indicate a higher degree of hyperfiltration the studied patients. This could be explained partly by the higher prevalence of overweight and obesity in our patients of 40%. The Cockroft-Gault equation was used to estimate the GFR; the formula results are weight dependent hence the possibility of overestimating GFR in individuals with a big weight.

Of the participants with low eGFR post-nephrectomy one was a 60 year old who had donated a kidney 15 years prior hence the possibility of the natural loss of nephrons with advancing age could probably explain. Also, some of the participants had a low weight hence the risk of underestimating the GFR since the formula used is weight dependent. However, majority did not have anything significant observed that could explain the low eGFR.

Proteinuria and microalbuminuria

A prevalence of proteinuria of 21.2% that was mainly mild was observed.
Massimo Gai *et al* (17), in their review of studies that have assessed kidney function in live kidney donors, noted a proteinuria prevalence of 20% and albuminuria prevalence of 30-40%. Forcade *et al* (12) noted microalbuminuria in a few patients while Michael siebels et al (10) noted a low incidence of proteinuria mainly in elderly patients.

The prevalence of proteinuria in the study compares with that of Massimo Gai *et al* (17). It is possible that the hyperfiltration observed in the study subjects could have contributed to the pathophysiology of proteinuria. No evidence of urinary tract infection was noted on the urine dip stick examination of the participants who had proteinuria. It has been postulated that persistent intraglomerular hypertension results in subtle injuries to the glomeruli with consequent increase in protein leakage into the tubular fluid (5).

Hypertension

The prevalence of hypertension of 9.6% and new onset hypertension of 6% was observed.

Nilay S. Patel *et al* (9) diagnosed new onset hypertension in 10% of his study subjects at one year post nephrectomy.

Massimo Gai *et al* (17) noted no significant difference in hypertension between live kidney donors and the general population.

Abdu *et al* (8) in South Africa documented the prevalence of hypertension in live kidney donors of 24%, range duration post nephrectomy of 1-16 years.

In a similar setting as the study', unpublished studies by Hassan and Njau for their Masters of Medicine in Internal Medicine dissertation found the prevalence of hypertension in the general population at 12.6% and 13% respectively. The lower prevalence in the study compared to that of the general population could be due to the fact that the kidney donors are highly selected, young and healthy group before kidney donation.

8.0 CONCLUSION

Post-nephrectomy, the donors regained renal function with a tendency towards hyperfiltration. Serum creatinine increased significantly and there was a corresponding significant decline in eGFR. The prevalence of proteinuria was low but compared well with those obtained in other studies. The prevalence of hypertension was low. The results of the study compares with those obtained in other studies.

10.0 RECOMMENDATIONS

In view if the results obtained from the study, protocol follow up of live kidney donors, for example 6 monthly to help establish the general trend of kidney function following live kidney donation was recommended. Further, controlled studies on this group of subjects needed to be carried out in order to establish factors that may be associated with the outcome of kidney function following live kidney donation. In addition, subtle changes observed in the form of single kidney hyperfiltration, proteinuria and new onset hypertension need to be monitored. Also quantitative tests for urinary protein to be carried out on individuals who had

positive tests on urinary dip stick for protein as part of follow up to ascertain the degree of proteinuria.

11.0 STRENGTHS OF THE STUDY

The strengths of the study are that to the best of our knowledge this is the first study to evaluate renal function among kidney donors in our setting. Thus, the results of this study may be used as a bench mark for future studies on the subject matter. Furthermore, to our knowledge, the study is the first to study a homogeneously African population by race hence it gives the first insight regarding renal function of the black African kidney donors.

12.0 STUDY LIMITATIONS

The limitations of the study include the fact that GFR was not determined isotopically using the DTPA method hence the GFR is an estimate. In addition, it was not possible to trace and study all eligible kidney donors: as a result it is not possible to tell whether their inclusion would have altered the results. Also the population studied was homogeneously African hence extrapolation of the results obtained from this study to other races may not be possible.

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APPENDICES

Appendix 1: CONSENT FORM

RENAL FUNCTION IN LIVING KIDNEY DONORS AT KNH

This is a study done in part-fulfillment of the degree of master of medicine in internal medicine

Purpose of the study

This study aims to establish baseline renal function in living kidney donors and lay ground for establishing guidelines for follow up of renal donors at Kenyatta national hospital renal unit.

Voluntary participation

Your participation in the study is voluntary and attracts no financial benefits.

A questionnaire will be administered to you as part of this study.

Benefits for participating

If any abnormality is found, the information shall be conveyed to the renal physician for appropriate action.

Risks and complications

No other risks are expected apart from a mild bearable pain during blood sampling

Confidentiality

- The principal investigator shall be charged with the responsibility of retrieving data from the patients' files and calling those recruited.
- Information volunteered to the researcher will be treated in confidence.
- Blood and urine sampled will be used as intended and the remaining shall be discarded promptly.

Declaration

I.....

