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Microalbuminuria in healthy kidney donors in pre transplant donor evaluation

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Abstract

Objectives: To determine the frequency of abnormal microalbuminuria in healthy kidney donors undergoing pre-transplant evaluation.

Method: The analytical cross-sectional study was conducted from January to June 2025 at the Sindh Institute of Urology and Transplantation, Karachi, and comprised living healthy prospective kidney donors aged 20-60 years. Clinical assessment and laboratory analysis of donors were performed, with quantitative variables being age, total protein excretion and albumin excretion, and qualitative variables being gender, smoking status, abnormal proteinuria and abnormal albuminuria. Abnormal albuminuria was established as albumin-to-creatinine ratio >30mg/g. Data was analysed using SPSS 25.

Results: Of the 195 donors with mean age 41.6±9.8 years, 112(57.4%) were females. The median excretion of 24-hour urinary protein was 107mg/day (interquartile range: 95-230mg/day), and donor's overt proteinuria was detected in 37(18.9%). Normal albumin excretion rates were found in 123(63.1%) subjects, and abnormal albuminuria occurred in 72(36.9%). Microalbuminuria was present in 49(25.1%) of the donors, while macroalbuminuria was found in 23(11.8). Age ≥40 years (p=0.021) and overweight/obesity (p=0.011) were significantly associated with abnormal albuminuria.

Conclusion: Abnormal albuminuria affected donor eligibility in older age and with higher body mass index. Incorporation of albumin-to-creatinine ratio into routine donor assessment enhanced risk stratification capability.

Key Words: Albuminuria, Body mass index, Donor screening, Kidney donation, Microalbuminuria.

Introduction

Kidney transplantation is known as the best renal replacement therapy (RRT) in patients with the end-stage renal disease (ESRD) as it provides excellent survival, quality of life, and economic effectiveness over the long term. [1] Specifically, living kidney donation offers superior graft survival and patient outcomes over deceased donor transplantation, and continues to be a staple of transplant programmes in most countries. [2-3] The overall safety notwithstanding, living kidney donation is not completely safe, and close long-term monitoring of the lives of the donors is mandatory to ascertain early signs of possible renal damage. [4]

Microalbuminuria has turned out to be a delicate marker of premature glomerular injury and endothelial malfunction, commonly prior to the aggressive decreases in glomerular filtration rate (GFR) or the emergence of a proteinuria of clinical importance. Microalbuminuria in the general population is linked with a high risk of chronic kidney disease (CKD), heart disease morbidity, and mortality. The existence of microalbuminuria is of specific concern in living kidney donors whose state is characterised by decreased nephron mass after unilateral nephrectomy, which can be prone to hyperfiltration injury with time. [5]

Obesity has become a significant and independent risk factor of albuminuria even with healthy individuals. High body mass index (BMI) correlates with elevated glomerular hyperfiltration, augmented intraglomerular pressure and morphological alterations, including glomerulomegaly, all of which are linked to elevated urinary albumin excretion. The albuminuria caused by obesity can be present without overt cases of diabetes or hypertension, and is said to be an early sign of kidney damage caused by

obesity. Within the context of living kidney donors, excess bodyweight can further enhance the adaptive hyperfiltration that occurs after nephrectomy, and increase the risk of further microalbuminuria and eventual renal dysfunction.[4-5]

Recent protocols have placed more emphasis on strict pre-donation assessment and post-donation monitoring, including the determination of GFR and urinary protein excretion, to verify the safety of the donors. [6] Historically, the screening of donor candidates and post-renal outcomes have been done through total protein excretion. Nevertheless, total protein measurements do not necessarily identify slight cases of glomerular damage since microalbuminuria could be present even when total protein excretion is within the normal range.[7] This difference highlights the need to consider microalbuminuria as a parameter of renal health, as opposed to using total proteinuria as the sole indicator of microalbuminuria.

