

## ORIGINAL ARTICLE

# Reduction in Glomerular Filtration Rate (GFR) Following Live Kidney Transplant Donor as a Consequence of Arterial Hypertension

AFSHEEN AKBAR<sup>1</sup>, MARYAM RAZA<sup>2</sup>, AMTUL HUDA<sup>3</sup>, SADIA ZIA<sup>4</sup>, SHAHEENA NAZ<sup>5</sup>, AASMA NIGHAT ZAIDI<sup>6</sup>, ZULFIQAR ALI<sup>7</sup>

<sup>1,4,5,6,7</sup>Department of Physiology Avicenna Medical College, Lahore

<sup>2</sup>Department of Physiology Rashid Latif Medical College Lahore

<sup>3</sup>Department of Physiology Abbottabad International Medical and Dental Colleges

Correspondence to Dr Zulfiqar Ali, Email: [dr.zulfiqarali53@gmail.com](mailto:dr.zulfiqarali53@gmail.com) cell: 0323-4800874

## ABSTRACT

**Aim:** Renal replacement therapy is best possible treatment for end stage renal failure, but current research suggestive of augmented long-term risk in renal function for the donor.

**Methods:** At this time, we evaluate the subjects for the risk of decreased (eGFR) estimated glomerular filtration rate within old 50 giver, who undergo pre-donation assessment and live benefactor nephrectomy among 2007 and 2015 by multiple centers of Pakistan.

**Results:** The mean pursue point in time was 8.5 years (0.9–28.2). Inco relational analysis, subject age and status of hypertension (arterial) by thereference line were considerably linked with a elevated hazard of unfavorable renal effect, in particular, eGFR <60 mL/min/1.73 m<sup>2</sup> (age/year: hazard ratio (HR) 1.03, 95% confidence interval (CI) 1.04–1.08, (HTN): HR 1.09, 95% CI 1.21–4.0), eGFR <60 mL/min/1.73 m<sup>2</sup> and a turn down of 39% from the initial measured line (age: HR 1.07, 95% CI 1.03–1.13, HTN: HR 4.22, 95% CI 1.71–10.35), and, eGFR <45 mL/min/1.73 m<sup>2</sup>. Age and HTN HR 2.13, 95% CI 1.04–1.21, HR 4.05, 95% CI 1.47–18.15 respectively, Adding together, eGFR levels at occasion of contribution was linked with a lesser hazard of eGFR <60 mL/min and eGFR <40 mL/min. The only significant predictor for adverse renal outcomes was Age.

**Conclusion:** Arterial hypertension, lower level of eGFR, and age at the time of donation are powerful prognosticating factor for undesirable kidney adverse effects in live renal donor.

**Keywords:** eGFR (per mL/min/1.73 m<sup>2</sup>) Estimated glomerular filtration rate, arterial hypertension HTN; ESRD

## INTRODUCTION

Live Renal donation is considered as most encouraging substitute treatment for chronic renal failure subjects in expression of optimal renal function, expectancy and good quality of life. On the other hand, present data scrutiny suggests an augmented donor encountered long term renal vulnerability. Even though end stage renal failure (ESRD) has significant inference on unhealthfulness and deadliness and observed as a rare incident, predominantly in subjects of live kidney donors<sup>1</sup>. Merely partial data is present on recurrent intermediate conclusions, and which recognized hazard issue for renal failure, acting as reduce estimated glomerular filtration rate (eGFR) mentioning the threat in 50 kidney donors following decrease in eGFR. Latter than 8.5 years of follow up 32% attains a GFR <60 mL, and 3.0% had an eGFR <30 mL with renal failure. In accumulation, donors will develop proteinuria around 5.0%. Hazards for a reduced eGFR include advance age, a elevated (BMI), body mass index and a elevated systolic BP<sup>2</sup>. Within multiple hospitals of Punjab incidence of proteinuria rising from 5.0% to 9.0% within 8 years of routine checkup. Eventually in subsequent checkups proteinuria be extensively elevated within hypertensive donors in comparison to non hypertension giver (14.3% vs. 5.1%– (p=0.02). Interestingly, excretion quantity of urinary albumin it will be only linked with donor age and not with the occurrence of (HTN) hypertension during the pace of kidney endowment<sup>3</sup>. Donor candidates with managed hypertension may be acceptable for

