RISK OF DEVELOPMENT OF HYPERTENSION AFTER DONOR NEPHRECTOMY

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ABSTRACT

Objective: To assess live donor nephrectomy for development of hypertension.

Study Design: Retrospective observational study.

Place and Duration of Study: The study was conducted at Armed Forces Institute of Urology (AFIU) Rawalpindi, from May 2016 to May 2020.

Methodology: All consenting kidney donors for live renal transplant were introduced with the process. Baseline blood pressure at time of workup of donation and annually afterwards after transplant on follow up examinations using retrospective data analysis of donor's workup and follow up was used. Comparison of 1,2,3 and 4-year occurrence of hypertension among (normotensive) donors with 1,2,3 and 4-year of donation using estimates from Framingham Hypertension Risk Score.

Results: A total of 79 donors with a completed annual follow-up rate of up to100 % during a 4-year period. The average age at donation was 33.96 ± 10.23 SD years; 50 donors (63.4%) were women. Overall 27% (22 out of 79) of all live donors developed post donation hypertension who were normotensive at the time of donation. Almost 2/3rd of the patients developing hypertension were females. There was a significant increase in blood pressure measurements each year after donation. Increased BMI of the patient was a risk factor for post donation development of hypertension. The donors who continue being normotensive 1-year post donation yielded an analogous risk to that fit Framingham populace.

Conclusion: Live organ kidney givers are at augmented risk of development of hypertension post kidney donation. The study ascertains the potential significance of following donors and handling risk factors aggressively to avert hypertension and to increase donor survival.

Keywords: Consent, Framingham Score, Hypertension, Living kidney donor.

INTRODUCTION

Living donor nephrectomy is increasing day by day as the candidates of kidney transplant are increasing enormously. Improved life probability and quality of life are significant benefits for recipients of live kidney donors as matched with dialysis or deceased donor transplantation[1]. The donor risks are usually lesser with some low postoperative deaths (nearly 3.1 deaths per 10 000 procedures)[2]. This is very important to ascertain extended span health risks related with kidney donation. There is no certain data available to show if such donors develop hypertension or any other complication in the long run.

To date multiple studies have beenconducted internationally. Very minor augmented risk of developing hypertension or proteinuria over longstanding follow-up was detected in a meta-analysis of 48 studies which reported on outcome of 5145 donors as equated to age accorded controls. But contrary studies are also available showing development of hypertension and microalbuminuriain donors in long term[3,4]. In a study conducted by Sanchez *et al*, their results establish that roughly as much as one third of population became hypertensive after donation and have almost alike chances to develop hypertension to what is seen in the general population[5]. They found that quarter of donors getting anti-hypertensive medications are poorly controlled (BP >140/90 mmHg) and ten percent of donors without a diagnosis of hypertension had blood pressure readings falling in hypertensive range. A better understanding of metabolic outcomes is paramount in choosing the potential donors which can help in developing a long term guideline to retain good health status. None of such studies are conducted in Pakistan yet.

Development of a new, multicomponent score, grounded on Framingham data has allowed calculation of hypertension risk by making appropriate groups has circumvented problems associated with previous studies. This Framingham score is a gender based algorithm used to estimate the 10-year cardiovascular risk of an individual. It permits creating clusters comparable for age, gender, systolic and diastolic blood pressures, smoking habits and family history of hypertension. This score hasn't been included in statis-

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tical analysis in studies until a recent study conducted in Switzerland[6].

Aim of this retrospective, long term study was to evaluate if nephrectomy is a risk factor for development of hypertension in kidney donors when compared with estimations of multivariate hypertension risk score of the Framingham cohort including pertinent risk considerations of hypertension for possible donors without nephrectomy.

METHODOLOGY

This retrospective observational study was conducted at Armed Forces Institute of Urology, from May 2016 to May 2020. It was a retrospective cohort study consisting of 79 donors. All participants who were registered for renal transplant donationwere well informed and written consent was taken for the use of data for clinical research purposes. Blood pressures were recorded before donation and followed yearly after donation. Hypertension was defined as systolic blood pressure >140 mmHg and/or diastolic >90 mm Hg, or use of any blood pressure-lowering medication. A mean of three separate measurements of blood pressure at each time taken before and yearly after donation during follow-up checkups was used for data report. Our inclusion criteria allowed only normotensive patients, all the patients who were hypertensive or were on antihypertensive medication were excluded. Newly identified cases of hypertension had to undergo 24h ambulatory blood pressure recording for confirmation, using cutoff figure of 135/85 mm Hg or higher. Only normal range blood pressure values were accepted as 'normal' if medicationsused the same day did exclude antihypertensive treatment. Only follow-up checkups with comprehensive data sets were analyzed. All this data was collected retrospectively by collecting information of consenting donors.

Variables which were interval-scaled were summarized with means and SDs or medians and IQRs, for statistical analysis, where appropriate. Dichotomous variates were labelled as ratios and percentages.