Some longitudinal studies have studied the onset of hypertension, decreased estimated GFR (eGFR) and albuminuria among living kidney donors with contradictory findings. Although renal stability is observed in several donors, others would experience microalbuminuria years after donation, indicating heterogeneity in the vulnerability of individuals. [8-9] These outcomes may be affected by age, baseline renal operation, blood pressure, metabolic profile and follow-up period. Exact assessment of GFR and sensitive identification of albuminuria are, thus, of paramount value in risk stratification and long-term care of donor. [10]

It is clinically relevant to assess microalbuminuria in healthy kidney donors with normal and abnormal total protein excretion. This type of evaluation can be used to detect early renal alterations which cannot be detected in the framework of traditional screening of proteinuria alone, therefore guiding subsequent intervention and adding to safer living kidney donation practices. Nevertheless, there is still a dearth of local and regional trials that assess microalbuminuria in healthy prospective living kidney donors, especially when it comes to obesity and other risk factors that can be altered. The study was planned to determine the frequency of abnormal microalbuminuria in healthy kidney donors undergoing pre-transplant evaluation.

Subjects and Methods

The analytical cross-sectional study was conducted from January to June 2025 at the Sindh Institute of Urology and Transplantation (SIUT), Karachi, following approval of the research synopsis by the College of Physicians and Surgeons Pakistan (CPSP) and institutional ethics review board. All the participants were aware of the aims, processes, possible risks and advantages of the study, and they signed an informed consent form. All information concerning the participants was kept confidential.

The sample comprised healthy proposed living kidney donors of both genders aged 20-60 years who visited the pre-transplant clinic of SIUT. Assessable donors with systolic blood pressure (SBP) and diastolic blood pressures (DBP) <140mmHg and <90mmHg, respectively, with no comorbidities and morphologically normal kidneys on ultrasound were included. Donors were not eligible with a dipstick-positive proteinuria of >1+, microscopic haematuria of >5 red blood cells/high-power field, eGFR of <80mL/min, or under- or over-collected 24-hour urine samples based on creatinine excretion beyond the estimated acceptable range. A consecutive sampling method was used to enrol the participants. The sample size was calculated using the standard formula for estimation of a single-population proportion, assuming a prevalence of abnormal proteinuria of 24% based on previous literature,[11] a 95% confidence level, and a margin of error of 6%.

Baseline demographic characteristics of the donors were recorded using a structured proforma. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m²). The participants were classified according to the World Health Organisation (WHO) Asia-Pacific criteria for South Asian populations as underweight (<18.5kg/m²), normal weight (18.5-22.9kg/m²), overweight (23.0-24.9kg/m²) and obese (≥25.0kg/m²).[12] The participants were educated about the correct 24-hour urine collection method, and the samples were examined in the institutional laboratory regarding total protein excretion. Moreover, each participant provided a midstream spot urine sample that was evaluated for albumin-to-creatinine ratio (ACR)

and protein-to-creatinine ratio (PCR). Abnormal proteinuria referred to a total protein excretion >150mg/24-hour urine, or spot PCR >0.2mg/mg. Abnormal albuminuria referred to an ACR >30mg/g creatinine in a spot urine sample. All findings were recorded on the study proforma.

Data was analysed using SPSS 25. Data normality was analysed using Shapiro-Wilk test. Quantitative variables, such as age, total protein excretion and albumin excretion, were expressed as mean ± standard deviation when normally distributed and as median with interquartile range (IQR) when not distributed normally. Qualitative variables were gender, smoking status, the presence or absence of abnormal proteinuria and abnormal albuminuria, and they were presented as frequencies and percentages. The association of age, occupation, smoking status, and BMI with abnormal albuminuria was assessed using cross-tabulation. The chi-square test or Fisher's exact test, as appropriate, was applied to evaluate associations among categorical variables. $P<0.05$ was considered significant.

Results

Of the 195 donors with mean age 41.6±9.8 years, 112(57.4%) were females. The majority of the participants were employed 118(60.5%) and 27 (13.8%) were current smokers. Of all the donors, 96(49.2%) had normal BMI (Table 1).

The mean random blood glucose (RBG) was 118.6±21.4 mg/dL, and the mean fasting blood glucose (FBG) was 96.2±12.8 mg/dL. The donor eligibility criteria were met in terms of renal function indices, and lipid profile parameters revealed borderline elevation, but no apparent dyslipidaemia (Table 2).