donation, according to the multiple clinical Guidelines for the Donors of Live Kidney. Those with a systolic BP of fewer than 130 mmHg and a diastolic BP of fewer than 85 mmHg who are taking one or two antihypertensive medications and no indication for the damage of target organ.<sup>4</sup> However, in transplanting strategies the level of long-standing hazard of ESRD and the donor's expected survival duration must be considered when approving a donor candidate with hypertension. During this analysis, looking adverse effects after donating kidney as lower eGFR in 50 donors, undergo nephrectomy in live donor at our centre among 8 years.

In this population, we also looked at the probability for the cumulative end result of serious cardiac complications and mortality<sup>5</sup>.

The objective of the study was to find out current research suggestive of augmented long-term risk in renal function for the donor.

## MATERIALS AND METHODS

At our unit, approximately 64 donors undergo examination before donation and afterwards nephrectomy for donation as live kidney. This research was approved by the Ethical Committee. 50 of the donors (78.1%) established follow-up results, while the left behind 14 were lost to follow-up. The information was gathered retrospectively from electronic patient charts. The level of creatinine serum was calculated, and according to modification of diet in renal disease formula (MDRD) was used to determine eGFR in initial check up and then afterwards. We looked at creatinine clearance in the early years of our research. DTPA renal scan (di-ethylene-triamine-penta-acetate)

Received on 24-02-2021

Accepted on 27-06-2021

dimensions were used to determine measured GFR (mGFR)<sup>6</sup>. Proteinuria and albuminuria were determined using one whole day proteins/ albumin in urine samples linked with creatinine ratios. At baseline, 78.1% of the subjects have no proteins or albumin in urine, 4.0% had proteinuria or microalbuminuria, and 19.0% had no results. Since our research looked at live renal transplantation for a long phase of time, the necessities for accepting live renal donors varied time to time, and they were approved to existing description<sup>7</sup>. There were nine selected donor with standard GFR of <60 mL in the early years of our programme. Owing to the lack of other co morbidities, in cooperation of donors who had a creatinine clearance or mGFR of >60 mL/min and were acknowledged for donating kidney. These donors were omitted from all subsequent studies to prevent producing skewed findings as a result of their inclusion. As a result, 50 donors were included in this report. Smoking was divided into two categories: current smokers and retired smokers, as well as nonsmokers. Subjects prescribed medication for managing arterial HTN (limit of 2 Anti HTN) or a blood pressure >130/90mmHg, two successive values >139/90mmHg in once tests is used to describe arterial hypertension. Multiple renal consequences were being assessed after live renal donation (1) an eGFR of 60 mL (2) an eGFR a decrease in 40% from initial result, and (3) an eGFR of 45ml fetal or a main cardiovascular incident myocardial infarction or cerebro-vascular accident together with transient ischemic attack or stroke were identified as cardiovascular outcomes<sup>8</sup>.

**Statistical analysis:** Nominally measured variables are expressed in a percentage, while quantitatively measured variables are expressed in a median (from lesser to greater). The Nominally measured variables are compared by chi-square test and quantitatively measured variables with help of Mann–Whitney U test. Age in years, gender, Body mass index, glomerular filtration rate, HTN, smoking status, and relationship to the recipient were used as baseline parameters in the univariate study with a p-value less than 0.1 and a univariate relation with the outcome variable were entered into model of multiple linear regression. The findings will be presented as hazards ratios by means of 95% confidence intervals (CIs).