We used hypertension risk score of the Framingham cohort for 1, 2,3 & 4-year risk of hypertension to our data to evaluate the outcome of donation on the manifestation of elevated blood pressure necessitating medication, as follows: for the initial year study we tailored the data to the dissemination prior to donation after discounting all cases of hypertension (n=79). For the consequent 4-year analysis, we fixated on all donors lasting normotensive 1-year post donation. Data documentation was also done for family history and smoking habits of the patients.

Comparison was made between the projected prospects from the Framingham calculations to the probabilities estimated from two multivariate logistic regression models, utilizing the manifestation of hypertension 1, 2, 3 & 4-years after donation as the dependent variate and the existing parameters of the Framingham equation (age, female gender, blood pressure both systolic and diastolic, BMI, smoking status, family history of hypertension and acollaborationspan of age and diastolic blood pressure) pre-donation (for the 1-year calculation) and at every 12 months after donation (for the 2, 3, 4-year assessment).

RESULTS

In the period of May 2016 to May 2020, all the patients included in the trial were contacted for retrospective examination of systolic and diastolic BP for assessment of development of hypertension after kidney donation. All of our population was local Pakistani community. Out of all the 79 patients 22 patients (27%) developed hypertension which included 14 female patients (17%) and 8 males (10%).

Age wise group distribution has been shown in table-I. Age range pre-donation visit showed 34.77 with standard deviation of 10.23 years in normotensive patients as compared to the patients who developed 33.96 ± 7.67 years. In BMI category, the normotensive donors had average pf 22.95 ± 3.18. As compared to hypertensive donors who were 25.08 ± 3.52 both groups had *p*-value of <0.001.

Table-I: Comparison of age and BMI of two groups.

	Normotensive	Hypertensive	*p*-value
Age	34.77 ± 10.23	33.96 ± 7.67	<0.001
Body Mass Index	22.95 ± 3.18	25.08 ± 3.52	<0.001

During the study the follow up of patients has been shown in figure. At the time of donation, all patients were evaluated and confirmed to be normotensive. The follow up of patients was phenomenal and up to 100%, as only one donor from 2017 could not be followed up after two years of donation.

A detailed data of the patients developing hypertension with systolic and diastolic measurements have been tabulated in tables-II-VI. This data shows that the donors who were to develop hypertension, had normal blood pressure even after one year of donation. They start to develop the hypertension from the second year after donation onwards, as can be seen in the table-II to

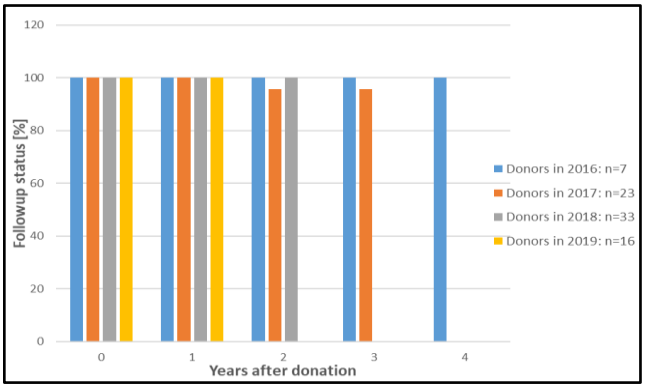

Figure: Percentage of follow-up of donors.

5. For this reason, there are no donors from 2019 to have reportedthe hypertension, since they are followed up only one year after the donation (table-IV).

Furthermore, it is observed that the number of donors developing the hypertension is increasing with time as shown in figure. For a four year follow up of the donors from 2016, 57.1% of the donors developed hypertension. For a three year follow up of the donors from 2017, 34.8% of donors developed hypertension whereas 30.3% of donors from 2018 developed hypertension during a two year follow up. This clearly establishes the increased risk of hypertension with time.

Table-II: Group wise systolic and diastolic blood pressure of donors in 2016 during follow up.

	Variable	Normotensive Donors		Hypertensive Donors	
		n	Mean ± SD	n	Mean ± SD
Donation time	Systole	3	116.67 ± 5.77	4	117.5 ± 5
	Diastole		76.67 ± 5.77		77.5 ± 5
Year 1	Systole	3	113.33 ± 5.77	4	120 ± 0
	Diastole		76.67 ± 5.77		80 ± 0
Year 2	Systole	3	113.33 ± 5.77	4	137.5 ± 15
	Diastole		76.67 ± 5.77		87.5 ± 5
Year 3	Systole	3	120 ± 10	4	130 ± 0
	Diastole		75 ± 5		90 ± 0
Year 4	Systole	3	113.33 ± 11.55	4	133.5 ± 16.01
	Diastole		71.67 ± 2.89		86.25 ± 7.5

Table-III: Group wise systolic and diastolic blood pressure of donors in 2017 during follow up.

	Variable	Normotensive Donors		Hypertensive Donors	
		n	Mean ± SD	n	Mean ± SD
Donation time	Systole	15	116 ± 5.07	8	117.5 ± 4.63
	Diastole		74.67 ± 6.4		75 ± 7.56
Year 1	Systole	15	112.67 ± 7.99	8	127.5 ± 28.16
	Diastole		71.33 ± 7.43		76.25 ± 9.16
Year 2	Systole	14	113.57 ± 4.97	8	126.25 ± 20.66
	Diastole		72.86 ± 4.26		85 ± 13.09
Year 3	Systole	14	120.71 ± 6.16	8	128.12 ± 14.62
	Diastole		71.29 ± 18.85		88.75 ± 8.76

Table-IV: Group wise systolic and diastolic blood pressure of donors in 2018 during follow up.

