Seifemichael Getachew, Mahteme Bekele, Engida Abebe, Tekleberhan Berhae, Mekdim Tadesse, Kenth wodside, Leja Hamza, Berhanu Worku, Hamelemal Gebeyehu, Berahne Redae, Balkachew Nigatu, Wondemagegn Gezhegn, Zerihun Abebe, Senait Fisha, Mersema Abate, Fasika Tedla, Aklilu A. Yishak, Jeffery D Punch, Alan Lechieman, Momina Ahmed. *Ethiop Med J, 2020, Supp. 1*

ORIGINAL ARTICLE

CLINICAL OUTCOME OF RENAL ALLOGRAFT DONORS AT NATIONAL KIDNEY TRANSPLANT CENTER IN ADDIS ABABA, ETHIOPIA

Seifemichael Getachew, MD[1*], Mahteme Bekele, MD[1], Engida Abebe, MD[1], Tekleberhan Berhae, MD[1], Mekdim Tadesse, MD, MHE[1], Kenth wodside, MD[2], Leja Hamza, MD[1],Berhanu Worku, MD[1], Hamelemal Gebeyehu, MD[1], Berahne Redae, MD[1], Balkachew Nigatu, MD[1], Wondemagegn Gezhegn, MD[1], Zerihun Abebe, MD[1], Senait Fisha, MD, JD[2], Mersema Abate, MD,MPH[5], Fasika Tedla, MD,Msc[3], Aklilu A. Yishak, MD,MPH,FASN[4], Jeffery D Punch, MD[2],Alan Lechieman, MD[2], Momina Ahmed, MD[1]

ABSTRACT

Introduction: *Chronic kidney disease is defined as the presence of one or more markers of kidney damage for greater than three months. The global burden of chronic kidney disease is increasing accompanied by increase in need of kidney transplantation and the number of living donors. Studies show that kidney donation has a medical risk to the donor with differences based on varying demographics. In Ethiopia, there is no report on the risk to the donors associated with possible medical complications.*

Objectives: *To assess medical outcome of renal allograft donors at the national kidney transplant center.*

Methods: *A cross-section chart review study was conducted at St. Paul Hospital's Millennium Medical College in Addis Ababa among 43 kidney donors who were on follow up from September 2015 to August 2018. Data was collected using pretested data abstraction tool. Epi-Info version 7.2.1.0 was used for data entry and SPSS version 23.0 and STATA version 14.1 were used for analysis.*

Results: *Median duration of follow up was 12 months. Majority of the donors were young less than 40 years, with mean pre-donation glomerular filtration rate 125ml/min and more than half were females. No cardiovascular event occurred during the follow up and 4(20.7%) of the females had post donation successful pregnancy without pregnancy related complications. Post donation hypertension and Chronic Kidney Disease were detected in 9.3 and 4.7 % of the donors.*

Conclusions: *The development of post donation hypertension and chronic kidney disease indicates the need for regular follow up of donors group .This study also recommend further study with a relatively longer duration of follow up to reach at a better conclusion.*

Key words: *Renal allograft donor, medical outcome, retrospective chart review, survival analysis, Ethiopia*

INTRODUCTION

Chronic kidney disease (CKD) is defined as the presence of kidney damage (urinary albumin excretion of 30 mg/day or more, or equivalent) **or** decreased kidney function (glomerular filtration rate (GFR) less than 60 mL/min/1.73m^2) for three or more months, irrespective of the underlying cause. Available evidence suggests that CKD is a risk factor for cardiovascular disease, premature mortality, and decreased quality of life. Among patients with CKD, the risk of death, particularly due to cardiovascular disease, is much higher than the risk of eventually requiring dialysis. Once the patient has reached GFR of less than 15 mL/min we call it end-stage renal disease (ESRD) (1,2).