## RESULTS

Table 1 summarizes the initial distinctiveness of the 50 donors. A donor ranged in age is 40 from 25 to 50 years old, with 60.8% being female. The majority of donors (50.4%) were of average weight (BMI 20–25kg/m<sup>2</sup>), with 41.9% having BMI values of 24 kg/m<sup>2</sup>. At the time of donation, 85mL (61–160) is discovered as median eGFR. About 2/3 of donors had a link to the receiver (65.2%). 36% of the people who donated were smokers. 15.5% of donors had arterial hypertension, and 11.0% taking treatment for HTN (one –two HTN therapy).

The average length of 8 years of follow up (between 1.0–28.1) during follow up time, the median eGFR was 60 mL (between 20–120) there will be no case of ESRD. 30.3% of subjects experience hypertension at the follow-

up. 4.4% of donors died from some cause or had a major coronary event, and no change in baseline eGFR substantially among donors by way of exclusive of this outcome (78 vs. 84mL, p value =0.676). Nephritic findings, such as first Only eGFR 60 mL, second eGFR 60 mL and a 40% fall from the initial values and third, eGFR 46 mL were seen in 40.2%, 12.3% and 7.5% of patients, respectively.

Table 1: Initial Variables of donors and are articulated as in percentage and medians from lesser to greater (n=50)

Age (years)	40 (25–50)
Female (%)	60.8
BMI (kg/m <sup>2</sup> )	24 (17.4–38.3)
eGFR (mL/min/1.73 m <sup>2</sup> )	85 (61–160)
Blood pressure mmHg Systolic	120 (79–159)
Blood pressure in mmHg Diastolic	80 (44–105)
Connected to recipient percentage	65.2
Smoker in (%)	36
Hypertension (%)	15.5
Anti HTN treatment (%)	11.0
Total time during Follow-up time (years)	8.0 (1.0–28.1)

Following donation, three donors developed proteinuria or albuminuria. However, we were unable to analyse risk factors for proteinuria/albuminuria in approximately half of the donors during follow-up because we did not have data on this marker of occurrence chronic kidney disease. Unfavorable renal consequences, main Cardiac disorders, and fetal risk factors during univariate study, the prevalence of HTN at start and was substantially correlated with unfavorable nephritic effects mention above. Simply age, along with eGFR, having prevalence of HTN at start were important interpreter of serious renal consequences, i.e. eGFR 60mL and a decline of 40% from start, and eGFR 46mL. HR 1.06, 95% CI 1.02–1.07 meant for eGFR of less than 60mL; HR 1.07, 95% CI 1.02–1.11 for eGFR 60 mL and less than 40% from start, HR 1.12, 95% CI 1.02–1.17 for eGFR 46 mL and loss of 40. Arterial hypertension was shown to have a score, important connection with poor renal results (HR 2.45, 95% CI 1.35–3.19 for eGFR 60 mL; HR 4.02, 95% CI 1.70–8.80 for eGFR 60 mL and a reduction of 40% from start; HR 6.01, 95% CI 1.60–21.01. The model's precision did not improve when the number of antihypertensive medication classes was increased.

Age factor is the only considerable risk coupled with fatality or most important cardiac complications follow up period (HR 1.07, 95% CI 1.02–1.15). Hypertension (HTN) is counted as major risk element for CRF, at baseline, subjects with HTN were slightly elder (median age: 54 between 32–67 in years vs. 43 between 22–71 years, p=0.001), had a higher BMI (27.5, range 17.5–34.1 vs. 23.9, range 16.9–37.9, p=0.018) lesser linked to the receiver (48.3% vs. 70.2%, p = 0.012).