Do hereby agree voluntarily to participate in this research on **renal function in renal donors at KNH.** The details of the study have been explained to me by **Dr. Ochwila.**

Signed..... (Participant)

Witness/researcher.....

Dated: .....

NB: For any questions or clarifications do not hesitate to contact the principal investigator, Dr Ochwila on cell phone number 0720428294.

Appendix 2: QUESTIONNAIRE

RENAL FUNCTION IN LIVING RENAL DONORS AT KNH

Dear sir/madam.

Thank you for accepting to participate in this important study. By doing so, you have agreed to be part of a scientific process which will positively impact on follow up and management of living kidney donors. Please answer a series of questions that I will read to you. Hopefully, you will do this to the best of your ability.

Thank you for accepting to spare this very valuable time.

Dr Ochwila (principal investigator)

Questionnaire Design

File no. .....

Patient's study no. .....

BIODATA

1. Name..... (optional)
2. Sex: Male ☐ Female ☐
3. Age .....years
4. Marital status: Single ☐ Married ☐ Other ☐
5. Level of education: Primary ☐ Secondary ☐ Tertiary ☐
6. Status of employment: Employed ☐ unemployed ☐ Retired and pensionable ☐

MEDICAL HISTORY POST NEPHRECTOMY

a. Have you suffered from any medical illness since the time you donated your kidney?
   1. Yes ☐ 2. No ☐
b. If yes in a above, specify the illness/signs and symptoms.
   .....
   .....

c. Have you been admitted in hospital ever since you had nephrectomy?
   1. Yes ☐ 2. No ☐

d. Reason for admission in c above and treatment

.....

.....

e. Do you routinely use analgesics/ NSAIDS?

1. Yes ☐ 2. No ☐

f. Do you suffer from diabetes mellitus?

1. Yes ☐ 2. No ☐

g. If yes in how long have you been diabetic? .....years

h. Do you have a family history of hypertension?

1. Yes ☐ 2. No ☐

OFFICIAL USE ONLY

1. Date of renal donation.....

2. Date of review/specimen collection.....

3. Blood pressure : pre-nephrectomy .....(mmHg)

Post-nephrectomy.....(mmHg)

4. Weight: pre-nephrectomy .....(Kgs)

Post-nephrectomy ..... (Kgs)

5. Height.....(M)

6. BMI.....

7. Serum creatinine: pre-nephrectomy .....umols/l

Post-nephrectomy .....umols/l

8. Urinalysis: proteins .....

   Spot urine microalbumin.....

9. Estimated GFR: Pre-nephrectomy .....

   Post-nephrectomy .....

Appendix 3: KENYATTA NATIONAL HOSPITAL-RENAL UNIT: RECIPIENT/DONOR EVALUATION FORM

RECIPIENT		
NAME..... IP NO..... AGE.....SEX..... WT.....HT.....BP.....		
STAGE 1	Counselling Consent	
STAGE 2	Blood group HIV HBV HCV	
STAGE 3	HLA	A B DR DQ T CELL X-MATCH
STAGE 4	UREA CREATITINE K,NA,CA,PO4 URIC ACID HB WBC,PLT,ESR FBS URINALYSIS LFT LIPID PROFILE	
STAGE 5	KUB U/S DOPPLER U/S OF FEMORALS/ILIACS PLAIN ABD XRAY	RT KIDNEY LT KIDNEY
STAGE 6	CT ANGIOGRAM* CXR ECG/ECHO CMV IgG/IgM STOOL O/C CYSTOSCOPY PAP/PDT/PSA	
STAGE 7	PROPOSED DATE PRE-OP WORKUP	

*CT angio if >40 years; Doppler U/S if <40 years

DONOR		
NAME..... IP NO..... AGE.....SEX..... WT.....HT.....BP.....		
STAGE 1	Counselling Consent	
STAGE 2	Blood group HIV HBV HCV	
STAGE 3	HLA	A B DR DQ T CELL X-MATCH
STAGE 4	UREA CREATITINE K,NA,CA,PO4 URIC ACID HB WBC,PLT,ESR FBS URINALYSIS LFT LIPID PROFILE	
STAGE 5	KUB U/S DTPA	24-HR CREAT CLEARANCE RT LT
STAGE 6	CT ANGIOGRAM CXR ECG/ECHO CMV IgG/IgM	
STAGE 7	PROPOSED DATE PRE-OP WORKUP	

CT angio (aorta/iliac/femoral incl venous phase)

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13th October 2011

Dr. Ochwila Bwire Austine
Dept. of Clinical Medicine & Therapeutics
School of Medicine
University of Nairobi

Dear Dr. Bwire .

Research Proposal: "Renal Function of Living Kidney Donors at Kenyatta National Hospital" (P301//08/2011)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and **approved** your above revised research proposal . The approval periods are 13th October 2011 – 12th October 2012.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing planned research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY. KNH/UON-ERC

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"PROTECT TO DISCOVER"