	Variable	Normotensive Donors		Hypertensive Donors	
		n	Mean ± SD	n	Mean ± SD
Donation time	Systole	23	117.39 ± 4.49	10	118 ± 4.22
	Diastole		77.39 ± 4.49		77 ± 4.83
Year 1	Systole	23	114.35 ± 6.62	10	124 ± 14.3
	Diastole		73.48 ± 4.87		87 ± 14.94
Year 2	Systole	23	116.96 ± 5.59	10	135 ± 7.07
	Diastole		75.22 ± 5.11		88 ± 7.14

Table-V: Group wise systolic and diastolic blood pressure of donors in 2019 during follow up.

	Variable	Normotensive Donors		Hypertensive Donors	
		n	Mean ± SD	n	Mean ± SD
Donation time	Systole	16	120 ± 6.32	0	-
	Diastole		78.75 ± 3.42		-
Year 1	systole	16	113.12 ± 4.79	0	-
	diastole		74.38 ± 5.12		-

DISCUSSION

First successful kidney transplant was done in 1954 when kidney was donated by identical twin of the donor[1]. Sincethen, the number of kidney transplant are on a rising verge. Effects on donor's health in long term weren't determined initially but surgery kept on going considering a good faith belief, assuming no damage to donor. In 1980s some experimental reports emerged that nephrectomy is associated with hyper filtration injury which ultimately leads to hypertension, proteinuria and glomerulosclerosis[2]. So rates of living donor transplant waned. Though this data was not derived from humans. Kidney transplant kept on being performed and for past few years, it's incidence has increased significantly and it surpassed cadaveric donors[3]. People involved in transplant acknowledge contribution if living donors and many safeguards are

in place for their protection. But no concrete well designed prospective studies are conducted to proof it[4,5].

In early studies, live donor transplant nephrectomy was not considered a risk factor for development of hypertension[6]. When matched to general population no significant difference was found in occurrence of hypertension and hence micro albuminuria[7,8]. These were small population studies with retrospective design, a small cohort, use of general population as control group, poor statistical designs and lost to follow up. In recent past some studies found contrary results with an increased risk of hypertension in donors[7,8].

In a prospective Swiss cohort, conducted over 18 years shows that it triplicates risk of hypertension in kidney donors in short term and leads to microalbuminuria too[9]. In a study conducted by Ramesh *et al* showed that 51 donors, who were consented, predonation blood pressure in normotensive persons was not correlated with post-donation cardiovascular and kidney functions[10].

In another study conducted by Kiberd *et al* in USA, the study showed that 1-5% of patients has chances to develop ESRD as a result of kidney donation[11]. The additional peril of ESRD caused a loss of almost 0.126–0.344 remaining life years. Obesity and smoking reduced life expectancy and amplified overall life spanhazards of ESRD.

In a meta-analysis of multiple studies conducted by Ommen *et al*, it was shown that living donors, particularly living related donors, are at enlarged risk for being hypertensive or developing kidney disease. It further argues that absence of proof is not proof of absence after conducting a thorough analysis across many trials[12].

Systematic collection of data of all donors allows to look for long term outcome and also gives opportunity for timely intervention. It will also allow to improvise policy for long term follow up.

In a meta-analysis Boudville *et al* concluded that after nephrectomy 5mm Hg average blood pressure rise occurs but risk of hypertension cannot be evaluated because of heterogeneity of data and weakness of study[13]. In the recent study conducted in Israel by Grupper *et al*, it was concluded that donors are more likely to developclinical picture of metabolic syndrome besidesdrop in GFR and greater than before urine albumin excretion[14].

Strengths of our study are its extensive retrospective design, large donor population, extensive follow up and complete data set hence strong hypertensive outcome classification. Details of smoking status and hypertension family history were also accessible for all donors. Most of the donors were available for follow up and those not making were contacted via telemedicine.

Among weakness of our study were retrospective design, inclusion of use of antihypertensive therapy in definition of hypertension as it leads to increased hypertensive population and weak system of telemedicine hence resulting in some degree of loss to follow up.

In summary our study supports nephrectomy a risk factor for hypertension but a life long follow up of donor and continuous observing of blood pressure and urinary albumin excretion are recommended to avoid any unfavorable outcome. Those who are diagnosed with hypertension should be placed on ACE Inhibitors or Angiotensin receptor antagonists. All transplant centers should have a centralized data registry with lifelong follow up of donor as well.

CONCLUSION

The patients donating kidney are at increased risk of developing hypertension in subsequent years post donation. Those patients who eventually develop hypertension are already at increased risk of developing hypertension post donation. These hypertensive donors are susceptible to worsening hypertension over period of 4 years and need medical attention. Kidney donors should be regularly followed up as a part of hospital health care policy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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