The overall global burden of CKD is showing an increase. According to the U.S Centers for Disease Control and Prevention (CDC) report , the prevalence of ESRD increased by more than double between 1990 and 2015 (3). The Global Burden of Disease Study shows that kidney disease was 18th global leading cause of death, accounting for 1.1 million deaths worldwide and the 17th leading cause of global years of life lost in 2015. This rising burden of CKD disproportionately impacts low- and middle-income countries, where growth in obesity and diabetes is showing an increase (3-5). A systematic review of literatures among African countries shows that in the community-level the prevalence of CKD ranged from 2% to 41% and in

[1]St. Paul's Hospital Millennium Medical College. [2]University of Michigan. [3]Icahn School of Medicine at Mount Sinai. [4]Tysons Corner Medical Center. [5]Zucker School of Medicine at Hofstra/Northwell.
*Corresponding Author E-mail: getseyfem@gmail.com

high-risk groups it ranged from 1% to 46% in patients with HIV, 11%–90% in patients with diabetes and 13%–51% in patients with hypertension and in sub-Saharan African countries the overall prevalence of CKD was 13.9% (6, 7). A study conducted in Butajira hospital, southern Ethiopia shows that 18.2% and 23.8% of the study participants were found to have CKD, as defined by eGFR < 60 ml/min/1.73 m2, according to the MDRD and Cockroft-Gault equations, respectively (8). The increase in CKD burden is accompanied by increase in need of renal replacement therapy particularly kidney transplantation increasing the number of living donors in parallel. Since the first kidney transplantation done over 60 years ago, living kidney donation is the gold standard among renal replacement therapy for ESRD (9). Studies show that rates of living donor kidney transplant have steadily risen in most regions of the world, increasing its global significance as a treatment option for kidney failure (10-12).

Studies conducted around the world regarding long term outcome of kidney donors shows different type and degree of complication based on difference in population characteristics, genetic make-up and other factors. Some studies show no increased risk or even lower risk of mortality, ESRD, hypertension, proteinuria, pregnancy complications, cardiovascular disease, quality of life, life expectancy and others as compared to the general population (13-15). Other studies show increased risk of complications with major associated factors being black race, male sex, old age in non black donors, higher Body Mass Index (BMI) and a close biological relationship to the recipient (13,14,16-24).

In Ethiopia, since the establishment of the National Kidney Transplantation Center at St. Paul's Hospital Millennium Medical College (SPHMMC) on 2015 a total of 52 living kidney transplantations have been done. Studies regarding medical risk of kidney donation have not been conducted at the center. Donors are individuals who volunteer to save others' lives with no known benefits but accepting the risks the donation may carry. Therefore, it is important to identify potential complications so that donors make a choice with the knowledge of potential risks that are associated with kidney donation.

Knowing the occurrence of post donation complications among donors will help to identify prospective donors with long term risk of ESRD, for planning medical follow up and treatment to minimize complications and their effects and for counseling and providing informed consent. There is also a need for data that can be used as baseline for further studies in the field.

The aim of this study was to fill this gap by analyzing data on the medical outcome of renal allograft donors at the national kidney transplant center-SPHMMC from September 2015 to August 2018.

PATIENTS AND METHODS

The study was conducted in Addis Ababa, the capital city of Ethiopia, which has ten sub-cities and a total population of 3,273,001 (25). During the study period, there were 12 governmental hospitals in Addis Ababa. The study was conducted from April to July 2018 at one of the governmental hospitals, SPHMMC national transplant center. The transplant center has three nephrologists, four transplant surgeons, 20 nurses, and other supportive staffs with a functioning 15-bed dialysis unit, a four-bed Intensive Care Unit (ICU), ward, 24 hour working pharmacy and laboratory. The study design was hospital based retrospective chart review. Medical records of renal allograft donors who donated kidney since the opening of the transplant center were reviewed. The dependent variable is donor incidence of: CKD, Hypertension, Proteinuria, Pregnancy related complications, Diabetes mellitus and Cardiovascular event. The independent variables are classified into three categories: socio-demographic, pre donation medical status and post donation medical status related variables. The data collection was carried out by donor chart review, clinical evaluation and relevant laboratory data using pre-tested data abstraction tool that consists of questions to assess all the variables. The data was collected by trained professionals from April to July 2017.