The median excretion of 24-hour urinary protein was 107mg/day (IQR: 95-230mg/day). Majority of donors had low-grade or borderline proteinuria, while 37(18.9%) showed protein excretion >300mg/day (Table 3). Microalbuminuria was present in 49(25.1%) of the donors, while macroalbuminuria was found in 23(11.8). Age ≥40 years (p=0.021) and overweight/obesity (p=0.011) were significantly associated with abnormal albuminuria (Table 4).

Discussion

The presence of abnormal proteinuria was evident in about one-quarter of healthy potential living kidney donors in the current study, and abnormal albuminuria was found in about one-tenth of the cohort. The results suggest that even well-screened donor candidates may have subclinical renal abnormalities. It is interesting to note that microalbuminuria was detected not only in donors who showed abnormal total protein excretion, but also in a small percentage of the donors who had normal proteinuria. This represents a key finding of the study and highlights the additional diagnostic value of ACR over conventional total protein measurements in detecting early renal abnormalities in donor candidates.

There is emerging evidence that despite the generally safe nature of living kidney donation, there is a group of donors who might have long-term renal and cardiovascular complications. A recent prospective cohort study has shown increased incidences of hypertension and slight decreases in kidney function after living kidney donation, which indicate the need to identify individuals at higher risk earlier. [11] Similarly, a systematic review and meta-analysis found a statistically significant but minor increase in the risk of ESRD in the long term in living kidney donors relative to matched non-donors even though the absolute risk was very low. [13] The results support the clinical impact of ensuring the presence of early signs of renal injury, like microalbuminuria.

The abnormal albuminuria prevalence found in the current study is in line with the current literature that highlights that nephron mass reduction could lead to glomerular injury associated with hyperfiltration in donors[14]. Recent surveys have noted that there have been gaps in knowledge of early predictors of adverse renal outcomes following donation, especially in resource-limited environments where long-term follow-up may not be ideal. [13] Microalbuminuria as a risk marker representing a very early evidence of endothelial dysfunction and glomerular damage can, thus, be used as a convenient instrument of risk stratification among healthy donors.

In addition to the medical outcomes, psychosocial and economic factors also have an impact on the donor assessment and long-term treatment. Surveys conducted on the general perception of the population towards the idea of living kidney donation have revealed that the issues of donor safety and future health are still widespread.[15] The financial consequences of donation have also been identified as one of the possible obstacles, and, therefore, there has been a call to put in place policies to achieve financial neutrality and overall donor support. [16-17] Proper evaluation of early renal alterations would do even more to enhance donor counselling and informed decision-making.

In this case, abnormal albuminuria was greatly related to an elderly age and high BMI in the current study, and these results are in line with previous findings that indicate that age-related nephron loss and metabolism can result in predispositions to the occurrence of renal injury subsequently to donation. The readiness to be a living organ donor was proven to be conditioned by the perceived health risks, and it is crucial to note that a communication of risks should be provided to individuals on a case-specific basis in the context of objective clinical indicators. [18] Evidence-based donor assessment has been found to enhance the understanding and acceptance of living donation as a result of the use of educational and family-centred interventions. [19]

A observational study carried over a long period of time showed that, although the majority of donors experience adaptive adjustments in kidney functioning following nephrectomy, inter-individual fluctuations do not disappear.[20] The meta-data of the analyses also proves that severe adverse events are still not common, but they are not insignificant, especially among donors who have other risk factors, like obesity or advanced age. [21] In this regard, the finding of microalbuminuria in seemingly healthy donors can be an early warning that requires more attention.

The current study has a number of limitations. Its cross-sectional design did not allow it to determine a temporal dependence or causal relationships between the attributes of the donors and the evolution of albuminuria. The study was carried out in only one tertiary care facility and, therefore, the findings might not be applicable to other populations or healthcare facilities. Moreover, proteinuria and albuminuria were

measured only once, and transitory measurements were not ruled out. Prospective longitudinal studies in the future should determine the course of albuminuria and renal outcome in the long term in living kidney donors. The studies would benefit more significantly by being metacentric and having a larger sample size, which would increase generalisability of the findings and risk stratification.