The median eGFR in donors among hypertension was slightly lower at follow up 51ml between 29–80 vs. 65mL, between 18–118 p=0.001. Donors of arterial hypertension have a slightly higher rate of adverse renal effects. (38.4% vs. 62.6%, p = 0.001 for eGFR 60mL; 41.0% vs. 12.3%, p=0.001 for eGFR 60mL and loss of 40% from start; and 18.9% vs. 8.0%, p = 0.065 for eGFR 46 mL/min

Table 2: Serious clinical effects along with risk factor (eGFR mL/min/1.73 m<sup>2</sup>, HR linked CI, and confidence interval

Clinical Outcome	Risk Factor	HR (95% CI)	p-Value
eGFR <60 mL/min (n = 50)	Age / year	1.06 (1.02–1.07)	<0.001
	Arterial hypertension	2.45 (1.35–3.19)	0.004
	eGFR (per mL/min/1.73 m <sup>2</sup> )	0.98 (0.97–1.00)	0.032
eGFR <60mL/min and loss of ≥40% from baseline (n=28)	Age / year	1.07 (1.02–1.11)	0.001
	Arterial hypertension	4.02 (1.70–8.80)	0.001
eGFR <46 mL/min 0.002 (n=17)	Age /year	1.12 (1.02–1.17)	0.002
	Arterial hypertension	6.01 (1.60–21.01)	0.007
	GFR/ mL/min	0.95 (0.90–1.00)	0.040
Fatality or most important cardiac complication (n= 10)	Age / year	1.07 (1.02–1.15)	0.019

Table 3. Baseline and follow up variables with and without HTNin donors and are mentioned in median and percentage (n=50).

	Without HTN (n=18)	With HTN (n=32)	P-Value
<b>Baseline variables</b>			
Age in years	43 (22–71)	54 (32–67)	<0.001
Female (%)	65.2	61.8	0.692
BMI (kg/m <sup>2</sup> )	23.9 (16.9–37.9)	27.5 (17.5–34.1)	0.018
eGFR (mL/min/1.73 m <sup>2</sup> )	87 (60–162)	82 (64–120)	0.747
BP Systolic (mmHg)	120 (80–155)	138 (118–159)	<0.001
BP Diastolic (mmHg)	80 (44–100)	84 (70–105)	<0.001
Connected to recipient percentage	70.2	48.3	0.012
Smoker (%)	35.8	34.3	0.864
Antihypertensive therapy (%)	0.0	65.7	<0.001
<b>Follow up variables</b>			
eGFR mL/min	65 (18–118)	51 (29–80)	<0.001
Arterial hypertension (%)	69.7	30.3	<0.001
eGFR <60 mL/min (%)	62.6	38.4	0.001
eGFR <60 mL/min/1.73 m <sup>2</sup> and loss of 40% from initial (%)	12.3	41.2	0.001
eGFR <46 mL/min (%)	8.0	18.9	0.065

## DISCUSSION

Our results indicate that at the period of live renal donation the HTNin spite of using of anti HTN medications, after the donation the new-onset CRF is a long-term cause considered as risk. For the duration of follow up for about 8.0 year 38.4% of the subject having an eGFR of less than 60 ml because of the retrospective sample style, these figures should be taken with caution, but these between series of incidence of 37% within 8 years of donating kidney<sup>9</sup>. Six of the 50 donors (3%) had an eGFR of 46mL after a mean period of follow-up of 4.8 -2.3 years, but not found in matched other stable non-donors eGFR of less than 60 mL after live kidney donation on health outcomes is up till now a hot topic for debate. On other hand, in large general population, the connection between a decrease eGFR and raised relative hazard for different destinations are evidently identified. Even though the above study identified an increased rate of cardiac fatality risk in 10 donors during an 8.5-year follow-up span, HTN at the time of donating kidney was not statistically correlated with cardiovascular complications and or death in our study. We may hypothesize that the link between systolic BP and raises the cardiac complication risk is difficult to detect incomparatively stable subjects of live kidney donors, predominantly in small population cohort with undersized follow up periods<sup>10</sup>. Donor candidates with managed hypertension should be evaluated and cared for according to the 2017 KDIGO Clinical Practice Recommendation on the Assessment and Care of Live Kidney Donors suggest if there is no proof of target organ injury, they could be eligible for donation<sup>11</sup>. However, our findings and those of other researchers show that, regardless of other risk factors, HTN at the time of donating kidney is linked to a lower eGFR after donation. As a result, we recommend that probable live renal donors with HTN, especially those of