The collected data was coded and entered into Epi-Info version 7.2.1.0, cleaned and stored and exported into SPSS version 23 for analysis. Descriptive statistics is presented with frequency tables, line graphs, Kaplan Meier (KM) plots and incidence density. Kaplan-Meier plots were used to compare survival experience of different groups of patients by using survival curves. Log-rank test was used to assess significant difference among survival distributions of groups for equality.

The study was conducted after ethical clearance was obtained from SPHMMC Institution Review Board (IRB) and written informed consent was obtained from the participants. The study had no risk/negative consequence for the participants. Medical record numbers were used for data collection and personal identifiers were not used in the research report. Access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the project.

RESULTS

Socio-demographic related variables

From the 52 donors, information was collected from 43. The rest were unavailable at the time of the study due to different reasons. Majority of the donors (51.2%) were in the age range of 23-29 years, 55.8% were females and more than half of the donors were married (58.1%).

Regarding educational status and occupation, majorities were College/University complete (44.2%) and were self employed (51.2%). Thirty-seven (86.0%) of them donated kidney to blood related (first degree) family members and the rest (14%) donated their kidney to their spouse **(Table 1).**

Table 1: Socio–demographic related variables among renal allograft donors at St. Paul Hospital's Millennium Mesial Center, Addis Ababa, 2018 (n=43)

Variable	Frequency	Percent (%)
Age		
23-29	22	51.2
30-39	13	30.2
40-49	4	9.3
>= 50	4	9.3
Sex		
Female	24	55.8
Male	19	44.2
Marital status		
Married	25	58.1
Single	18	41.9
Education		
Cannot read and write	6	14.0
Primary school	4	9.3
High school	14	32.6
College/University	19	44.2
Occupation		
Government employee	12	27.9
Self-employee	22	51.2
No job	6	14.0
Student	3	7.0
Relationship with the recipient		
Blood related	37	86.0
Spouse	6	14.0

Pre donation medical status related variables

The mean glomerular filtration rate (GFR) measured before donation among the donors were 125.1 +- 21.3 SD.

Regarding blood pressure measured before donation, the mean systolic and diastolic pressure among the donors were 112.8 +- 9.7 SD and 74.7 +- 7.4 SD respectively **(Table 2)**.

Table 2: Pre donation medical status related variables among renal allograft donors at SPHMMC, Addis Ababa, 2018 (n=43)

Variable	Mean	Standard deviation
Pre-GFR	125.1	21.3
Systolic blood pressure	112.8	9.7
Diastolic blood pressure	74.7	7.4

Post donation medical status related variables

Regarding post donation health status, none of the donors developed diabetes mellitus or cardiovascular event. Only one sixth (16.7%) of the female donors got pregnant post donation but none of them developed pregnancy related complications.

Among the 43 donors, two (4.7%) of them has developed CKD after one year of donation while 41 (95.3%) did not develop CKD during the three years observation period. Only four (9.3%) of the donors developed post donation hypertension and the rest (90.7%) had normal post donation blood pressure and none of the donors had post donation dipstick proteinuria (Table 3).

Table 3: Post donation medical status related variables among renal allograft donors at SPHMMC, Addis Ababa, 2018 (n=43).

Variable	Frequency	Percent (%)
Diabetes mellitus		
Yes	0	0
No	43	100.0
Cardiovascular events		
Yes	0	0
No	43	100.0
Pregnancy		
Yes	4	16.7
No	20	83.3
Pregnancy related complications		
Yes	0	0
No	4	100.0
Post donation BP		
Normal	39	90.7
Hypertensive	4	9.3
Post donation dipstick proteinuria		
Yes	0	0
No	43	100.0
CKD		
Yes	2	4.7
No	41	95.3

The change in post donation blood pressure over time shows that, the systolic blood pressure shows a highest and lowest peak at the 12 month and 24 month of follow up respectively. The curve indicates a smooth flow till 12 months and then a relatively sharp decline till 24 months of follow up.