Conclusion

The majority of the potential kidney donors had a good renal function with largely low-grade or marginal proteinuria. In spite of the fact that abnormal albuminuria was noted in a subgroup of donors, microalbuminuria was found in a small proportion of individuals with abnormal protein excretion, and overt albuminuric disease was rare. Advancing age and obesity were important risk factors of abnormal albuminuria, and they affected donor eligibility. The findings indicate the necessity of evaluating urine as a whole during the donor evaluation process, and the need to assess the risk appropriately, especially in the elderly and overweight donors, so as to safeguard long-term donor safety.

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Table 1: Baseline demographic and anthropometric characteristics of the donors (n = 195).

Continuous variables		
Variable	**Mean ± SD**	
Age (years)	**41.6 ± 9.8**	
BMI (kg/m²)	**24.9 ± 3.6**	
Categorical variables		
Variable	**Category**	**n (%)**
Gender	**Male**	**83 (42.6)**
	Female	**112 (57.4)**
Occupational status	**Employed**	**118 (60.5)**
	Unemployed	**77 (39.5)**
Smoking status	**Smoker**	**27 (13.8)**
	Non-smoker	**168 (86.2)**
BMI categories		
BMI category (kg/m²)	**n (%)**	
Underweight (<18.5)	**32 (16.4)**	
Normal (18.5–22.9)	**96 (49.2)**	
Overweight (23.0–24.9)	**49 (25.1)**	
Obese (≥25.0)	**18 (9.2)**	

BMI: Body mass index, SD; Standard deviation.

Table 2: Biochemical and glycaemic profile of the donros.

Parameter	**Mean ± SD**	**Reference Range**
Random blood glucose (mg/dL)	**118.6 ± 21.4**	**<140**
Fasting blood glucose (mg/dL)	**96.2 ± 12.8**	**70–100**
Serum creatinine (mg/dL)	**0.86 ± 0.14**	**0.6–1.2**
eGFR (mL/min/1.73 m²)	**104.8 ± 18.9**	**≥90**
Total cholesterol (mg/dL)	**182.4 ± 34.6**	**<200**
Triglycerides (mg/dL)	**146.2 ± 39.8**	**<150**

LDL cholesterol (mg/dL)	**108.7 ± 28.5**	**<100**
HDL cholesterol (mg/dL)	**46.3 ± 9.6**	**>40 (M), >50 (F)**

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, eGFR: Estimated glomerular filtration rate.

Table 3: Urinary protein excretion and albuminuria profile of the donors.

Variable	**Value**
24-hour urinary protein (mg/day), median (IQR)	**107 (95–230)**
24-hour urinary protein categories	
Category	**n (%)**
<150 mg/day	**68 (34.9)**
150–300 mg/day	**90 (46.2)**
>300 mg/day	**37 (18.9)**
Spot urine ACR (mg/g), median (IQR)	
Variable	**Value**
ACR	**21.4 (10.6–58.2)**
Albuminuria status	
Category	**n (%)**
Normal albumin excretion	**123 (63.1)**
Microalbuminuria	**49 (25.1)**
Macroalbuminuria	**23 (11.8)**
Total abnormal albuminuria	**72 (36.9)**

ACR: Albumin-to-creatinine ratio, IQR: Interquartile range.

Table 4: Association of clinical variables with abnormal albuminuria.

Variable	**Category**	**Normal Albuminuria n (%)**	**Abnormal Albuminuria n (%)**	**p-value**
Age	**<40 years**	**82 (77.4)**	**24 (22.6)**	**0.021**
	≥40 years	**47 (49.5)**	**48 (50.5)**	
Gender	**Male**	**57 (68.7)**	**26 (31.3)**	**0.44**
	Female	**72 (64.3)**	**40 (35.7)**	
BMI category	**Underweight/Normal**	**99 (77.3)**	**29 (22.7)**	**0.011**
	Overweight/Obese	**36 (45.0)**	**43 (55.8)**	
Smoking status	**Smoker**	**18 (66.7)**	**9 (33.3)**	**0.33**
	Non-smoker	105 (62.5)	63 (37.5)	

BMI: Body mass index.

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