early age, be carefully evaluated. In this study, 30.2% of donors experience emergence of HTN at some point in follows up of 8.5 years. Nevertheless, frequency of decline eGFR and outset of HTN in donor subjects with prolong follow-up time period greater than 12-15 years, will have to be interpret with vigilance. Donors who experience low levels of eGFR and disorders, such as HTN, are probably to be follow in a expertise centers, consequently assortment prejudice may be there, some researchers observed a link between a increase in eGFR prior to donating kidney and a decrease risk for two of the renal resultant (eGFR 60 ml and eGFR 45 ml) with comparable hazard ratios to those seen in our research. (2–3% increased chance of developing an increased eGFR per 1 mL/min/1.73 m<sup>2</sup> reduction in pre-donation eGFR). As a result, it's fair to assume that RFR is decreased not only in HTN donors, but also observed in those with a low levels of eGFR at donation time period<sup>12</sup>.

## CONCLUSION

The best cure for ESRD is living kidney donation, but it is a complicated moral and medicinal problem. We all anticipate that the psychological advantages of altruism and better beneficiary welfare will outweigh any minor risks to the donor. Inaccessible medical disorders like asthma may not be a contraindicated in donating live kidney, but donors should be advised of possible complications and harms, and donors with known co-morbidities, in particular, should be closely monitored on a daily basis.

**Conflict of interest:** Nil

## REFERENCES

1. Levey AS, Inker LA. GFR evaluation in living kidney donor candidates. *Journal of the American Society of Nephrology*. 2017;28(4):1062-71.

2. Gaillard F, Legendre C, White CA. GFR assessment of living kidney donors candidates. *Transplantation*. 2019;103(6):1086-93.
3. Inker LA, Koraihy FM, Goyal N, Lentine KL. Assessment of glomerular filtration rate and end-stage kidney disease risk in living kidney donor candidates: A paradigm for evaluation, selection, and counseling. *Advances in chronic kidney disease*. 2018;25(1):21-30.
4. Lentine KL, Levey AS, Segev DL. Integrated Risk Assessment Versus Age-Specific GFR Thresholds for Living Donor Candidate Evaluation. *Transplantation*. 2020;104(12):2464-6.
5. Akoh JA, Schumacher KJ. Living kidney donor assessment: Kidney length vs differential function. *World Journal of Transplantation*. 2020;10(6):173.
6. Prasad N, Gupta A, Kaul A, Bhadouria D, Patel M, Behera M, et al. TA Comparison of the creatinine clearance by gfr estimating equations with measured gfr by isotope scan in voluntary living kidney donor. *Transplantation*. 2020;104(S3):S411.
7. Knight SR, Cao KN, South M, Hayward N, Hunter JP, Fox J. Development of a clinical decision support system for living kidney donor assessment based on national guidelines. *Transplantation*. 2018;102(10):e447-e53.
8. Lam NN, Lentine KL, Garg AX. Renal and cardiac assessment of living kidney donor candidates. *Nature Reviews Nephrology*. 2017;13(7):420.
9. Ibrahim HN, Hebert SA, Murad DN, Adroque HE, Nguyen DT, Graviss EA, et al. Outcomes of hypertensive kidney donors using current and past hypertension definitions. *Kidney international reports*. 2021;6(5):1242-53.
10. Haugen AJ, Langberg NE, Dahle DO, Pihlstrøm H, Birkeland KI, Reisæter A, et al. Long-term risk for kidney donors with hypertension at donation—a retrospective cohort study. *Transplant International*. 2019;32(9):960-4.
11. Ickx B, Mokhtari Z, Obbergh L, Lucidi V, Collange V, Naili S, et al. Mild Increases in Plasma Creatinine after High-Risk Abdominal Surgery Are Associated with Long-Term Renal Injury: A Retrospective Cohort Study. 2020.
12. Wainright JL, Robinson AM, Wilk AR, Klassen DK, Cherikh WS, Stewart DE. Risk of ESRD in prior living kidney donors. *American Journal of Transplantation*. 2018;18(5):1129-39.