The DBP curve shows that there were sharp increase and decrease except between the 1st and 6th months of follow up where it remained relatively constant (**Figure 1)**.

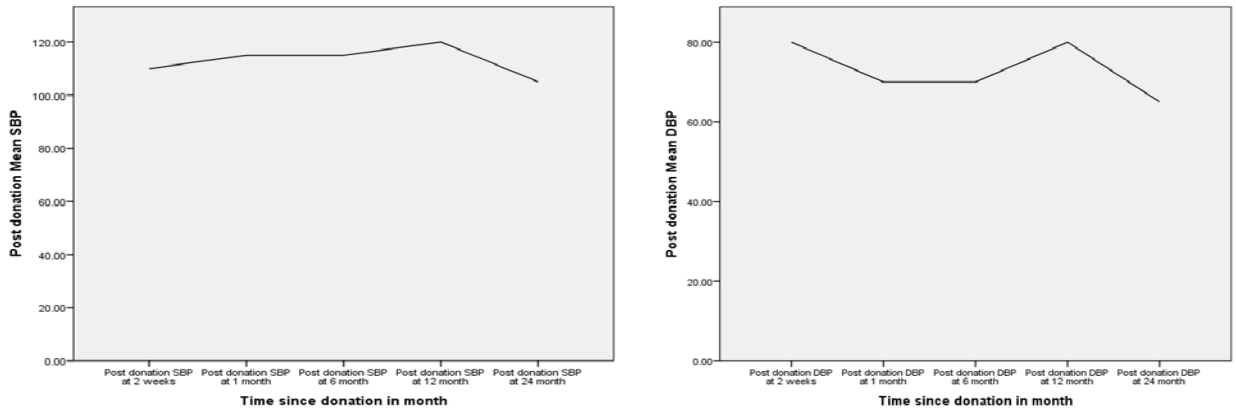

Figure 1: Liner graph of post donation mean SBP and DBP by time, Addis Ababa, 2018

The BMI curve shows a less steep increase throughout the time. The GFR curve shows that the mean GFR of the donors showed a relatively sharp decline from the 1st to 6th month of follow up and then it shows a progressive increase till the end of the follow up period (**Figure 2)**.

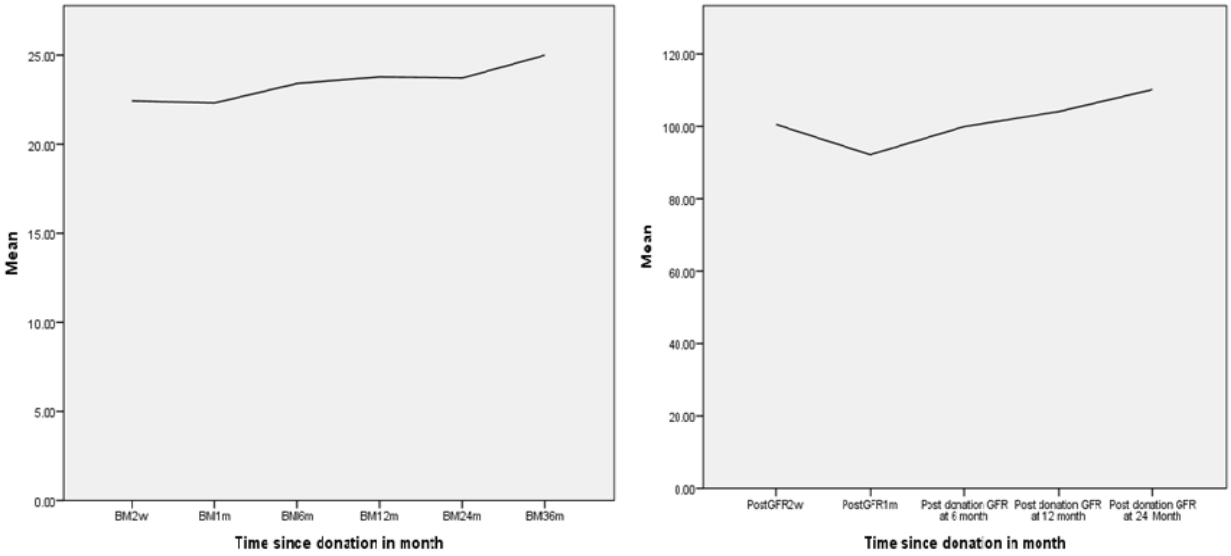

Figure 2: Line graph of post donation mean body mass index and glomerular Filtration Rate by time, Addis Ababa, 2018.

Censoring status

Among the 43 donors, two (4.7%) of them has developed CKD after one year of donation while 41 (95.3%) did not develop CKD during the two years observation period. Only four (9.3%) of the donors developed post donation hypertension and the rest 39 (90.7%) had normal post donation blood pressure and none of the donors had post donation dipstick proteinuria or pregnancy related complications.

On the other hand, during the two years observation period, any of the donors did not develop proteinuria (dipstick) and pregnancy related complications. The incidence rate ratio among the groups classified by the above independent variables did not show significant difference (P values >0.05).

Comparison of survival experience

KM plot and log rank test were used to assess the difference in the survival distribution among groups. It doesn't show statistically significant difference among the groups.

DISCUSSION

The main purpose of this study was to assess clinical outcome of renal allograft donors at the national kidney transplant center-SPHMMC. The study revealed that two (4.7%) of the donors has developed CKD after 1 year of donation while 41 (95.3%) did not develop CKD during the three years observation period.

Only four (9.3%) of the donors developed post donation hypertension and the rest (90.7%) had normal post donation blood pressure. This is in contrast to other studies conducted in the US which reported a median risk of kidney failure of 34/100,000 donors and risk of 0.24% among black men, 0.15% among black women (19, 24). This difference could be due to the difference in the duration of follow up among the studies and also could be because of the varying socio demographic and population characteristics. On the other hand, it is comparable with another study showing a prevalence of hypertension to be 7% (17,22).

The post donation CKD and hypertension among the donors during the three years observation period was on average 4.1 per 100 person years of observation (95% CI=1.0194, 16.2969) and 8.2 per 100 person years of observation (95% CI= 3.0594, 21.7192), respectively. This is less than findings in a study done with long term follow up resulting higher level of donors with CKD up to 14.5% and hypertension of 32.2 %(10).

On the other hand, during the three years observation period, any of the donors did not develop proteinuria (dipstick), diabetes mellitus, cardiovascular events and pregnancy related complications. This is in line with the above systematic review and meta analysis study showing no such complications across countries (13).

Conclusion

Majority of our donors were young with normal mean pre donation GFR. No post donation cardiovascular event happened to all donors and no pregnancy related complication happened among the pregnant donors.

The development of post donation hypertension and chronic kidney disease indicates the need for regular follow up of donors group .This study also recommend further study with a relatively longer duration of follow up to reach at a better conclusion.

ACKNOWLEDGMENT

We would like to express our great appreciation to all the staffs of transplant center for their professional and technical support in accessing medical charts of patients and in data collection. We would also like to thank St. Paul's Hospital Millennium Medical College for sponsoring the research work.

Conflict of Interest

Authors have no conflict of interest to declare.

REFERENCE

1. Kumar P, clark M. Kumar and Clark Clinical Medicine. 6th ed2014. 248-58 p.
2. Fauci A, Braunwald E, Kasper D. Harrison Principles of Internal Medicine 18th edn ed. New York NY: McGraw Hill Medical; 2015.
3. Wang H, Naghavi M, Allen C, al e. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study. Lancet 2016;388:1459-544.
4. Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(9888):260-72.
5. Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States 2015. Available from: http://www.cdc.gov/ckd.
6. Samar AE, Davide B, Graziella D, Evangelia D, Giovanni T, Carmine Z. Prevalence and burden of chronic kidney disease among the general population and high-risk groups in Africa: a systematic review. BMJ. 2107;8(1).
7. John WS, Bocheng J, Scott T, et al. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. 2014;2(3):174-81.
8. Temesgen F, Mehidi K, Tilahun Y. Prevalence of Chronic Kidney Disease and Associated Risk Factors among Diabetic Patients in Southern Ethiopia. American Journal of Health Research. 2014;2(4):216-21.
9. Gabriel MD. Handbook of renal transplant 6th ed: LWW; 2017. 624 p.
10. Horvat LD, Shariff SZ, Garg AX, the Donor Nephrectomy Outcomes Research (DONOR) Network. Global trends in the rates of living kidney donation. Kidney Int. 2009;75(10):1088–98.
11. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major non communicable diseases. Kidney Int. 2011;80(12):1258-70.
12. Bal MM, Saikia B. Gender bias in renal transplantation: are women alone donating kidneys in India? Transplant Proc. 2007;39:2961-63.
13. O'Keeffe LM, Ramond A, Oliver W, et al. Mid- and long-term health risks in living kidney donors. Ann Internal Med. 2018;168(4):276-84.
14. Kasiske BL. Outcomes after living kidney donation: what we still need to know and why. American journal of kidney diseases: the official journal of the National Kidney Foundation. 2014;64(3):335-7.
15. Ibrahim HN, Foley R, Tan L, et al. Long-term consequences of kidney donation. N Engl J Med. 2009;360 (5):459-69.
16. Reisaeter AV, Roislien J, Henriksen T, Irgens LM, Hartmann A. Pregnancy and birth after kidney donation: the Norwegian experience. Am J Transplant. 2009;9(4):820–24.
17. R. W. Steiner, J. H, D. E. Rifkin, B. Gert. Estimating Risks of De Novo Kidney Diseases After Living Kidney Donation. American Journal of Transplantation. 2014;14:538-44.
18. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. JAMA. 2014;311(6):579–86.
19. Morgan EG, Yingying S, Andrew SL, et al. Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate. N Engl J Med. 2016;374:411-21.
20. Mjoen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. Kidney Int. 2014;86(1):162-7.

21. Krista LL, Anita P. Risks and Outcomes of Living Donation. Adv Chronic Kidney Dis. 2102;19(4):220–8.
22. Grams ME, Sang Y, Levey AS, et al. Kidney-failure risk projection for the living kidney-donor candidate. N Engl J Med. 2016;374:411-21.
23. Bryce AK, Karthik KT. Lifetime risks of kidney donation: a medical decision analysis. BMJ Renal medicine research. 2017;7(8).
24. Allan B, Massie, Abimereki D, et al. Quantifying Post donation Risk of ESRD in Living kidney donors. Journal of the American Society of Nephrology. 2017.
25. Federal Demcratic Republic of Ethiopian MoH. Health and Health Related Indicators. . Addis Ababa, Ethiopia: 2016.
26. KIDGO. Clinical Guideline for Evaluation and Management of Chronic Kidney Disease. 2nd ed2012.
27. JNC 8. Hypertension Guideline Algorithm2014.
28. Richard J, John F, Jurgen F. Comprehensive Clinical Nephrology. 5th ed2014.
29. The American College of Obstetricinas and Gynecologists. Clinical Management Guidelines for Obstetrician-Gynacologists. ACOG Practice Bulletin2013.
30. American Diabetes Association. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes. Diabetes Care. 2018;2018(41):S13–S27.
31. Karen AH, H M James H, Kenneth WM, al e. Draft Definition for CDISC2014.